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Poster abstract book

The poster abstract book is divided per topic and in alphabetical order on last name
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Cerebral Palsy

ICNC-0287: Hypoxic ischemic encephalopathy (HIE) treated by hypothermia: prognostic value of EEG and aEEG in a cohort of 20 patients

Background: The aim of this work is to assess the prognostic value of EEG and aEEG in hypoxic ischemic encephalopathy (HIE) newborns during hypothermia (HT) treatment. Methods: The study included 20 newborns with HIE treated by HT who had a BSID-III at 2 years. EEG and aEEG were analyzed by 2 readers (LS and AA) and graded according to Murray’s and al Naqeeb’s classifications respectively for EEG and aEEG. Receivers operating characteristic (ROC) curves were used to assess the prognostic value of EEG and aEEG during 4 periods (<24h, 24-48h, 48-96h, <24h-96h). We considered significant p values < 0.05. Results: 13 newborns had a good outcome, 6 died and 1 suffered from cortical blindness. EEG demonstrated a statistically significant predictive value for the 48-96h period (AUC 0.95-0.80)(p<0.05) and for <24h-96h (AUC 0.74-0.77)(p<0.05). A grade 1 EEG after 24h was always associated with a good outcome and a grade 3 EEG after 48h was always associated with a bad outcome. Patient with a good outcome showed an improvement of their EEG grade during HT. Prognostic value of aEEG did not reach statistical significance (AUC 0.525-0.687). Interpretation: In newborns with HIE treated by HT, EEG has a good prognostic value after 48h. Moreover, improvement of EEG grade during HT is associated with a good outcome. In our study, prognostic value of aEEG did not reach statistical significance.

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Cerebral Palsy

ICNC-0001: Correlation of clinical signs and MRI-picture of the brain in children with CP and spastic diplegia

Pathognomonicity of brain MRI data depending on the CP type is poorly described in children. Study objective: determination of correlation of the brain MRI-picture with clinical signs in children with spastic diplegia. Material and methods. 324 children with spastic diplegia were followed-up. All children underwent double MRI of the brain: at the age of six months to three years old and at the age of four to seven years old. Results. MRI of 98.1% of children demonstrated symmetrical bilateral dilation of the lateral ventricles of three degrees: 46.8% - moderate, 29.4% - mild and 23.8% - expressed. In 85.9% of children a hydrocephalus ex vacuo was revealed, in 2.5% - an obstruction of the cerebrospinal fluid pathways. Leukomalacia of the white substance in both hemispheres and axonal degeneration along the pyramidal tracts were typical for 97.9% of children, and localized along the lateral ventricles walls (65.2%), spread up to the subcortical regions (28.9%) or involved the whole white substance (5.9%). Damage of the corpus callosum was observed in all patients: in 57.4% - hypoplasia in the form of shortening and thinning, in 17.5% - dysgenesis in the form of shortening under unchanged thickness, in 25.9% - atrophy in the form of thinning along the unchanged length. A proved interrelation between the side of predominant periventricular leukomalacia signs and the side of mainly expressed neurological disorders was revealed. Conclusions. The neuroimaging correlations in children demonstrated expressed and widespread leukomalacia with axonal degeneration of the pyramidal, reticulospinal, rubrospinal and vestibulospinal tracts, as well as corpus callosum pathology.

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Cerebral Palsy

ICNC-0002: Principles of rehabilitation of children with CP during the first 7 years of life

Rehabilitation of children with CP presupposes an integrated evaluation of moving ability of a child and determination of cognitive and sensory impairments, impeding successful biosocial adaptation. Objective. Determine the main principles of effective rehabilitation of children with CP during the first 7 years of life. Material and methods. The 25-years’ experience of rehabilitation of 4,530 children with CP is presented. All children were followed-up from the first months of life till 7 years old. Regularly, four times per year the 1.5-2-months courses of in-patient/out-patient medical, social and pedagogic rehabilitation were performed. The effectiveness of the rehabilitation was monitored with the help of EEG, brain MRI, neuromyography. Results. It was revealed that the rehabilitation effectiveness in children with CP depends on the rehabilitation process initiation terms: in 65% - at the age of 3 months, in 35% - at the age of 6-9 months. In 30% of children the rehabilitation program was performed during the whole day. Before each rehabilitation course for an individual child started, a specific program with possible effect prediction was developed. By the age of 3 in 41% of children, by the age of 5 – in 64% of children and by the age of 7 in 76% of children a satisfactory development of gross
Cerebral Palsy

ICNC-0003: Rehabilitation effectiveness in premature children with spastic forms of CP

Functional activity of the motion analyzer is especially relevant in rehabilitation of premature children with spastic forms of CP. OBJECTIVE. Study of rehabilitation effectiveness in children with spastic forms of CP. Material and methods. The analysis of rehabilitation effectiveness in 546 premature children with CP and spastic diplegia (269 patients) or paraplegia (277 patients) during the first 3 years of life was performed. The estimation of rehabilitation effectiveness in children was based on the degree of spasticity according to Ashworth Scale, clinical examination results, EEG, neuromyography, brain MRI, video-monitoring. Results. During the first year of life spastic impairments in 38% of children corresponded to 4 points (a paretic limb couldn’t be completely passively flexed or straightened - flexion or extension contracture). In 31% of children a significant muscular tone increase was observed, passive movements were impaired – corresponded to 3 points. 29% of children suffered from increased muscular tone of moderate to mild degree, manifesting – corresponded to 2-1 points. Decrease of the extensors tone in children of the first 6 months of life was contributed by the fetal position. By the age of 3 years in 82% of children the spasticity did not exceed 2 points, 18% of children had tone increase of 4-3 points. In 42% of children with mild paresis the presence of legs muscles spasticity even facilitated standing and walking, and its decrease resulted in worsening of mobility. The analysis of the long-term systematic rehabilitation effectiveness in premature children with spastic forms of CP demonstrated that the character, severity degree and clinical manifestations dynamics directly correlated with the results of the paraclinic studies.

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Cerebral Palsy

ICNC-0288: Comparative analysis of risk factors for CNS perinatal affection in children, born by ethnic women from the Republic of Dagestan.

Social and cultural lifestyle peculiarities of many fertile age ethnical Dagestan women have changed during the last decades, and these changes are mainly related to the tendency of transition from social life to “Islamic traditions”, which has coincided with an increase in frequency of CNS perinatal affection in newborns. Objective: Comparative analysis of risk factors for CNS perinatal affection in children, born by ethnic women from the Republic of Dagestan, depending on social or religious way of life. Materials and methods. For almost 20 years we had studied 5,650 children with perinatal CNS pathology, of them 2,760 were born by ethnical Dagestan women, living social life (1 group), and 2,890 – by women, adhering to the religious traditions (1 group). All women were aged 20–25, pregnancy was 1–3, labour was 1–2. Results. The following risk factors were found in the women of 1 and 11 groups, respectively: 1. Lack of planning for pregnancy and labour (98% and 61%), data on health condition before pregnancy (96% and 43%), and timely systematic medical supervision (82% and 41%). 2. Presence of vertically transmitted infections, metabolic disorders, iron deficiency anemia, endocrine disorders (61% and 94%). 3. Irregular and non-balanced nutrition during pregnancy with deficit of protein, vitamins, iron, magnesium and phosphorus (58% and 99%). 4. Multiple religious fasts during pregnancy lasted for 1–3 months (26% and 100%). 5. Miscarriage (22% and 39%). Conclusions. There are definitely more risk factors for CNS perinatal affection in children born by ethnical Dagestan women, adhering to the religious traditions, versus those living social life.

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Cerebral Palsy

ICNC-0863: Experience of drug-free medical rehabilitation of children with perinatal CNS affection

Disorder of the statokinetic development of infants is determined by untimely inhibition of the tonic labyrinthine and neck reflexes, as well as by the delayed reflexes, which contribute to vertical body orientation. Objective. Study the possibilities of the drug-free medical rehabilitation of children with perinatal CNS affection. Material and methods. 340 infants with perinatal CNS affection were followed-up: 168 infants were under intensive drug-free rehabilitation only (kinesitherapy,
Cerebral Palsy

ICNC-0290: Lissencephaly with dysmorphic features
Lissencephaly (LIS) is a diffuse brain malformation manifested by smooth cerebral surface, abnormally thick cortex with four abnormal layers that includes a deep zone of neuronal heterotopia and enlarged dysplastic ventricles (Barkovich et al., 1991; Forman et al., 2005). It encompasses the pathologic terms of agyria, and pachygyria. Several different types of LIS have been recognized, based on pathological features. They are most readily distinguishable based on the number of layers, and include four-three-, and two layered forms (Forman et al., 2005). Clinical Case: We report a LMT, newborn product of urgent C/S due to fetal distress, 37 weeks GA, cord 9 times around the legs, decreased fetal movements, oligohydramnios. Maternal History of two previous abortions at 4, and 5 weeks respectively, Parents not related. The patient had the following problems: (1) Resuscitation needed and put on mechanical ventilation. (2) NN convulsion, AED used (Phenobarbital). (3) Hypotonic with frog like position and arreflexia. (4) Bilateral talipus equinovarus. (5) Scoliosis. (6) Brain CT scan: ventriculomegaly with pachygyria. Baby died at 10 days of age Conclusion: Repeated abortions during the first trimester, and hypotonic neonate with fatal migrational disorders raise the need for molecular genetic study for proper genetic counseling for future pregnancies.

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Cerebral Palsy
ICNC-0004: Specific indicators of diffusion weighted magnetic resonance imaging in child cerebral palsy with Symptomatic Epilepsy
The purpose of the study was to determine the characteristics of diffusion weighted Magnetic Resonance imaging indicators in children with symptomatic epilepsy with cerebral palsy. Materials and Methods: The study was based on the results of the study 54 children with symptomatic epilepsy with cerebral palsy aged 1 - 14 years. All of 54 studied children underwent routine MRI imaging with diffusion weighted sequence. Main group consisted of 26 epilepsy patients with cerebral palsy. The control group consisted of 20 children without clinical manifestations of epilepsy and no signs of seizure activity on EEG. FA (fractional anisotropy), values and MD (mean diffusion) were calculated on the same sections for all the resulting images. The results of the study. In the study we found a significant decrease in the FA values in fronto-temporal areas (P <0.01). Mean diffusion (MD) is calculated, which an increase of values is associated with a defect in neurogenesis or loss of cells, followed by an increase in the extracellular space. In children with symptomatic epilepsy cerebral palsy was observed the significant increase the MD values in all studied areas (P <0.01). Conclusion: The obtained results prove that diffusion weighted MRI in children with symptomatic epilepsy and cerebral palsy reveals the structural changes of white matter of brain. A significant increase of diffusion capacity of the brain due to lower fractional anisotropy in the fronto-temporal lobe, indicates the permeability and damage of the myelin sheath in white matter.

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Cerebral Palsy
ICNC-0005: Imaging possibilities of children with symptomatic epilepsy with cerebral palsy
Objectives: Epilepsy is one of the most complex medical and social problem at present time. The aim of the study was to determine characteristics of MRI studies in symptomatic epilepsy with child cerebral palsy. Methods: MRI studies were performed in 28 patients with symptomatic epilepsy with cerebral palsy. Their age ranged from 1 to 10 years. The debut of seizures was observed from birth to 2.5 years, the average age at onset 5.6 ± 0.16 months. Results: According to the
MRI studies most (57.1%) lesions of white matter of the brain were mainly as multiple and single foci pathological intensity. Lesions of the basal ganglia have been reported in 50% of children. Deformation of the brain stem was recorded in 57.1%, flattening the pituitary gland - in 36% of children, expanding the periventricular subarachnoid space in 14.3%. According to MRI findings in 25% of children have severe intracranial hypertension. Moderate atrophy of the cerebral hemispheres were reported for 53.5% of the surveyed children. Symmetrical lesion of the basal ganglia was observed in 39.3% of children with symptomatic epilepsy with cerebral palsy. Conclusions: Thus, according to information received atrophic changes in the cerebral cortex mainly in the anterior frontal and temporal lobes of the brain are determined almost the majority of the surveyed children with symptomatic epilepsy with cerebral palsy.

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Cerebral Palsy

ICNC-0864: Balance training therapy in early childhood intervention - The Huple® program
Introduction: Early childhood intervention covers the areas of secondary prevention, habilitation and rehabilitation, which begins early, even right after the NICU period, and regular control lasts until the beginning of school. The quality of medical attendance of children with special needs has changed dynamically in the last decades. Keystones of early therapy in Gezenguz Foundation in Hungary consist of different coherent parts, which are early sensory stimulating program, neurodevelopmental treatment, neuro-hydrotherapy and balance training therapy (Huple®-program).Method: Huple® is a special equipment for balance training and vestibular stimulation, which is used in the early intervention of infants and children from the beginning of life. Huple®-program supports the ontogenetical development of children in various situations and positions. The first step of the early intervention is a complex neurologic examination, in which Huple® is also included. During therapy – using Huple® even on land or in the water – we focus on supporting the regulation of central nervous system, development of the postural control and coordinated movement of the extremities, which is also based on the postural stabilization. Results: Effect of Huple® is affirmed by a research, in which we found that development of the postural control in hypotonic children was better after six weeks balance training than in the control group. Conclusion: Huple® can also be attached by a recently developed special 3D acceleration sensor so that we can make quantitative examination of balance skills, and we can follow up the effectiveness of the therapy.

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Cerebral Palsy

ICNC-0865: Neuro-hydrotherapy in early childhood intervention
Introduction: Hydrotherapy is a widely used method in treating various motor deficiencies. However, in early childhood intervention it is much less prevalent. The Gezenguz Foundation treats babies with brain injuries and/or developmental risks (e.g. prematures) between 0-6 years of age. It provides a complex program to prevent or treat motoric, cognitive, and psychological problems. This contribution will offer an overview of Neuro-hydrotherapy developed by the Foundation that plays a crucial role in the complex therapy of this age cluster. Method: Neuro-hydrotherapy (NHT) can be applied from birth until stabilization of final seno-motoric patterns. It is a method developed along neurophysiologic principles and according to functional demands. It always affects the motoric regulatory system that is organized on the highest level. It influences the organization of the neuromuscular system by activating complex movement patterns. Axis of the method is stimulation of the vestibular system that can influence muscle tone, raise attention level, and it creates the conditions of harmonious movement and manipulation by forming balance, coordination and postural control. Results: At the Foundation movement therapy begins after an examination done by a neurologist and a physiotherapist. Control is due every third month. Movement development is checked by Bayley 2 and WOTA tests. Some children receive only land therapy. Those who participate in neuro-hydrotherapy sessions as well showed better results in sensomotoric development. Conclusion: Neuro-hydrotherapy is a motoric development method that can be applied independently in prevention and as an efficient part of a complex therapy in the treatment of motoric deficiencies.

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Cerebral Palsy

ICNC-0006: Pseudobulbar affect in survivors of extreme prematurity with cerebellar injury: Support for the cerebellar link in pathological laughter and crying
We report two children with cerebral palsy (CP) who have structural cerebellar injury as a result of their being born extremely premature who have pathological crying and laughter. Case #1: A 9 year old male born 23 weeks weighing
Cerebral Palsy

500gm. He has CP with a mixed motor deficit characterized by mild dystonia, mild spasticity and ataxia. Brain MRI shows almost complete cerebellar loss, atrophy of the pons and upper medulla. His mother describes episodes occurring over the last two to three years where he will suddenly; with no apparent reason begin to cry for 2-5 minutes then return to normal with no explanation or emotional content. Case #2 SP is a 5 year old girl born at 23 5/7 weeks gestation weighing 560gm. Brain MRI shows moderate left hemisphere and vermis atrophy. Parents are disturbed by several minute long episodes of inappropriate crying and laughing for no obvious reason. CP is common among those infants who survive extreme premature birth (gestational age less than 28 weeks, birthweight less than 1kg). The cerebellum is injured in 2/3 of the these infants.2 Dementia and colleagues proposed that pathological laughter and crying (PBA) is due to lesions in the cerebro-ponto-cerebellar pathways.3 The phenomenon has been well described as pseudobulbar affect in adult patients with MSA, MS, dementias etc. but has not been described in children with CP. The incidence of this phenomenon is unknown but the occurrence may provide support for the role of the cerebellum in the pathogenesis of PBA.

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Cerebral Palsy

ICNC-0291: Assessment of the association between Apgar scores and seizures in infants less than 1 year old
Objectives: To assess the association of Apgar scores 1 and 5 minutes after birth with the seizure in infants less than 1 year old. Design: A retrospective, observational, hospital-based study. The medical records from the Chung-Ang University Hospital for the period January 2006–May 2015 were used to identify infants less than 1 year old who had a history of seizure. Population: Using electronic medical records, infants who were diagnosed with infantile seizure in the Chung-Ang University Hospital from January 2006 – May 2015 were included in the seizure group (n = 93) and a control group consisting of 296 age-matched cases without history of seizure were selected from the group of infants born at Chung-Ang University Hospital during the same periods. Results: We found that Apgar scores were significant risk factors for infantile seizure among all the measured perinatal factors. When classified by sex and delivery mode, Apgar scores were different when classified by gestational age and birth weight. We found strong associations between Apgar scores and infantile seizures in the full-term and the normal birth weight group (bodyweight ≥ 2.5 kg) regardless of delivery mode. The Apgar scores all had an inverse correlation with EEG class but only the 1-minute Apgar score correlated with MRI findings. Summary: Low Apgar scores are significant perinatal factors that can be risk factors to the infantile seizure especially, in the full-term and normal birth weight and had a strong negative linear relationship with the EEG and brain MRI results in the seizure group.

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Cerebral Palsy

ICNC-0008: Reasons for acute hospital admissions among children, adolescents, and young adults with cerebral palsy, a nationwide population study
Introduction: To find out common reasons for acute hospitalizations among children (4-12.9y), adolescents (13-17.9) and young adults (18-32.9) with cerebral palsy (CP). Methods: We completed a secondary analysis of data from the Taiwan National Health Insurance Research Database (NHIRD) to find out the most frequently observed reasons for admissions and the associated lengths of stay (LOS). CP patients aged 4 to 32.9 years were identified by CP registry in the catastrophic illness patient registry of 2010 NIIRD. Data of Admission claims during 2010-2011 were analyzed. Claims indicated admitted before 2010 were excluded. Health records data from children with CP (n=1200 youth with CP (n=555) and young adults with CP (n=713) contributed to this study. Results for admissions were identified according to ICD codes from the admission claims. Common reasons, frequencies of admissions for each reason, and mean LOS were reported. Results: Pneumonia, epilepsy and other respiratory problems as the top 3 reasons for admissions in all groups. All groups were commonly admitted because of other infections, upper and lower gastrointestinal (GI) problems. The reasons that were specific to children included orthopedic issues especially congenital hip dislocations, ENT problems, UTIs, contractures and hydrocephalus. In youth, scoliosis, contractures and fractures were unique reasons for admission. In young adults, UTIs, blood problems, mental illness and visual problems were relative common reasons. Conclusion/Discussion: The reasons for hospital admissions reported here reflect the range of comorbidities experienced by each age groups with cerebral palsy. It also provide important clinical information for physicians, and guide future planning of ambulatory care services.

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Cerebral Palsy

ICNC-0866: Association between neuromotor stimulation and functional elastic bandage: a follow-up study of a child with craniofacial anomalies

Introduction: Craniofacial anomalies (CFA) are among the most common birth defects and are associated with increased mortality and, in many cases, the need for lifelong treatment. Over the past few decades, dramatic advances in the surgical and medical care of these patients have led to marked improvements in patient outcomes. However, none of the treatments currently in clinical use address the underlying molecular causes of these disorders. Aim: Follow-up a child with craniofacial anomalies submitted to physical therapy. Participant and methods: Single-case study of an 11 month male child with craniofacial anomalies referred to the physical therapy clinic of FACULDADE METROCAMP, a college located in Campinas (São Paulo/Brazil). The physiotherapy treatment began in August 2015, and was realized twice a week. During evaluation in the initial assessment, delayed motor development, hypotonic, underactive movements were observed. Treatment was focused on patient/environment and patient/therapist interactions, stimuli for motor acquisition and therapeutic touch. Functional elastic bandage using Therapy Taping Methods applied in the lower limb and trunk. During the first four weeks the bandage was not tensioned over 20% of its maximum length in order to offer cutaneous stimulation of the skin receivers to arouse a motor response. The bandage was tensioned over 20% of its maximum tension, aiming correct positioning of the segment. Results: After physical therapy intervention the child began to accept therapeutic touch; improved her interaction with both the therapist and the environment; started to play with some of the toys and explore your hands. Also, motor acquisition postures like prone and supine are more tolerated and start a movement prone/supine. Although not sit, but remains when facilitated with support and greater stability, stands to maintain a lightly head in the middle line. The child supported standing, variable movement of legs. Conclusion: According to the results presented neuromotor stimulation combined with Therapy Methods Taping seemed to be effective and this study may contribute to future application in patients who requires this type of intervention.

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Cerebral Palsy

ICNC-0292: Neutral head position and tilting to reduce the incidence of intraventricular hemorrhage in very preterm neonates

Background: Intraventricular hemorrhage (IVH) remains a frequent, serious complication of premature birth. Neutral head position and tilting may contribute to the prevention of IVH in preterm infants. Objective: The aim was to provide a systematic review of the effect of neutral head position and cautious head tilting (less than 30 degrees) on the incidence of IVH and cerebral hemodynamics in very preterm infants (gestational age < 30 weeks). Methods: Literature was searched in the following electronic databases: Medline, Embase, CINAHL, SCOPUS and several trial registers. Two researchers independently assessed the quality of the studies. Results: There is insufficient evidence to support that neutral head position and/or tilting affects the incidence of IVH in preterm infants. Neutral head position appears to have no significant effect on cerebral oxygenation. However, most studies were performed in small groups of neonates. Most children were clinically stable and assessed at variable postnatal age (often > 1 week old). Few neonates were born extremely prematurely. Conclusion: There is insufficient evidence that neutral head position and/or cautious tilting affects the incidence of IVH in preterm infants. Results were inconclusive due to small sample sizes. Future perspectives: We are conducting a prospective observational study in 560 preterm children (GA < 30 weeks) to study the effect of neutral head position during the first 72 ours after birth on the incidence of IVH, cerebral hemodynamics and cerebral oxygenation as assessed by means of near infrared spectroscopy and ultrasonography.

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Cerebral Palsy

ICNC-0867: The joint neuro-thoracic clinic, collaboration between adult chest physician, neuro-rehabilitation physician and paediatric neurologist as a model for transition of young people with complex neuro-disability

Introduction: There are a significant number of young people with complex neuro-disability and most adult services are not ready to receive these. Within paediatric services a paediatrician acts as a point of access and coordinates care provided by multiple professionals. Such a pivotal person is often lacking within adult services. GPs may take on a coordinating role within transition, however, in adolescents with complex medical needs GPs often lack the expertise to do this without specialist support. Description: Considering the health needs of these young people, collaboration between a chest physician and a neuro-disability physician is essential. Joint working with a paediatric neurologist facilitates the transfer of care, including provision of historical background and expert advice around neurometabolic conditions. A 2 monthly MDT clinic provides care for 37 young people, including 13 patients with ventilators. Providing a regional service, the
Cerebral Palsy

ICNC-0052: Characteristics of children presenting with cerebral palsy in a neuropaediatric clinic in the United Republic of Tanzania

ABSTRACT Introduction: Cerebral palsy (CP) is the single most important chronic neuropaediatric condition in Sub-Saharan Africa. Prevalence and attribution of preventable causes cerebral palsy here is regarded to be large but exact figures are not well known. Objective: To clinically characterise children with CP aged 2-14 years visiting two neuropaediatric clinics in Moshi, Tanzania. Furthermore to obtain an impression of the degree of potentially preventable risk factors. Study design: Cross-sectional study Methodology: All children with cerebral palsy aged 2-14 years visiting regular neuropaediatric clinics in Moshi, Tanzania fulfilling all inclusion criteria were consecutively included over a two-month period. Results: Half to 2/3 of any neuropaediatric clinic population was accounted for by cerebral palsy patients. Fifty patients were enrolled into this study. Risk factors were prenatal (78%), natal (80%) and postnatal (88%). Over half (64%) were rated as severely disabled according to the GMFCS. Ninety-two percent of children had potentially preventable risk factors. Conclusion: Most common, mixed type CP was seen, with the majority classified as severely disabled. The largest proportion of risk factors was postnatal, perinatal asphyxia being the single most important risk factor. The vast majority of the risk factors were herewith potentially preventable. These first data from the United Republic of Tanzania sadly correspond to data from studies performed in other very low income countries around the world.

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Cerebral Palsy

ICNC-0009: Cerebral Palsy profile in Hasan Sadikin Hospital, Bandung, Indonesia

Introduction Cerebral palsy (CP) is the single most important chronic neuropaediatric condition in Sub-Saharan Africa. Prevalence and attribution of preventable causes cerebral palsy here is regarded to be large but exact figures are not well known. Objective: To clinically characterise children with CP aged 2-14 years visiting two neuropaediatric clinics in Moshi, Tanzania. Furthermore to obtain an impression of the degree of potentially preventable risk factors. Study design: Cross-sectional study Methodology: All children with cerebral palsy aged 2-14 years visiting regular neuropaediatric clinics in Moshi, Tanzania fulfilling all inclusion criteria were consecutively included over a two-month period. Results: Half to 2/3 of any neuropaediatric clinic population was accounted for by cerebral palsy patients. Fifty patients were enrolled into this study. Risk factors were prenatal (78%), natal (80%) and postnatal (88%). Over half (64%) were rated as severely disabled according to the GMFCS. Ninety-two percent of children had potentially preventable risk factors. Conclusion: Most common, mixed type CP was seen, with the majority classified as severely disabled. The largest proportion of risk factors was postnatal, perinatal asphyxia being the single most important risk factor. The vast majority of the risk factors were herewith potentially preventable. These first data from the United Republic of Tanzania sadly correspond to data from studies performed in other very low income countries around the world.

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Cerebral Palsy

ICNC-0293: Evaluation of sympathetic fiber involvement in cases with congenital brachial plexus injury

Introduction: Congenital brachial plexus paralysis (CBPP) causes some autonomic dysfunctions. However, there is not sufficient data on the occurrence of autonomic dysfunction in CBPP and the efficiency of some tests for measurement of autonomic functions. In the present study, we aimed to demonstrate the autonomic dysfunction in CBPP and to clarify the effectiveness of some specific tests.

Materials-Methods: Twenty-five patients with CBPP were included in this study. Sympathetic skin responses were measured by surface electrodes at three different locations on the upper extremity.
Other supplementary tests, such as the iodine starch test and histograms, skin pH measurement, skin temperature measurement, and arterial tension measurement. Cases were evaluated by using movement assessment systems such as the Gilbert-Raimondi scale and others.

Results: Eleven male patients and 14 female patients, with a mean age of 22.52 ± 37.2 months, were assessed. According to electroneuromography (ENMG), 7 cases had root avulsion, and 18 cases had brachial plexus lesions of varying degrees. When injured and healthy extremities were compared, no statistical relationship was found between the sympathetic skin responses and other autonomic parameters. Discussion: Sympathetic skin responses can occur in patients with cases of CBPP and even in patients with root avulsion. In these cases, reinnervation may be ensured using an alternative route, such as the first and second intercostals nerves, the second thoracic nerve, or Kuntz’s fiber. These results have introduced considerations relative to requirements for these studies, such as describing the anatomic variations and anatomic distribution of the autonomic system in pediatric cases.

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Cerebral Palsy

ICNC-0053: Are we speaking the same language? A pilot study to evaluate the agreement in clinical phenotyping of children with cerebral palsy

Introduction: Cerebral palsy (CP) consists of a group of syndromes characterized by abnormalities of posture and motor activity. Patients are phenotypically classified as spastic, dyskinetic, ataxic or combined CP. Correct classification is essential for communication between medical professionals especially to gain optimal treatment for the individual patient. The aim of this pilot study was to determine the agreement of phenotypical classification of children with CP among clinicians.

Methods: Fifteen children with CP (8 boys, 11y±4y, GMFCS range 1-5) were videotaped with a standardized protocol. A total of nine clinicians (three pediatric neurologists, three pediatric rehabilitation doctors and three movement disorder specialists) scored the presence, severity and localisation of spasticity, dyskinesia and/or ataxia in each patient based on the videos. Inter- and intrarater agreement were assessed using the Fleiss’ and Cohen’s Kappa. Results: Preliminary results show an only slight agreement (κ = 0.186) for the clinical phenotype (i.e. spastic-dyskinetic) and moderate agreement (κ = 0.416) for the dominant symptom in the nine physicians. Agreement only slightly differed within the three groups of specialists (κ = 0.360-0.545). Intra-observer measurements are currently retrieved and will be presented at the conference.

Conclusion/discussion: These preliminary results highlights the large differences in classification of neurological symptoms in CP. There is a large disagreement between specialist, not only between different specialisms but also within specialisms. The specific features in CP may require specific medical treatment strategies. We suggest a multidisciplinary evaluation with good discussions to increase agreement on phenotypes and optimize management of children with CP.

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Cerebral Palsy

ICNC-0010: The subclinical epileptiform discharges among non-epileptic cerebral palsy patients

Background: Subclinical epileptiform discharges (SEDs) are assumed to play a role in development of cognitive dysfunction in cerebral palsy (CP) patients. Purpose: to estimate the prevalence of SEDs among non-epileptic CP patients and their cognitive correlates. Patients and methods: Fifty one non-epileptic CP patients were subjected to history taking, neurological examination, assessment using gross motor function classification system for cerebral palsy (GMFCS), Stanford-Binet scale (5th edition), encephalography, and magnetic resonance imaging (MRI) brain. They were divided into two groups. 19 CP patients without SEDs in group 1 and 32 CP patients with SEDs in group 2. A comparison between patients’ features studied in group 1 and 2 was done using independent-samples t-test and Chi-square (X2). A correlation between SEDs and the studied features was done using Spearman's rank correlation coefficient (rho). Results: The prevalence of focal SEDs among non-epileptic CP patients was 62.7%. The presence of MRI abnormality and moderate mental retardation (MR) showed highly significant positive correlation with SEDs. Meanwhile, CNS malformation and severe MR showed significant positive correlation with SEDs. On the other hand normal intelligence showed highly significant negative correlation with SEDs. Kern-icterus and dyskinetic CP showed significant negative correlation with SEDs. Conclusion: SEDs are common finding among non-epileptic CP children. They are positively correlated to cognitive dysfunction. This finding supports the assumption that SEDs are therapeutic target in mentally subnormal children. Larger studies are needed to confirm our results and to evaluate the clinical benefit of treating SEDs.
Cerebral Palsy

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Cerebral Palsy

ICNC-0011: COL4A1 de novo mutation in a child with cerebral palsy and microcephaly and normal perinatal history

The COL4A1 gene encodes the alpha1 chain of type IV collagen, a component of basement membranes in vasculature, renal glomeruli and ocular tissues. Mutations in COL4A1 were associated with familial porencephaly, prenatal, neonatal and adult intracerebral hemorhages, aneurysms, ocular manifestations and nephropathy. We describe an infant with normal perinatal history, in whom a de novo COL4A1 mutation was identified. A seven-month-old male, the first-born child to healthy non-consanguineous parents, was examined because of developmental delay and decelerating head growth. He was born at term, after a normal delivery, with birth weight 2600 g, Apgar score 9/10, and head circumference of 33 m (10th percentile). During pregnancy his mother was carefully monitored with repeated ultrasound evaluations which were all normal. At 3 months, his ophthalmologic examination for strabismus revealed a posterior subcapsular cataract. On examination he presented with prominent microcephaly (-4SD), but otherwise no dysmorphic features. Neurological examination revealed spasticity, increased DTRs and extensor plantar response in the lower extremities. His social and cognitive developments were appropriate for his age. Brain MRI showed bi-frontal, periventricular and cerebellar cystic lesions with hemosiderin deposition consistent with old hemorrhages. Evaluation included TORCH serology, metabolic work-up, ultrasound of kidneys and liver, cardiac evaluation and chromosomal micro-array without any pathology. COL4A1 mutation was suspected and genetic studies confirmed that he had a heterozygous variant p.Gly1239Arg in the COL4A1 which was not detected in both parents. The COL4A1-related disorders are underdiagnosed and can be the cause of spontaneous intracranial hemorrhage and stroke and of “idiopathic” cerebral palsy.

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Cerebral Palsy

ICNC-0950: Clinical and radiological profile of dyskinetic Cerebral Palsy in preterm infants- A developing country experience

Introduction: We studied the clinico-radiological profile, etiology, motor-functional ability and severity of dystonia in preterm children with dyskinetic cerebral palsy (CP) Methods: Nineteen consecutive children with preterm birth and dyskinetic CP seen over 2 years, underwent detailed neurological, neuroimaging, gross-motor function and video-recording-based dyskinesia assessment using Burke–Fahn–Marsden-Scale. Results: Mean gestational-age was 35.5+1 week (range 32-36 weeks); birth-weight 2231±457 gm; age at presentation 48.7±34.6 months (range 12-120 months). Majority were males (N=11)58% and first-borns (N=13)68%. Chief concerns were global developmental-delay (95%), abnormal twisting postures (58%), feeding (21%) and speech difficulties (21%). Causes of preterm birth were multiple gestation (21%, N=4/19), leaking (16%, N=3/19); gestational diabetes, chorioamnionitis and antepartum-hemorrhage (5.3%, N=1/19 each); no cause ascertained in 47%(N=9/19). Etiological insults were hyperbilirubinemia 68%(N=13/19), perinatal asphyxia 16%(N=3/19) and multiple postnatal events 16%(N=3/19). Amongst preterm hyperbilirubinemia (N=13), mean maximum-bilirubin-level 28.7±8.8 (range 12-44mg/dl), acute-bilirubin-encephalopathy stage2 62%(N=8/13); exchange-transfusion 77%(N=10/13); G-6-PD deficiency 23%(N=3/13), non-Rh-isoeimmunization (85%,N=11/13), upgaze palsy 62%(N=8/13), abnormal brain-stem-auditory-responses 62%(N=8/13) and enamel staining 39%(N=5/13) were noted. Overall, majority of children had GMFCS level-4 (32%,N=6/19) and level-5 (58%,N=11/19); dystonic 90%(N=17/19) CP with mean Burke-Fehr-Marsden-dystonia-score 51.1±20.5 (range 25-88). Kernicterus predominantly affected basal-ganglia alone (N=6/13)46%, both basal-ganglia and periventricular white-matter (PVWM) 38%(N=5/13), PVWM alone (N=1/13)7%; one child had normal MRI. Kernicterus affected globus-pallidi (N=11/13)85%, subthalamus-nucleus (N=3)23% and substantia-nigra (N=2/13)15%. Perinatal-asphyxia (N=3/19) affected putamen and thalamus alone, PVWM alone and both in 1 patient each. Conclusion: This is the largest study of dyskinetic preterm children from a single centre in a developing country. Radiologically, kernicterus in preterm children affects globus-pallidi, subthalamic-nuclei and substantia-nigra causing marked dyskinesia.

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Cerebral Palsy

ICNC-0014: Relationship between brain derived neurotrophic factor (BDNF) and homocysteine level in cerebral palsy children with methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphism

Cerebral palsy (CP) is a major neurodevelopmental disorder in children. CP risk factors largely occur during the prenatal period, therefore genetic factor is one of the risk factors for the occurrence of CP. Methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphism is presumed to be related to the incidence of CP. Brain derived neurotrophic factor (BDNF) plays role in brain plasticity. The purpose of this study was to assess the relationship between BDNF and homocysteine level in cerebral palsy children with MTHFR C677T gene polymorphism. This was an analytic observational study conducted in several hospitals, school for children with special needs, and rehabilitation centers in Bandung since March – November 2014 with cross-sectional design. Sampling was done by consecutive and purposive sampling. Identification of MTHFR C677T gene polymorphism using PCR-RFLP, homocysteine serum levels using CMIA, BDNF serum levels used ELISA. Statistical analysis used Mann Whitney test and T test. The results showed the frequency of the MTHFR C677T gene polymorphism was 18% with the T allele frequency of 11%. Homocysteine level in subjects who have the MTHFR C677T gene polymorphism was significantly higher than in subjects without polymorphism, 8.22 vs 7.46 µmol/L (p = 0.046). BDNF levels in CP subjects with the MTHFR C677T gene polymorphism was higher, 41.530 vs 39.060 pg/ml (p = 0.190) as compared to subjects without polymorphism.Conclusion: There is no relationship between BDNF and homocysteine level in CP children with MTHFR C677T gene polymorphism.

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Cerebral Palsy

ICNC-0294: Decreased risk of cerebellar hemorrhage in premature newborns exposed to antenatal magnesium sulfate

Decreased risk of cerebellar hemorrhage in premature newborns exposed to antenatal magnesium sulfateIntroductionCerebellar hemorrhage (CbH) is now recognized as a common form of brain injury in premature newborns. Our objective was to determine clinical predictors of CbH in a prospective cohort of premature newborns evaluated with MRI.Methods A cohort of 68 preterm newborns (<33 weeks gestation) imaged with 3T-MRI soon after birth was studied. Exclusion criteria included clinical evidence of a congenital syndrome, congenital infection, or clinical status too unstable for transport to MRI. A blinded pediatric neuroradiologist scored T2 sequences for the presence of CbH. Clinical predictors were compared by the presence of CbH using descriptive statistics. Predictors associated with CbH (P<0.1) were evaluated using multivariable logistic regression. ResultsCbH was present in 26/68 (38.2%). Newborns with CbH were younger at birth (mean 27.6±2.3 wks vs. 28.7±1.8 wks, P=0.03), and of lower birthweight (median 919g, IQR:760-1140 vs. 1200, IQR:1000-1450, P=0.002). CbH was associated with antenatal magnesium sulfate (RR 0.42, 95%CI:0.24-0.73, P=0.003), hypotension (RR 2.54, 95%CI:1.17-5.5, P=0.008), patent ductus arteriosus (RR 2.14, 95%CI:1.2-3.8, P=0.02) and mechanical ventilation≥7 days (RR 2.05, 95%CI:1.13-3.73, P=0.02). Adjusting for predictors associated with CbH, antenatal magnesium sulfate was independently associated with decreased CbH (OR 0.11, 95%CI:0.029-0.44, P=0.002). Conclusion/Discussion The rate of CbH in our cohort is higher compared to other studies, suggesting 3T-MRI may be more sensitive for the detection of CbH. Antenatal magnesium sulfate is independently associated with a decreased risk of MRI-detected CbH, which may help explain the reason underlying the neuroprotective effects of magnesium sulfate in premature newborns. Acknowledgements: NIH/NINDS NS035902 and EB009756.

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Cerebral Palsy

ICNC-0295: Foetal Neurology: A study of referral pattern and outcomes in a tertiary centre

IntroductionScreening for foetal abnormality is an important part of antenatal care. When a neurological abnormality is detected in the foetus the woman is referred to the Paediatric Neurosciences team for counselling(1). This study investigates the pattern of abnormalities found and their outcome. MethodsPatients were identified from the Paediatric Neurosciences departmental database, which contained referrals from 2005-2015. Further information on the patients and their outcomes was collected from their electronic notes. ResultsOf the 68 patients identified in the database, 66 pregnancy outcomes were documented. Ultrasonography (US) was used in all patients, and US combined with Magnetic Resonance Imaging (MRI) were the most used investigation methods. Myelomeningocele was the most frequent
abnormality detected (n=30). The pregnancy was terminated in 39% (n=22) cases. The pattern of decision to terminate was different for the various abnormalities: 75% of open lipped schizencephalies were terminated, in comparison to 0% of Dandy Walker malformations. 32 children were alive at recent follow up of which 31 had the correct diagnosis prenatally; 18 of which had had additions to their diagnosis. Conclusions There is little literature on the patterns of antenatal referrals to the Paediatric Neurosciences teams and their subsequent outcomes. This study describes the pattern of abnormalities detected, their frequency and ultimate outcomes. This study can be used to assist the Paediatric Neurologists and Neurosurgeons when counselling women who have been found to have neurological abnormalities on antenatal screening. References 1. Scher, Mark S. J Child Neurol 2003; 18(2); 85-92.

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Cerebral Palsy

ICNC-0016: A randomised control trial of Botulinum toxin-A administration under ultrasound guidance against manual palpation in spastic cerebral palsy

Introduction Botulinum toxin is a drug of choice for localised spasticity in cerebral palsy. Objective of this study was to compare the efficacy of botulinum toxin, ultrasound guidance versus manual palpation. Methods Randomised trial conducted between May 2012 and May 2014. Children, aged up to 6 years, with cerebral palsy were included. Children were randomized to 2 groups. A feedback questionnaire with four point ordinal scale was used subjective assessment of effectiveness. Clinical effectiveness was defined as a change of 5° in ankle dorsiflexion, a decrease of 1 in Modified Ashworth scale and functional improvement was defined by an increase in GMFM score by 6%. Results Thirty children in the study were categorised into group I, who were given botulinum with ultrasound (n=14) and group II, who were administered the toxin without ultrasound (n=16). The two groups were matched with respect to baseline characteristics. There was no significant difference in the GMFM scores between the groups (p=0.45). The mean feedback scores were similar in both the groups. No side effects were noted in both the groups. Discussion A G Py et al (n=54), found a functional improvement by using ultrasound guidance (p < 0.02). Berweck et al did more than 6000 sonography guided injections and recommended sonography for precise injection of botulinum toxin. This discordant outcome of our study was probably because gastrocnemius is a bulky muscle and does not need ultrasound guidance. Conclusion There is no significant difference in the outcome with regard to technique of administration of botulinum toxin with or without ultrasound into Gartrocnemius muscle

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Cerebral Palsy

ICNC-0296: Relation between the Bayley Scales of Infant Development–II (BSID-II) and Stanford Binet Intelligence Scale (SB) scores of the children born extreme /very preterm with risk factors

Introduction We examined the cognitive skills of the 3 years-old children with SB born between 24-29 weeks of gestational age who had normal scores in cognitive development evaluated with BSID-II. Materials and Methods 109 extremely/very preterm babies (47 girls, 62 boys) treated in NICU were prospectively evaluated at 24 months of corrected age with BSID-II, at 3 years with SB. Their gestation ages were between 24-29 weeks (27.12±1.40), birth weights were between 530–1900 gr (1066gr±247.77gr). Results The IQ of the 8 patients (9.9%) were between 74-84 (dull-normal), 63 (77.8%) between 90-109 (average), and 10 (12.3%) between 110-112 (bright-normal). Those 8 patients having IQ between 74-84 had multiple risk factors (ventilator treatment, oxygen therapy, seizures, chronic lung disease, multiple pregnancy and sepsis) in the neonatal period. 10 children (12.4%) were treated with speech-therapy because of expressive language delay and speech disorder. 7 (8.6%) were supported with home-programme due to ADHD problems. The sensitivity and specificity of BSID-II at 2 years to predict normal outcome at 3 years by SB was 70.32 and 90.47 respectively. Conclusions Due to multiple risk factors impaired cognition, motor and neurosensory deficits occur frequently in extremely/very premature survivors age. A through longitudinal assessment even in those who has normal scores at 24 months of age is of paramount importance to catch those morbidities , for improved outcome.

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Cerebral Palsy

ICNC-0017: Nemaline Myopathy: next generation sequencing (NGS) significantly improving the molecular classification of Brazilian families

Introduction: Nemaline myopathy (NM) is one of the most common congenital myopathies with a significant genetic heterogeneity. Pathogenic mutations have been described in the genes NEB, ACTA1, TPM3, TPM2, CFL2, KBTBD13, KBTBD5, KBTBD10, KFHL40, KFHL41, which turn the screening of individual mutations very expensive and time consuming. During the last 10 years we studied some Brazilian Nemaline patients using SANGER sequencing of genomic DNA for small genes (ACTA1, TPM2 and TPM3), or through the international NM consortium. More recently we introduced the use of next generation sequencing and here we describe our preliminary molecular data of 16 Brazilian families with nemaline myopathy. Methods: 20 patients from 16 unrelated families were selected based on the presence of nemaline bodies in the muscle biopsy. Molecular studies were performed using Sanger or the next generation sequencing NGS: whole exome (Nextera – Illumina) or target NGS customized panel of 88 known neuromuscular genes (NGS-NMD). Results: Among 8 families studied by whole exome we identified 5 patients from 4 families with novel nebulin mutations (2 frame shift and 4 splicing mutations) and 1 patient with a previously described ACTA1 mutation. Among the other six families, which up to now have been studied only by target NGS-NMD panel, no pathogenic mutations were found in the TPM3, TPM2 or ACTA1 genes. The nebulin gene is not included in this panel due to its huge size. Two families previously described showed: two siblings with nebulin mutation and a sporadic case with TPM2 mutation. Conclusion: considering that mutations in the nebulin gene were found in 5 among the 9 Brazilian studied families studied for this gene, this form can be considered the main cause of NM in Brazilian patients. Thus, this large gene certainly must be included in the screening for mutations using NGS sequencing, and the whole exome analysis seems to be more effective for the study of nemaline patients. Apoio: CNPQ e FAPEMIG

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Cerebral Palsy

ICNC-0287: Submission title: Duration of Phenobarbital Treatment for neonatal seizures

BACKGROUND Neonatal seizures affect 2-4/1000 live births, and about 25% of these children later develop postnatal epilepsy. The ideal duration of anticonvulsant treatment is still unclear. In this study, we sought to determine whether the duration of phenobarbital treatment was predictive of the risk of later developing epilepsy. We also examined the factors affecting clinical decision making. METHODS We conducted a retrospective chart analysis of all neonates treated with phenobarbital for symptomatic seizures before 44 weeks postmenstrual age at a single center from 2010 to 2013. Infants were included if seizures were due to central nervous system infection, hypoxic ischemic encephalopathy, ischemic perinatal stroke, intracranial hemorrhage, and other transient provoking factors. Neonates with complex cardiac disease or a diagnosis of neonatal epilepsy were excluded. RESULTS 96 infants met inclusion criteria. Infants who developed postnatal epilepsy (26/96, 27%) were more likely to have protracted neonatal seizures (OR 1.16, 95% CI 1.029-1.308), longer initial treatment with phenobarbital (OR 1.007, 95% CI 1.001-1.013), and treatment with a second anticonvulsant, most commonly levetiracetam (p=0.02). CONCLUSIONS This study suggests that the severity of symptomatic neonatal seizures predicts the risk of later developing epilepsy. Clinicians likely choose to prolong phenobarbital treatment in these cases, and are more likely to add a second anticonvulsant. It is not possible to conclude whether the duration of phenobarbital treatment causally influences the risk of epilepsy. This emphasizes the need for prospective multicenter trials to determine the ideal anticonvulsant treatment in neonates at risk for postnatal epilepsy.

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Cerebral Palsy

ICNC-0019: Specific characteristics of abnormal general movements are associated with functional outcome at school age

Introduction: assessing the quality of general movements (GMs) is a non-invasive tool to identify infants at risk for developmental disorders. We investigated whether specific characteristics of definitely abnormal GMs are associated with outcome at school age.Method: Parents of 40 children (median age 8.3years, 20 girls) participated in this follow-up study. In infancy (median corrected age 10 weeks), the children had shown definitely abnormal GMs. Information on specific GM characteristics such as the presence of fidgety movements, degree of complexity and variation, and stiff movements, was available. Outcome at school age was assessed using a standardized parental interview (Vineland Adaptive Behaviour Scale) and questionnaires (Developmental Coordination Disorder Questionnaire and Child Behaviour Checklist). Results: six children had cerebral palsy (CP), ten children attended a school for special education, and eight children had behavioural problems. Both absence of fidgety movements and presence of stiff movements were associated with CP (fidgety absent: 56% CP, present: 0% CP, p=0.001; stiff movements present: 35% CP, absent: 0% CP, p=0.003). Stiff movements were also related to need of special education (stiff movements present: 47%, absent: 9% special education, p=0.009). A lack of movement complexity and variation was associated with behavioural problems.
(variation absent: 55%, some variation present: 9% behavioural problems, p=0.007). Conclusion: evaluation of fidgety movements and movement stiffness may increase predictive power of definitely abnormal GMs for motor outcome - in particular CP. This study endorses the notion that the quality of GMs reflects the integrity of the infant's brain, assisting prediction of long-term outcome.

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Cerebral Palsy
ICNC-0298: Knee jerk responses in infants at high risk for cerebral palsy: an observational EMG study
Background: Following our clinical observation of tonic responses (TRs) in response to the knee jerk in infants at very high risk for cerebral palsy (VHR infants), we systematically studied TRs, clonus and reflex irradiation. We compared responses in VHR infants and typically developing (TD) infants and evaluated possible associations with general movement (GM) quality. Method: 24 VHR (11 girls; median gestational age 30.5 weeks; median birth weight 1470 grams) and 26 TD (12 girls; median gestational age 40.2 weeks; median birth weight 3710 grams) infants were assessed around 3 months corrected age. Surface electromyograms of leg, trunk, neck and arm muscles were recorded while eliciting the knee jerk. GMs and the knee jerk examination were video-recorded. Results: The median number of appropriate trials was 17 (range 6-37). More VHR than TD infants showed TR (VHR 22 out of 23, TD 7 out of 26; p=0.005) and clonus (18 out of 23 infants and 4 out of 26, respectively; p=0.0005) in the ipsilateral quadriceps. VHR infants more often than TD infants demonstrated phasic responses in the contralateral quadriceps (p=0.002) and hamstring (p=0.003). Widespread reflex irradiation occurred in VHR and TD infants. Definitely abnormal (DA) GMs and stiff movements were associated with TRs (DA GMs; p=0.0005, and stiff; p=0.007) and clonus (DA GMs; p=0.003, stiff movements p=0.0005) in the ipsilateral quadriceps. Conclusion: Similar to clonus, TRs may be regarded as a marker of a loss of supraspinal control. Reflex irradiation primarily is a neurodevelopmental phenomenon of early ontogeny.

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Cerebral Palsy
ICNC-0615: Demographic profile, Neurological status and Outcome in children with Tubercular Meningitis
Introduction: We studied the clinical profile, radiological characteristics, outcomes and its predictors in children with tubercular meningitis (TBM). Methods: Records of 350 children admitted from Jan 2010 to Dec 2014 in Advanced Pediatric Centre with diagnosis of TBM were screened. Data was recorded on pre-structured questionnaire and prospective follow-up was done. Results: Mean age at presentation was 43.8+40.5 months (range 3-150 months); 71% were males. Mean duration of illness was 40.5+51.5 days (range 1-365 days). At presentation, 91% fever (91%), intracranial hypertension (85%), seizures (63%), vomiting (51%), irritability (48%), cranial nerve involvement (36%), focal deficits (33%) and headache (25%) were noted. Mean GCS was 10+3.1 (range 3-15). Majority of children presented in stage III (44%), followed by stage II (41%) and stage I (15%). Severe (50%) and moderate (14%) malnutrition, history of contact with a case of tuberculosis (47%), positive family screening (40%), BCG scar (36%), positive mantoux-test (30%) and abnormal chest-radiograph (26%) were noted. CSF showed predominant lymphocytes (64%) followed by neutrophils (26%); elevated proteins (71%) and hypoglycorrhachia (70%). Neuroimaging showed hydrocephalus (91%), basal exudates (57%), infarcts (39%) and tuberculomas (15%). Hydrocephalus was categorized as grade 3 (63%), grade 1 (18%) and grade 2 (8%); ventriculo-peritoneal shunts were inserted in 67% patients. Extracranial tuberculosis was noted in 10%. All patients were started on anti-tubercular therapy (ATT); 10% patients were already on ATT; compliance was good in majority (94%); paradoxical reactions were noted in only 2 patients. Mortality was 20%; at discharge 63% had sequelae while 17% were normal. Long-term outcome is being assessed and will be presented. Presence of basal exudates (p=0.01) and hydrocephalus (p=0.03) correlated significantly with outcomes. Conclusion: Our study provides important clinical data from a single centre in a developing country. In this cohort of children in resource constraint setting, in-hospital mortality and morbidity at discharge was high.

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Cerebral Palsy

**ICNC-0020: Basal ganglia lesions in term newborn**

The term “basal ganglia” refers to caudate and lentiform nuclei, substantia nigra and subthalamic nuclei. These deep gray matter structures belong to the extrapyramidal system and have a selective vulnerability. There are scanty reports in the literature of these insults in newborns. Aim: To describe a consecutive serie of term newborns with insult to basal ganglia and thalamus. Methods: Patient charts were reviewed with regard to etiology, neuroimaging and outcome. Neonatal cerebral magnetic resonance imaging was reviewed with special emphasis on basal ganglia and thalamus findings. Results: Thirty-two neonatal cases were included in this study. In 12, 11, 5 and 4 out 32 patients, an ischemic stroke, hypoxic ischemic encephalopathy, bilirubin encephalopathy and inborn errors of metabolism were identified respectively. The ischemic stroke pattern and the inborn errors of metabolism was asymetrical basal ganglia involvement with or without affectionation other cerebral areas. Hypoxic–ischemic brain injury and bilirubin encephalopathy were presented as symmetrical involvement of putamen and/or thalami in HIE while globus pallidus and subthalamic nuclei were affected in BE. At follow up, seven patients died, twelve were identified with cerebral palsy, eight with psychomotor retardation, four were normal and one patient was lost. Conclusions:A high percentage of term newborns with basal ganglia lesions have a poor outcome (mortality and neurological sequels). The acute insult vascular and hypoxic ischemic encephalopathy are the principal cause. The pattern of lesions could help us to the etiologic diagnosis.

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Cerebral Palsy

**ICNC-0868: To assess the balance functions of children with Down’s Syndrome attending selected paediatric clinical settings in Colombo district, Sri Lanka**

Introduction: Down’s syndrome (DS) is known to exhibit specific balance problems and reasons found as deficits in the postural control system, hypotonicity etc. Specific areas affected in the balance due to DS, and how it varies with age are yet to find. Aims: To assess balance variations among children with Down’s syndrome in three different age groups (3 to 5, 6 to 9 and 10 to 12) and to compare with age-matched healthy children.Methods: A descriptive study was conducted on 64 DS children. Paediatric Balance Scale (PBS) which is a 14-item validated scale assessing three different aspects of balance i.e. static, dynamic and transfer stability was used. Each item was scored from 0-4. Scoring was performed by pre-trained investigators. Results: Total PBS score for DS group (mean = 46.46) is less than that of normal (N) children (mean=54.57) (p<0.001). Out of three aspects, dynamic skills were highly affected, and among them, DS children exhibit lowest balance skills for standing on one foot (mean=1.47) and placing an alternate foot on a stool (mean=2.58). Balance skills show an improvement with the age. (3 to 5 → DS=39.34, N=52.83), (6 to 9 → DS=47.53, N=55.57), (10 to 12 → DS=50.95, N=55.80). Interestingly, the balance gap between normal and DS group seems to narrow with age. Conclusion: Balance skills of DS children are significantly less than normal children. They demonstrate the least balance for dynamic balance skills. Balance skills of DS children improve and they become closer to normal peers with age.

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Cerebral Palsy

**ICNC-0021: Functional outcome following Botulinum Toxin type-A injection in children with cerebral palsy; experience from a Sri Lankan tertiary care Paediatric Neurology Unit**

Introduction: Botulinum Toxin type A (BTX-A) is widely used to treat focal spasticity in children with cerebral palsy (CP), however it has not been systematically studied in Sri Lanka. Objective: To systematically evaluate functional outcome of children with CP after BTX-A injection in a busy Paediatric Neurology Unit.Methods: Functional status of all children receiving BTX-A over two years was evaluated before and several months after injection, using Gross Motor Functional Classification System (GMFCS), Manual Ability Classification (MAC), achievement of individual predetermined goals as identified by Therapists and families. An individualized therapy program was recommended based on specific goals set for the injection. Paired T test was used to compare GMFC and MAC, before and after BTX-A.Results: Seventy seven children met inclusion criteria (male 58%, Mean age 5.8 years). Diagnoses included spastic diplegia (21%), spastic hemiplegia (38%) and spastic quadriplegia (31%). Statistically significant improvement in GMFCS level was noted after BTX-A to the lower extremities (p <0.05), as well as in MAC improvement after upper extremity BTX-A (p <0.05). Therapy goals were achieved in 62% of all children after BTX-A injection, and 82% of parents expressed satisfaction regarding improvement following injection.Conclusion and recommendations: Similar to prior published results from other countries, we found that significant functional improvement occurs following BTX-A injection coupled with an individualized therapy program in children with CP. Neurorehabilitation for children with CP in Sri Lanka presents unique challenges: further work.

Cerebral Palsy
Cerebral Palsy

ICNC-0299: Venlafaxine Abstinence in Neonates: a Neurological Syndrome

Introduction: Up to two thirds of infants born to mothers using the antidepressant venlafaxine are estimated to display features of withdrawal. Here we present literature review on neonatal venlafaxine abstinence with comments upon practical management.

Methods: A PubMed search yielded nine relevant articles on neonatal venlafaxine withdrawal. Selected further references were also examined.

Results: Reported characteristics of venlafaxine withdrawal include restlessness, hypoand hypertonia, jitteriness, irritability, poor feeding, seizures, tachypnoea, poor perinatal adaptation and hypoglycaemia. Onset occurred from shortly after birth to 4 days of age, with complete resolution between day 5 of life and 7 weeks age (including weaning of anticonvulsant drugs). Seizures were described as myoclonic in three neonates, two having abnormal electroencephalograms, with discordance between resolution of clinical seizures and electroencephalogram normalisation. Phenobarbitone was used in five neonates to control seizure activity. In one case, withdrawal was allowed to resolve with supportive care only; notably, administration of a small dose of venlafaxine temporarily improved symptoms. Three studies measured low or undetectable levels of venlafaxine and its metabolites in affected neonates. Together with their predicted half-lives in the neonate and symptom improvement upon venlafaxine administration, this supports a withdrawal phenomenon as responsible rather than toxicity. No subsequent adverse neurodevelopmental effects from withdrawal were reported.

Discussion: It is important that paediatricians are aware of the manifestations of neonatal venlafaxine abstinence. We recommend antenatal counselling for motherstaking venlafaxine and observation of their at-risk neonates for 4 days following delivery.

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Cerebral Palsy

ICNC-0301: Lethal Zellweger Spectrum Syndrome due to a novel mutation in the pex3 gene

Background: Zellweger spectrum syndromes (ZSSs) are a heterogeneous group of autosomal recessive neurodegenerative disorders that affect multiple organ systems. A high incidence of ZSSs in the South African population has been observed in the last 20 years. Most of these patients were diagnosed in the first 8-10 weeks after birth and lived an average of 2 years. Three cases however presented with a severe phenotype and these patients died within 1 to 30 days after birth.

Patient: A neonate, presenting with facial and finger dysmorphia as well as lactic acidosis after birth, was recently referred to the Potchefstroom laboratory for inborn errors of metabolism, South Africa for a metabolic work-up.

The patient unfortunately died a day after birth. Results: Initial metabolic investigations on plasma indicated an elevated level of C26 as well as C24/C22 and C26/C22 ratios. In addition, increased pipecolic acid was also observed. A ZSS was suspected after plasma bile acids analysis revealed elevated dihydroxycholestanoic acid, trihydroxycholestanoic acid and C29-dicarboxylic bile acid. Complementation studies, for accessing peroxisomal biogenesis disorders on fibroblasts, were done and revealed PEX3 gene as a probable candidate. The sequenced mutation analysis of the PEX3 gene showed that the patient had a novel homozygote frameshift mutation namely c.203_204dup (p.Val69Glnfs*9).

Conclusions: It was concluded that this pathogenic mutation results in the expression of a non-functional truncated protein and consequently a severe and fatal phenotype. Our findings on and experience in ZSSs gives merit to the investigation of peroxisomal biogenesis disorders in neonates presenting with dysmorphia and metabolic decompensation.

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Cerebral Palsy

ICNC-0302: CXCL5 Signaling is a shared pathway of Neuroinflammation and Blood-Brain Barrier Injury contributing to White Matter Injury in the immature brain

White matter injury (WMI) is a prominent brain injury in very preterm infants. A common signaling pathway may cause neuroinflammation and blood–brain barrier (BBB) damage to the immature brain. CXCL5 is produced in inflammatory and endothelial cells in response to insults, and is markedly increased in the amniotic cavity in response to intrauterine infection and preterm birth. We determined whether CXCL5 signaling is a shared pathway of neuroinflammation and BBB injury that contributes to WMI in a postpartum day-2 (P2) rat pup model of lipopolysaccharide (LPS) and hypoxic ischemia (HI). We found that predominant increases in microglial activation and BBB damage were observed 24 hours after LPS-sensitized HI, and WMI (decreased myelination and increased astrogliosis) was observed on P12 compared with controls. Immunohistology revealed increased CXCL5 expression in the white matter 6 and 24 hours after insult. Immunofluorescence experiments revealed upregulated CXCL5 expression in activated microglia and endothelial cells 24 hours post-insult. CXCL5 inhibition by SB225002, a selective nonpeptide inhibitor of CXCR2, significantly attenuated microglial activation and BBB damage, increased myelination, and reduced astrogliosis in the white matter after LPS-sensitized HI. In addition, CXCL5-sensitized HI or CXCL5 alone significantly induced BBB damage and WMI in association with different neuroinflammation mechanisms. CXCL5-sensitized HI induced microglial activation and neutrophil infiltration, whereas CXCL5 alone predominantly caused neutrophil infiltration. In conclusion, CXCL5 is a potential biomarker for WMI in preterm infants. Pharmacological blockade of CXCL5 signaling that attenuates dysregulated neuroinflammation can be used a therapeutic strategy against WMI in the immature brain.

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Cerebral Palsy

ICNC-0870: Properties of joined WHO ICF-CY body functions b codes and activity and participation d codes in childhood disability

Aim To examine the possibility of joining ICF-CY body functions b codes and activity and participation d codes to create a common disability variable Methods The parents of 332 children with 8 different disabilities were visited and 47 body functions b codes and 57 activities and participation d code qualifiers were scored. Each code had 5 qualifier levels. Following Rasch analysis fifty four of retrieved codes were selected to cover the full spectrum of disability in the best possible way. After joining them, they underwent psychometric and Rasch data analysis to create a disability variable based on both ICF-CY coding systems. Results The mean score of the joined b and d codes was 0.96, with SD 1.0 and range 0.28–2.15. Variance was 1.69, range 0.49–3.13 and Cronbach’s alpha 0.98. Inter-code correlation was 0.67, range 0.10–0.98. Rasch analysis documented good coverage on the whole range of the disability variable. The lowest score was −4.97, and the highest was 4.86. The mean location was −1.52. The joined codes were ordered. Furthermore, the distribution of the b and d codes on the child-code map documented a better measure of disability with d codes, in children with relatively less disability. Conclusion Joined ICF-CY body functions b codes and activities and participation d codes can cover the whole spectrum of disability in childhood. ICF-CY codes thus selected, when added to ICD-10 diagnosis registering, can contribute to better information on disability across health sectors for both individual children and groups of children.

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Cerebral Palsy

ICNC-0024: Influence of Spinal Manipulation on Muscle Spasticity in Cerebral Palsy Patients

Muscle spasticity is one of the treatment targets in Cerebral Palsy. According to preliminary studies, spasticity reduction could be achieved by special chiropractic technique - spinal manipulation that is a component of the Intensive Neuropsychological Rehabilitation System (INRS), multimodal rehabilitation approach that combines different treatment modalities: physical therapy, reflexotherapy, massage, rhythmical group exercises, mechanotherapy, rehabilitation computer games. The aim of the study was to evaluate influence of one spinal manipulation and two-week treatment course according to INRS on wrist muscle spasticity.Group of 29 children with spastic forms of Cerebral Palsy, without fixed wrist contractures, aged 7-18 years, were included into the study. Children were evaluated before, after one spinal correction and in the end of treatment course.Spasticity of wrist muscles was assessed using Neuroflexor device (Aggero MedTechAB, Sweden) that measures resistance while applying passive movements to the wrist at two different velocities. Neuroflexor was proved to reliably measure the muscle tone and distinguish between its components: neural component (NC), attributed to spasticity from viscoelastic components, attributed to muscle and tendon mechanical changes.Significant decrease of NC was noted after the spinal manipulation (mean difference 1.65, p < 0.01). After the treatment course level of spasticity has further decreased to mean difference 2.09 (p<0.01). For patients with low level of
spasticity significant decrease of NC was noted already after the first correction. In case of pronounced spasticity decrease of NC was achieved only after treatment course. Spinal manipulation may have influence on the muscle spasticity; further studies are required.

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Cerebral Palsy

ICNC-0871: Modern treatment approach: Importance of neurorehabilitation in remediation of cognitive deficits in children with partial epilepsy

Objectives: Epilepsy causes attention and visuospatial impairments in children. Attention is a key element in acquiring new information. Modern neurorehabilitation methods are crucial in remediation. We investigated short- and long-term rehabilitation effect of computer-based intervention for children with partial epilepsy (PE). Methods: 35 children with PE and cognitive deficit (under antiepileptic treatment): 17 in study group (mean age=10.07yrs, SD=1.149) and 18 in waiting-list control group (mean age=10.51yrs, SD=1.766) participated. Study group received individual rehabilitation twice a week during 5 weeks with attention and visuospatial modules from FORAMENRehab software (Sarajuuri et al, 2000; adapted for children). Primary intervention effect was evaluated comparing baseline performances before and after 5-week-period. Follow-up assessment was conducted after 1.27 years (SD=0.374). Results were analysed with Wilcoxon-Mann-Whitney test. Results: No differences on baseline performances existed before intervention between study and waiting-list groups (p>0.05). Immediately after training, study group showed significantly better results (p<0.05) in all attention components: focused (omission errors), sustained (processing speed), complex (correct responses; commission errors) and tracking. Also, in visual recognition (accuracy), visual organization (correct responses) and visual attention (processing speed)(p<0.05). Long-term positive intervention effect persisted 1.27 years later: study group outperformed waiting-list group in two attention and two visuospatial components. Conclusions: Computer-based neurorehabilitation design with FORAMENRehab is effective for children with PE. Significant improvements were seen in study group in all attention and visuospatial functions compared to children without rehabilitation. Furthermore, the intervention effect was persistent. We recommend modern computer-based interventions with minimum 10 sessions for treating cognitive impairments in children with epilepsy.

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Cerebral Palsy

ICNC-0304: Early EEG markers may inform prognostication of cognitive outcomes in very preterm infants

Introduction: Infants born very preterm (<30 weeks gestational age) are at substantial risk of developing cognitive, motor, behavioural, and social impairments. However accurate prognostication of such impairments is challenging. This study investigates the predictive values of quantitative electroencephalography (EEG) markers acquired at term equivalent age, in relation to cognitive outcome at 12 months corrected age. Methods: 38 very preterm infants without any major congenital or chromosomal abnormality were studied. EEG was recorded at term equivalent age (40-42 weeks gestational age) and relative power was computed for frequency bands: delta (0.49-1.95Hz), theta (2.20-5.86Hz), alpha (6.10-12.94Hz), and beta (13.18-29.79Hz) at each of 19 electrodes of the international 10-20 system. Cognitive outcome was assessed at 12 months corrected age using Bayley Scales of Infant and Toddler Development (BSITD-III). Univariate linear regression was carried out to assess the relationship between EEG relative power and cognitive score. Results: Univariate linear regression showed for each unit increase in relative alpha and beta power at electrode CZ, the cognitive outcome decreased by 603 (95%CI: -1179 to -27, p<0.05) and 2309 units; (95%CI: -4179 to -439, p<0.05) respectively. Relationships at other electrodes were non-significant. Conclusion/Discussion: These preliminary results suggest that at term equivalent age in very preterm infants, relative power of higher-frequency EEG activity at the vertex may prognosticate cognitive outcomes at 12 months. We are investigating further infants and additional outcome measures.

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Cerebral Palsy

ICNC-0307: Change of Cytokine Levels in Neonatal Seizures induced by Hypoxic Ischemic Encephalopathy

Introduction: We investigated any change of cytokine levels in response to neonatal seizures induced by hypoxic ischemic encephalopathy (HIE) serially to assess any meaningful cytokine levels in relation to neonatal seizures with various parameters. Method: The HIE induced seizure group consisted of 13 patients, and another 15 normal newborns were enrolled as a control group. The initial samples in the seizure groups were obtained within the first 24 hr of seizure onset, while the samples in the control group were obtained within the first 24 hr of admission. The second samples were obtained between 48 and 72 hr in both groups. The third samples were taken only in the seizure group on the 5th day of seizure onset. Results: During neonatal seizures, the levels of cytokines increased within 24 hr and the levels of cytokines decreased after 48 to 72 hr of seizure onset. Among the 10 interested cytokines, the levels of IL-8 significantly increased for 72 hr in the seizure group (p < 0.05). IL-10 was not significant for the first 24 hr, but increased significantly between 48 to 72 h of seizure onset (p < 0.05). Meanwhile, IL-1Ra decreased significantly in the 2nd sample (p < 0.05).

Conclusion: Our findings suggest that serial examination of serum cytokine concentrations may serve as a biomarker for brain damage of neonatal seizure when detected within 72 hr of the seizure.

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Cerebral Palsy

ICNC-0286: Long term cognitive outcome in preterm infants with mild Periventricular Echo-enhance

Mild periventricular echo-enhance (PVE) is common in preterm infants, which is considered a possible evidence of brain damage. We did a 6 years follow-up study to explore the long term prognosis of mild PVE during the first two week of preterm newborn. Sixty three preterm infants, who were admitted in NICU during September 2002 to August 2003, were enrolled and divided into three cohorts judged by transcranial ultrasound examination, including A cohort with normal scans (n=26), B with mild intravascular hemorrhage (IVH, n=23), C with both IVH and PVE (n=14). Both Raven’s progressive matrices and Peabody picture vocabulary test were assessed before they entered primary school at the age of 6 Gestational age, birth weight, gender and average hospitalized duration in the three cohorts has no significant differences. The average age of cohort A, B and C were 6.46±0.30, 6.47±0.23, 6.21±0.16 respectively. The average Score of Raven’s progressive matrices in cohort A, B and C were 113.3± 15.1, 112.3± 15.0, 117.6± 12.9 respectively, with no cohort differences (P=0.56). The average Score of Peabody picture vocabulary test were 119.9± 16.0, 118.9± 16.3, 111.6± 17.1 respectively, with no cohort differences ( P=0.36). Vision problem ratio in cohort C (50%) was much higher than in cohort A (19%) and B (39%) with significant differences (P=0.037). Mild PVE during the first two weeks in preterm newborns usually have a good cognitive outcome. Both IVH and PVE in preterm infants have much more vision problems at school age.

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Cerebral Palsy

ICNC-0303: Safety and efficacy of Levetiracetam in pre-term neonates with seizures: A retrospective study

Background & Objectives: There is paucity of data regarding safety and efficacy of newer anti-epileptic drugs in pre-term neonates. This study evaluated safety and efficacy of Levetiracetam (LEV) compared to Phenobarbital (PHB). Study methods: In this retrospective record review, 65 pre-term neonates with seizures who had received either Phenobarbital (n=35) or Levetiracetam (n=30) were included. Results: The mean gestation, birth weight, gender, mode of delivery, APGAR score and seizure characteristics were comparable between two groups. The seizures were controlled with 1st drug alone in 26/30 in LEV group and 20/35 in PHB group (86.7% Vs 57.1%; p=0.005). After administration of second drug, seizure control was better in LEV group (100%) compared to PHB group (84.7%), but was not statistically significant (p=0.057). Late preterm neonates (34 to 36+6 weeks) had better seizure control with LEV than PHB (86.6% Vs 55.2%; p=0.048). There was no significant difference in seizure control between the groups for other gestational ages. Birth weight did not show any association with seizure control by both the drugs. No statistically significant adverse effects were noted after administration of both the drugs. There were no deaths during the hospital stay in LEV group, one death in PHB group, which was attributed to chronic lung disease.Conclusions: This retrospective study has shown that Levetiracetam has better efficacy in seizure control as first line drug compared to PHB in preterm neonates. Levetiracetam was safe and well tolerated without any major adverse effects. Prospective, randomized controlled studies are needed to confirm these findings.
Cerebral Palsy

ICNC-0028: Multiple regression analysis of quality of life in children with Cerebral Palsy

Objective: To analyze the correlation factors influencing quality of life (QOL) in children with cerebral palsy (CP). Methods: 80 children with CP and 80 healthy children were measured by Pediatric Quality of Life Inventory Version 4 (PedsQL4.0) to assess their QOL and then compared differences in QOL of children between two groups. Children with CP were also assessed using Gesell Developmental Scale (GDS) and Gross Motor Function Classification System (GMFCS) to test their developmental quotient (DQ) and severity degree (GMFCS), and then the correlation among QOL, age, sex, family income, clinical type, severity degree, intelligence degree of children with CP were analyzed by multiple regression analysis. Results: Significant differences in mean scores favoring control group were found in physical functioning/aspect, emotional functioning, social functioning, psychological aspect and total score (P<0.01). Intelligence degree and severity degree correlated to total score of QOL. Severity degree, intelligence degree and age correlated to physical aspect. Intelligence degree correlated to psychological aspect. Conclusion: CP reduces children's QOL in full-scale. Severity degree and intelligence degree are two important factors influencing QOL in children with CP.

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Cerebral Palsy

ICNC-0029: The study on quality of life of children with cerebral palsy

Objective To study the quality of life of children with cerebral palsy. Methods With the PedsQL4.0, 113 children with cerebral palsy were studied, and 52 children with common illness and 314 normal children were also studied and compared. With the PedsQL of school functioning, the children of these three groups who had been to school or kindergarten were also studied and compared. Result The score of physiology functioning, communication functioning and total score of PedsQL in children with cerebral palsy were lower than those in the children with common illness and normal children. The difference has statistic significance. The score of emotional functioning in children with cerebral palsy was only lower than that in the normal children, the difference has statistic significance. The score of school functioning in children with cerebral palsy was significant lower than that in children with common illness and normal children(P<0.01). Conclusion The quality of life of children with cerebral palsy is much lower than children with common illness and normal children. The illness has sever effect on the school functioning of children with cerebral palsy. Therefore, the whole improve of quality of life is the goal for the rehabilitation of children with cerebral palsy.

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Cerebral Palsy

ICNC-0031: The clinical research of early intervention to cerebral sub-health infants by traditional Chinese medicine

OBJECTIVE To observe the effect of early intervention to cerebral sub-health infants by TCM (Traditional Chinese Medicine). METHODS 60 cases clinical cured cerebral sub-health infants aged 2m~6m with moderate to severe brain damage in perinatal period were early intervened mainly by our TCM, mainly by massage of attacking vital points of DU meridian, benefiting kidney, strengthening the qi of spleen and five-elements music listening treatment, assisted with physical therapy etc. The course of the intervention was 3 months. The QO of Gesell were compared before intervention, 3months and 18 months after intervention. RESULTS 3 months and 18 months after the intervention, the QO of the infants were increased compared with the QO before the intervention. And the difference is significant for statistics(P<0.001). 18 months after the intervention, the QO of 45 cases were higher than 70. CONCLUSION The intervention by TCM can reduce the probability of the occurrence of cerebral palsy, mental retardation and other sequelae which were caused by perinatal brain damage, and promote the development of movement, cognitive, language, social and other functions. And its mechanism may be related to the promotion of brain development, promoting damaged neuronal repair.

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Objective: To explore the effect of music therapy on children with cerebral palsy about the the physical coordination, cognition and music development level, emotional communication level. Methods: 30 children with cerebral palsy, collected in the Nanhai Affiliated Maternity and Children’s Hospital affiliated to Guangzhou University of Chinese Medicine from January 2009 to January 2010, 22 boys and 8 girls, age (3.9±1.2) years, 20 cases of HIE, 15 cases of premature birth, 13 cases of pathologic jaundice. At the beginning of treatments, the cases were diagnosed with mental retardation. According to the individual situation of each child, we would choose the specific music therapy program, such as RBT music therapy, creative music therapy, Orff music therapy, improvisational music activities, music prompt behavioral therapy, individual music therapy, group music therapy, body training, music listening, music desensitization training, body feeling music therapy. 60 times is a period of treatment. Before and after the treatment, we would evaluate the behavior, emotional communication and music development level by using the music therapy assessment scale. Results: 8 cases (26.7%) is markedly effective, 19 cases (63.3%) effective, 3 cases (10%) invalid, the total efficiency 90%. About the total scores, scores of before treatment is (32.3±6.9), after treatment (46.3±6.5), t value -8.0, p value 0.00 (p < 0.00); About the physical coordination and cognition, scores of before treatment is (15.8±4.1), after treatment (18.6±4.1), t value -2.6, p value 0.01 (p < 0.05); About music development level, scores of before treatment is (13.8±2.5), after treatment (17.0±2.5), t value -4.8, p value 0.00 (p < 0.01); About the emotional scores, scores of before treatment is (1.5±1.3), after treatment (5.5±1.7), t value -10, p value 0.00 (p < 0.01); About the communication scores, scores of before treatment is (1.2±1.3), after treatment (5.1±1.4), t value -10.7, p value 0.00 (p < 0.01). Conclusion: Music therapy for cerebral palsy can improve the level of body movement coordination, the cognitive, emotional communication.

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Cerebral Palsy

ICNC-0034: A randomized controlled study and evaluation of children with Cerebral Palsy by mind acupuncture

Abstract Objective: To investigate the effects of clearing the Governor Vessel and refreshing the mind needling in neural development and remediation of children with cerebral palsy. Methods: 200 cases of children with cerebral palsy were randomly divided into the treatment group (n = 100) and the control group (n = 100). The treatment group was given the combined therapy of acupuncture and rehabilitation training, and the chosen acupoints were 13 points of the Governor Vessel, Shenhu (BL 23), Taixi (KI 3), Yanglingquan (GB 34), Zusani (ST 36) and Sanyinjiao (SP 6), and points of refreshing the mind were also selected, which included puncturing Shenting (GV 24) toward Qianling (GV 21), puncturing Qianding (GV 21) toward Baihui (GV 20), puncturing Baihui (GV 20) toward Naohu (GV 17) and Sishencong (Ex-HN 1). The control group was only treated with rehabilitation training. A contrastive analysis of the therapeutic effect of acupuncture combined with rehabilitation training and pure rehabilitation training was made after a treatment course of 3 months. The Gross Motor Function Measure (GMFM) and Beijing Gesell Developmental Scale were adopted to assess the neural development and rehabilitation outcomes of the two groups. In addition, skull CT/MRI was adopted to evaluate the plerosis of injured cerebral nerve after treatment. Results: The total effective rate in treatment group was 87%, significantly higher than the 55% in the control group. The children’s development quotient (DQ) tested by Gesell Developmental Scale and scores tested by GMFM in the treatment group was obviously higher than the control group (P < 0.01). The improving and curing rates presented by skull CT/MRI in the treatment group were higher than the control group (P < 0.01). Conclusions: Clearing the Governor Vessel and refreshing the mind Needling could accelerate the recovery of injured brain nerve and the reconstruction of brain function. The acupuncture therapy could ameliorate both the motor development and cognitive development. On the other hand, the forward curative effect of acupuncture combined with rehabilitation training was significantly better than the pure rehabilitation training.

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Cerebral Palsy

ICNC-0036: Exploratory development of combined rehabilitation treatment for children with Cerebral Palsy

Objective: To investigate suitable rehabilitation modality of our country to spread. Methods: We studied the applying of integrated traditional and western medicine-home rehabilitation modality for children with cerebral palsy (tri-combined cerebral palsy rehabilitation modality) form Oct 1999 to Oct 2005. It was the first time that to study the combination of TCM rehabilitation with Western medicine rehabilitation and home rehabilitation modality in international and have an advantage of the technique of same kind. Results: The effective rate of 684 patients (80.4%) was significantly higher than that of Western medicine rehabilitation group (32%). And we took the leader of reporting the recovery rate of cerebral atrophy and dysplasia (31%) of cerebral palsy after treatment, significantly higher than that of treated by rehabilitation training only (2.56%). The study illuminated the dominantposition of TCM and western medicine rehabilitation. After the
study of molecular biology, etiology, haemodynamics, and microcirculation, brain electrophysiology, imaging, we also proved that the combined rehabilitation modality can promote the function rebuilding of nerve cell. We carried out home rehabilitation for children with cerebral palsy at home, edited and published series teaching material including book and VCD and replenished the vacant of internal. We published 20 paper's articles and one was included by ISTP and 20 times were cited. The opinion of the evaluation committee is that the study achieved the level of domestic leading and international advanced. Conclusion: The rehabilitation modality can effectively degrade mutilation rate of cerebral palsy and relieve mind and economy burden of family and society.

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Cerebral Palsy
ICNC-0038: Observation of effect on neural development on massage Chinese in the brain damage in preterm infants

Objective The effects of the two groups is compared to see whether there are superiority in early intervention of brain damage in preterm infants with the Massage of Tongduxingn ao and Yishenjianpi. Whether to further established the important position of traditional Chinese medicine in the early intervention of brain damage in premature infants. Methods 82 infants with Brain demage in preterm infants were selected, randomly divided into two groups. The experimental group received the treatment of Massage of Tongduxingn ao and Yishenjianpi combined with routine intervention. The control group received Massage of Sensory Stimulation combined with routine intervention. The Gross Motor Function Measure, Bayley scales of infant development II （MDI、PDI） and the Gesell Developmental Scales were tested before, right after and 3 months after the treatment designed. Results The children’s development quotients (DQ) and GMFM(A,B) areas in both groups are improved. The experimental group has a significant superiority in improving the DQ of gross motor function by Gesell Developmental Scales and GMFM(B area) compared to the control group(P ＜ 0.05), but no discrepancy in the others. After the treatment, the score of experimental group reach normalization in Mental Development Index(MDI) and Psychomotor Development Index(PDI) by BSID is higher compared with the control group(P＞0.05). Conclusion The Massage of Tongduxingn ao and Yishenjianpi and the Massage of Sensory Stimulation can promote the developmental level of the intelligence and gross motor function, and The Massage of Tongduxingn ao and Yishenjianpi has a significant superiority in improving the DQ of gross motor function and sitting position(B area of GMFM).

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Cerebral Palsy
ICNC-0039: Increase in ankle muscle strength and rate of force development after 6-weeks gait training in adults with cerebral palsy - a randomized controlled clinical trial

Introduction: Reduced muscle strength is a severe functional problem in adults with cerebral palsy (CP). Strength training interventions, which increase muscle strength, have failed to demonstrate functional relevant improvements. Here we report data from a randomized clinical trial (RCT) of the effect of treadmill training on muscle strength and gait kinematics in adults with CP. Methods: 32 adults with CP (GMFCS 1-3) aged 38.1 years +/-12 (SD) years were randomly allocated to either a training group (n=16) where daily gait training on a treadmill was performed for 30 min for six weeks in addition to their usual activities or a control group that performed their usual activities. Evaluation of maximal voluntary contraction (MVC), rate of force development (RFD), torque responses to supramaximal electrical stimulation (Mmax) in the ankle joint plantar- and dorsi flexors, ultrasound determined thickness of tibialis anterior (TA) and medial gastrocnemius (MG), gait kinematics by 3D video analysis was made before and after the intervention/control period. Results: Significant increase in dorsi and plantarflexor MVC and RFD was observed in the intervention group compared to the control group. No significant difference in muscle thickness and Mmax was found between the groups. Significant improvements were found in gait speed, active range of motion and amplitude of toe lift during gait in the intervention group as compared to the control group. No correlation between kinematic improvements and muscle function were found. Conclusion: The increased strength and RFD are likely caused by increased neural drive since no increase in muscle thickness and Mmax was observed. These data demonstrate that it is possible to achieve functionally relevant increases in muscle strength through intensive daily gait training in adults with CP.

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3University of A Coruña, A Coruña, Spain
Cerebral Palsy

**ICNC-0310: Punctate white matter lesions: correlation to gestational age and SWI appearance**

Background: punctate white matter lesions (PWML), often are included in the spectrum of periventricular leukomalacia (PVL), still have controversial prognostic meaning. We investigated differences between PWML with and without loss of signal on an advanced MRI technique, the susceptibility weighted imaging (SWI), in correlation to gestational age (GA) of a group of Very Low Birth Weight (VLBW) neonates. Methods: we have retrospectively reviewed brain MRI scans performed in 263 VLBW admitted to our NICU, searching for PWML. All scans were performed routinely at term equivalent age (TEA) on a 1.5T system using “feed and wrap” technique. PWML were then divided into 2 groups based on the evidence of blood degradation products as visualized by SWI, and the prevalence of this finding was assessed in 2 GA groups (<28 weeks and 28-32 weeks) according to previous hypothesis concerning the highest risk of developing PVL. Results: Out of 263 VLBW babies, 53 patients with PWML on MRI were selected. Among these, 17 (about 1/3) presented lesions visible on SWI as limited zones of lower signal in the periventricular zone, often following the distribution of deep medullary veins. The incidence of punctate lesions In the group <28 week GA was of 12.8% (78/263), with half of the lesions positive on SWI (Tab. 1). In 28-32 week group the total incidence of PWML was almost twice as high, although the share of SWI± abnormalities went down (28% of PWML). Of interest, the incidence of SWI+ PWML remained stable (6.4%) throughout the whole population of very preterm (<32 weeks), highlighting a potential different vulnerability pattern when compared to SWI - lesions. Conclusion: About 1/3 of PWML present low SWI (SWI+) signal suggesting potential haemorrhagic-transudative process, as opposed to activation of ischemic-inflammatory pathway in SWI- lesions. The share of SWI+ PWML goes down with the increase of GA, similarly to the risk of intraventricular haemorrhages. Punctate SWI± lesions could present a separate nosologic entity and should be studied further, especially in terms of follow-up. References - Kersbergen KJ et al. Different patterns of punctate white matter lesions in serially scanned preterm infants. PLoS One. 2014 Oct 3;9(10):e108904 - Ramenghi LA. Magnetic resonance imaging assessment of brain maturation in preterm neonates with punctate white matter lesions. Neuroradiology. 2007 Feb;49(2):161-7 - Bassi L. Diffusion tensor imaging in preterm infants with punctate white matter lesions. Pediatr Res. 2011 Jun;69(6):561-6 Table 1 - Punctate white matter lesions (PWML) in VLBW: gestational age and SWI appearance. GA (weeks) TOTAL <28 28-32 Any PWML 10 43 53 % of population 12.8% 23.2% 20% SWI PWML 5 12 17 % of PWML 50% 28% 32% % of population 6.4% 6.4% 6.4% Population (VLBW neonates) 78 185 263

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Cerebral Palsy

**ICNC-0330: Neurological examination, head circumference and brain sonography as predictors for neurodevelopment in preterms at 24 months**

Introduction: Head circumference, neurological examination and brain sonography findings are independent predictors for neurodevelopmental outcomes of preterm babies. Objective: To assess the prognostic value of the combination of neurological examination at term age, head circumference z score at term age and brain sonography findings in the prediction of neurodevelopment at 24 months corrected age. Methods: Abnormal neurological examination was determined with at least one abnormality item in the Hammersmith Neurological Examination Score at term age. Serial brain sonography was performed at 5 and 21 days and at term age. Microcephaly was defined when head circumference z score was less than -2.0 at term age. Abnormal neurodevelopment was defined as the composite score of Mullen Early Learning Test of less than 70 at 24 months corrected age. Results: 185 patients completed follow up. 22 patients had abnormal neurological examination. 15 patients had major brain abnormalities and 10 were microcephalic. 32 patients had abnormal neurodevelopment. The sensibility and specificity for neurological examination were 18.75 and 89.5%, respectively. When combined with head circumference at term age or with major brain sonography findings sensibility and specificity were 12.5 and 100%. PPV and NPV were 100 and 84.5%. When the three methods were combined sensibility and specificity were 62.5 and 100% and PPV an NPV were 100 and 83.6%. Conclusions: The combination of these methods performed at term age could be a useful and accessible tool for prediction of neurodevelopment in preterm infants in limited-resource settings.

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Cerebral Palsy

ICNC-0312: Bell’s palsy in a neonate, a case report
Background: Idiopathic Bell’s palsy is the commonest cause of unilateral fascial paralysis in children. Although being idiopathic by definition, possible infectious, inflammatory and ischemic triggers have been suggested. Bell’s palsy has very rarely been described in neonates and young infants. Case report: We are reporting a two days old neonate with no prior illnesses. He has presented with acute left fascial palsy. Clinical findings & normal brain imaging has been consistent with the diagnosis of bell’s palsy. The patient has satisfactory response to oral steroids. This is the youngest infant reported with bell’s palsy in current medical literature up to our knowledge. Discussion: Bell’s palsy is thought to be responsible for up to three fourths of cases of acute unilateral fascial paralysis worldwide. The diagnosis is ideally to be only made after other causes of acute peripheral palsy have been excluded. Steroids may have some role in the treatment but antivirals have doubtful evidence of benefit. Prognosis is generally good, though residual dysfunction is occasionally encountered. Conclusion: Bell’s palsy is the commonest and benign cause of acute fascial nerve dysfunction in children, however it is very unusual to be seen in young infants. We are reporting what we believe the youngest neonate with acute bell’s palsy with good response to steroid treatment. Keywords: Bell’s palsy, fascial nerve.

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Cerebral Palsy

ICNC-0313: Neurological outcomes in critically ill infants with seizures
Background: Continuous video-electroencephalography monitoring (cEEG) remains the gold standard for seizure diagnosis and quantification in infants with critical illness, and may help to predict long-term neurological outcomes. Aim and Methods: We reviewed critically ill infants (0-4 months) who underwent cEEG at Mayo Clinic between 2010 and 2013. We sought to evaluate predictors of favorable long-term neurodevelopment, including seizure freedom. Results: Of 72 patients identified, 45 (62%) were male. At the time of cEEG, their median conceptional age was 40 weeks (IQR 38.5-42.0). The median duration of cEEG monitoring was 45 hours (IQR 23.0-86.2). Forty-nine (68%) infants were monitored in the neonatal ICU and 23 (32%) in the pediatric/cardiac ICU. The most common etiologies included ischemic or hemorrhagic stroke (n=18, 25%) and acute hypoxic-ischemic encephalopathy (n=18, 25%). Forty-two patients (58%) had electrographic seizures and 19 (26%) had status epilepticus. The majority experienced electrographic seizures without clinical correlate (n=28, 67%). Seizures were identified within the initial 30 minutes of cEEG recording in 33 (79%) infants. Among infants who experienced seizures, 37 (88%) underwent follow-up with a pediatric neurologist at a median of 23.0 months (IQR 9.0-37.0). Thirty-one (84%) were seizure-free and 26 (70%) were off all antiepileptic medications. Normal neurodevelopment was only reported in 13 (35%) infants. Motor (n=21, 57%) and cognitive (n=21, 57%) deficits were frequent. Discussion: Seizures were common among our critically ill infants and cEEG was essential to their diagnosis. However, most infants were seizure-free and off antiepileptic drugs at last follow-up, although most had suffered long-term neurodevelopmental sequelae.

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Cerebral Palsy

ICNC-0315: Tale of two cities- Comparison of asphyxiated infants managed with therapeutic hypothermia in a developed country (Centre 1) and a developing country (Centre 2)
Background: Perinatal Asphyxia in full-term infants is a leading cause of morbidity and mortality. Therapeutic hypothermia has been shown to reduce asphyxia associated mortality and disability. The effect of this intervention might not be similar in developed and developing countries. Objectives: To compare experiences in use of therapeutic hypothermia between two neonatal units from developed and a developing country using a similar protocol (TOBY). Methods: Retrospective record review. Characteristics and outcomes of patients with perinatal asphyxia and therapeutic hypothermia at a Level 3 NICUs in a hospital in Utrecht, The Netherlands, (Center 1) and those at Johannesburg, South Africa, (Center 2) were compared. Results: A total of 124 patients in centre 1 and 104 in centre 2 were cooled. There were no differences between gestational age, birthweight and the time to hypothermia between the two centres. The median 5 minute Apgar score was lower in centre 1; 4 (IQR 0-10) vs 5 (IQR 1-10) (p<0.001). There were more outborn patients (109 vs 2, p<0.001) in centre 1. The pH and base deficit was significantly lower in centre 1 (6.91 vs 7.00,
p<0.001 and 18.2 vs 20.6 p<0.001 respectively). All the patients in centre 1 had an aEEG tracing with the commonest tracings being BS (34%), DNV (33%) and FT (19%) compared to 54 patients in centre 2 with the commonest tracings being DNV (48%), BS (19%) and CLV (30%). 9 patients were ventilated in centre 2 as compared to 119 in centre 1 (p<0.001). More babies died in centre 1(35%) with half following redirection of care (p=0.015). In Center 1, 53% had a DQ>100 vs 5 in centre 2. Of the survivors in centre 2, half had a DQ < 85% vs 5 in centre 1 (p<0.001). 33% of patients were lost to follow up in centre 2 compared to 1% in centre 1. Conclusion: There are significant differences between the two cohorts. This could not be explained by the increased mortality due to redirection of care in the developed country. Resources – selection to cool and ventilation may play a role in the differences in the developing country.

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Cerebral Palsy

ICNC-0041: Altered force-length relation of ankle plantarflexor muscles may contribute to toe walking in persons with cerebral palsy

Optimal forward propulsion during gait requires that ankle plantarflexor muscles are activated at a length where cross-bridges between myofibrils are formed most efficiently and the muscles are capable of producing most force. In persons with cerebral palsy (CP), muscle and connective tissue show structural changes secondary to brain lesion and activation at a less optimal muscle length may therefore contribute to functional deficits. Here we used combined ultrasound, electrophysiological and biomechanical measures to determine the optimal muscle fiber length for force production in ankle plantarflexor muscles and compared this to the actual muscle fiber length in the stance phase during gait in 15 persons with CP and 15 healthy control persons. Subjects were seated in a reclining arm chair with the examined foot attached to a computer controlled foot plate. The length of muscle fibers was measured by ultrasound at 3-8 different positions (depending of each individuals range of motion in the ankle joint) of the ankle joint covering the whole range of movement. At each position changes in muscle fiber length, plantarflexor muscle EMG and torque were measured in relation to 1) a maximal voluntary contraction (MVC), 2) a maximal muscle contraction elicited by supramaximal stimulation of the tibial nerve (Mmax) and 3) slow stretch of the muscle (6 deg, 10 deg/s). Persons with CP were found to produce less torque and change in muscle fiber length during MVC and Mmax. Slow stretch also produced smaller changes in muscle fiber length than in healthy persons. The maximal MVC and Mmax were produced at a more plantarflexed position in the persons with CP than in the healthy subjects. This was well correlated to a more plantarflexed position of the joint during the stance phase of gait in the persons with CP. We suggest that structural changes of ankle plantarflexor muscles during development results in an altered force-length relation so that persons with CP have to activate the plantarflexor muscles at a more plantarflexed position in order to generate force most efficiently. This may be an important explanation why children and adults with CP walk on their toes.

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Cerebral Palsy

ICNC-0316: Neurologic complications after neonatal ecmo: A case series

Introduction: Neonatal extracorporeal membrane oxygenation (ECMO) is a supportive intensive care technique for severe cardio - respiratory failure. Several long-term complications are reported, especially developmental delay, hearing loss and learning disabilities. This is the first description of neurologic outcome in Chilean patients. Objective: To describe neurologic complications after neonatal ECMO in a case series in Chilean patients. Method: Descriptive study, we included patients requiring ECMO in neonatal period from 2003 and 2011, which were on follow-up in our hospital protocol. Institutional Review Board approval was obtained. Results: 51 neonatal patients, 60.8% male, mean follow-up 38.4 months (5 – 60), mean gestational age 38.6 weeks (34 – 42), 48/51 required ECMO because of a respiratory disease (31 congenital diaphragmatic hernia). Intracranial hemorrhage was observed in 14.5% (7/48). Bayley evaluation at 4-6 months of age demonstrated developmental delay in 74.4%, whereas 52.5% had delay at 12 – 18 evaluation. At age 3, 14/23 (60.9%) had abnormal neurological examination, whereas this was observed in 8/20 (40%) at age 5. Brainstem auditory evoked potentials were abnormal in 4/17 at discharge and in 5/40 at 12 – 18 months of age, only in 1/8 conductive hearing loss was confirmed by audiometry. Epilepsy was diagnosed in 6/51 (11.8%). Conclusions: First case series of neurologic outcome in Chilean patients, a high percentage of them had complications in several degrees. Introduction: Neonatal extracorporeal membrane oxygenation (ECMO) is a supportive intensive care technique for severe cardio - respiratory failure. Several long-term complications are reported, especially developmental delay, hearing loss and learning disabilities. This is the first description of neurologic outcome in Chilean patients. Objective: To describe neurologic complications after neonatal ECMO in a case series in Chilean patients. Method: Descriptive study, we included patients requiring ECMO in neonatal period from 2003 and 2011, which were on follow-up in our hospital protocol.
protocol. Institutional Review Board approval was obtained. Results: 51 neonatal patients, 60.8% male, mean follow-up 38.4 months (5 – 60), mean gestational age 38.6 weeks (34 – 42), 48/51 required ECMO because of a respiratory disease (31 congenital diaphragmatic hernia). Intracranial hemorrhage was observed in 14.5% (7/48). Bayley evaluation at 4-6 months of age demonstrated developmental delay in 74.4%, whereas 52.5% had delay at 12 – 18 evaluation. At age 3, 14/23 (60.9%) had abnormal neurological examination, whereas this was observed in 8/20 (40%) at age 5. Brainstem auditory evoked potentials were abnormal in 4/17 at discharge and in 5/40 at 12 – 18 months of age, only in 1/8 conductive hearing loss was confirmed by audiometry. Epilepsy was diagnosed in 6/51 (11.8%). Conclusions: First case series of neurologic outcome in Chilean patients, a high percentage of them had complications in several degrees.

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Cerebral Palsy

ICNC-0331: Neonatal EEG Monitoring
Neonatal EEG monitoring is useful to assess the severity of encephalopathy and for determining prognosis. In addition, neonatal seizures cannot be diagnosed without ictal EEG recordings, because electro-clinical dissociation is their most prominent feature. Conventional EEG (cEEG) has been considered as a gold standard of neonatal brain function monitoring. Amplitude-integrated EEG (aEEG) has also been widely used in NICU. The duration and severity of suppressed EEG activities is correlated with neurodevelopmental outcome of the neonates. The patterns of serial cEEG/aEEG changes are different according to the mode of brain injury. Maturationals changes of EEG activities of preterm infants can be assessed by cEEG and delay in cEEG maturation is observed in infants with worse developmental outcome. Although maturational changes are also recognized by aEEG, the relation between aEEG maturation and neurological outcome in preterm infants remains to be determined. The efficacy of antiepileptic treatment for neonatal seizures must be judged on the basis of continuous EEG monitoring. Seizure burden is suggested to correlate with developmental outcome and can be reduced using continuous EEG monitoring by treating both clinical and subclinical seizures.

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Cerebral Palsy

ICNC-0042: Quality of care provided to children with Cerebral Palsy attending Alexandria University Children’s Hospital, Egypt
Introduction: Cerebral palsy is the most common cause of childhood motor disability. High-quality health care depends on collaborations among parents; care providers, and community agencies with ongoing monitoring of the child's health and function. Methods: The study was conducted at Alexandria University Children’s Hospital, Egypt. Data collection was done through two separate checklists that have been distributed to 15 pediatric neurology residents and 4 senior staff of the hospital. The checklists were structured based on “Standards for integrated care pathways for child and adolescent mental health services”. Also, the medical records of 84 children with cerebral palsy regularly attending the outpatient clinics were reviewed. Face to face interview of caregivers of 88 children with cerebral palsy using a self-structured client satisfaction questionnaire. Results: Most of the standards were partially met and some standards were not met at all including the presence of efficient recording system of diagnostic and assessment information of children with CP. 89.3% of the caregivers reported their dissatisfaction regarding absence of a system to help them gain benefits from different community agencies. 86.9% were not satisfied with absence of multidisciplinary assessment. Also, 86.9% reported that the planned outcomes were not achieved. Conclusions: The present study made it possible to identify areas for improvement in the services. These areas included: needs assessment and needs based plan of care, system delivery of care, information management and education and training of care providers.

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Cerebral Palsy

ICNC-0873: Mapping of child and adolescent mental health services in Alexandria, Egypt
Introduction: Mapping of health services is a powerful tool for decision makers, health care providers and the users of the services. The importance of providing mental health services has lead to a rise in the number and types of services provided. Mapping of child and adolescent mental health services helps decision makers decide on type and location of new services, as it highlights areas of deficiency, it may also help in the reallocation of resources to better meet the
needs of the target population. Methods: Data collection was done through a structured interview with 15 selected child and adolescent mental health care providers; data was also collected from governmental records. Google maps were used to map the different services on one map. Results: 96 locations providing child and adolescent mental health services were found with 7 types of providers; 4 of which are governmental and 3 private and Nongovernmental. Inpatient psychiatric beds for children and adolescents are clearly deficient and provided only at one location and are not exclusively for children and adolescents. There is duplication of some services by the same provider and there is clear deficiency in some services by area or by type. Conclusions: Geography is a factor to be considered while providing and re-allocating child and adolescent mental health services. Also, Social networks may provide an easy practical way for mapping services.

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Cerebral Palsy
ICNC-0043: Understanding the etiology of ataxic and unclassifiable types of Cerebral Palsy
Introduction: The progress achieved in understanding the etiopathogenesis of spastic and dyskinetic Cerebral Palsy (CP) is not shared by the less common types of ataxic or unclassifiable CP. The purpose of this study is to report on identified etiologies in patients who met diagnostic criteria for these types of CP. Methods: Upon review of data collected in a hospital-based CP registry, we identified 17/288 (5.9%) ataxic and 4/288 (1.3%) unclassifiable cases. Clinical data, neuro-imaging, metabolic and genetic studies were systematically reviewed. Results: 14/17 patients with ataxic CP (82.3%) had post-neonatal brain MRIs and 1/17, post-neonatal brain CT, (average age, 75 months), reporting normal pattern in 5/17 (29.4%); maldevelopments in 2/17 (11.7%), predominant white matter injury in 2/17, miscellaneous changes in 6/17 (35.2%). Genetic abnormalities were documented in 4/17 (23.5%) [2=Angelman syndrome, 1 = EAST syndrome (KCNJ10 mutation), 1= Dravet-like phenotype (de novo GABRA1 mutation)]; Angelman-like syndrome was clinically documented in another patient. In the unclassifiable group; non-progressive hypotonia, without ataxia, predominated clinically; 3/4 had a postneonatal brain MRI; average age of 32 months, reporting normal pattern in 2/4 (50%); predominant grey matter injury in 1. Genetic abnormalities were documented in 2/4; patients (50%); [3p25.3 duplication = 1, MCT8 mutation (Alan-Herndon-Dudley syndrome) =1]. Conclusion: Normal neuro-imaging was frequently present in ataxic and unclassifiable CP patients. Genetic studies were particularly helpful in the diagnosis of specific syndromes or de novo mutations, suggesting that these investigations could be relevant to all CP types, particularly those of obscure etiology.

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Cerebral Palsy
ICNC-0045: Assessment of attitudes among parents of children with cerebral palsy about provided health care
The goal behind this survey is to answer the question whether there is a gap between the rights and benefits of people with cerebral palsy given by law and their experiences. The attitudes among parents of children with cerebral palsy regarding health management of their children were assessed with the aim to provide appropriate and better health care for their children. A structured questionnaire was created covering health, social and welfare domains. The answers were given on a Likert scale ranging from completely satisfied to completely unsatisfied. Seventy (70) parents of children with cerebral palsy were included. The mean age of children was 7.7 years (4 to 11 years). The additional diagnostic procedures were offered to 40% of children between 6-12 months of age. Only 11% of the parents were satisfied with diagnostic procedures provided. When asked about the waiting list for neuropsychiatrists, the majority of parents were partly or completely unsatisfied, as well as with long waiting lists for physio/speech therapists. All parents were not satisfied (completely or partially) with accessibility to information regarding their children’s social and welfare rights and health medico-legal regulations. The obtained results show a great dissatisfaction among parents with children suffering from cerebral palsy regarding provided health care. Our study suggests that these parents need more help in order to improve the welfare of their families. These data may contribute to a better understanding of specific needs and help the future planning of health management in children with cerebral palsy.

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Cerebral Palsy

ICNC-0318: Incidence and outcome of children with prenatally diagnosed central nervous system malformations

The aim was to study the incidence and outcome of prenatally detected central nervous system congenital malformations (CNS-CM). The data was collected retrospectively and partially prospectively during the last decade (2006-2015) by the European registry for monitoring congenital anomalies protocol. During the study period there were 29,886 births with a total of 53 fetuses with isolated or multiple CNS-CM, which makes a total of 0.18% births. There were 57 malformations. The most common malformations were defects of the neural tube 26/57 (46%), hydrocephalus 10/57 (18%), agenesis of the corpus callosum 5/57 (9%), holoprosencephaly 4/57 (7%), Dandy-Walker malformation 4/57 (7%), and other malformations 8/57 (14%). Medical abortions due to CNS-CM were performed in 31 fetuses (58.5%) and there were 18 (34%) live births. Four children were stillborn. The long-term outcome was evaluated in 16 of the 18 live births (89%), while the data for two children was unknown (11%). The average length of the follow-up was 5.3 years (1-9 years). None of the infants died during the perinatal period but two died within a period of three months. A favourable outcome is considered, by age appropriate, normal mental/motor development and adverse outcome slow mental/motor development with dependence on the parents in daily activities. The favourable outcome have 7/16 (44%) and the adverse long-term outcome have 9/16 (56%) children. These results indicate a good prenatal screening in detecting CNS-CM, but the long-term outcome was not favourable in the majority of children.

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Cerebral Palsy

ICNC-0874: Early rehabilitation in children with Hypoxic brain injury: An outcome study

Objectives: Children with hypoxic brain injuries have been considered to make poorer recovery than children with traumatic brain injuries. We aim to highlight that early rehabilitation may contribute to better outcomes than widely appreciated. Methods: Retrospective study. Setting: two hospitals in the UK with paediatric intensive care units (ICU) and neurorehabilitation wards. Inclusion criteria: children under 16 years; admitted to ICU for ventilation; encephalopathy following cardiorespiratory arrest January 2010 to December 2014; survived to discharge from ICU. Exclusion criteria: children under 1 year of age. Results: 16 children (8 male) were identified. Mean age: 99 months.

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Cerebral Palsy

ICNC-0319: Novel GLRB gene mutation in a Saudi baby with Hyperekplexia

Hyperekplexia is considered a rare, autosomal dominant neurological disorder that presents early in life with: Hypertonicity, Exaggerated startle response and Life threatening neonatal apnea. It can be caused by mutation in : alpha-1 subunit (GLRA1) on ch 5q32. Beta subunit (GLRB) gene on ch 4q31 of the “inhibitory glycinereceptor”, GLYT2 gene (SLC6A5) on ch 11p15 which encodes a “presynaptic glycine transporter”. GLRB gene mutations have been previously reported; about 113 mutations are registered within the exome variant server. Most of them are insignificant though a significant proportion due to missense mutation were associated with probably damaging effects. In our case we report a new gene mutation that enables confirmation of laboratory diagnosis. The latter will be a determining factor of counselling and long term prognosis and treatment. Raising awareness of the presence of this treatable disease will prevent unnecessary exposure to antiepileptic medications, prevent life threatening apneas and improve long term outcome.
Cerebral Palsy

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Cerebral Palsy
ICNC-0875: Social communication difficulties in children with severe traumatic brain injuries and early intervention benefits

Objectives: Children with severe traumatic brain injuries (sTBI) often have behavioural and/or communication impairments that result in isolation - suffering from unpopularity, rejection by peers, and lack of friendships. Using modern and attractive rehabilitation methods is important in paediatric social skills remediation. Aim of the pilot study was to identify the extent of social deficits and communication strategies in children with sTBI. Methods: 2 patients with sTBI (4 months post-injury, boy aged 12yrs., girl 10yrs.) and 2 healthy age- and sex-matched controls participated. Social Perception tasks from NEPSY-II and Theory of Mind (ToM) tasks were used to estimate social perception deficit. For comparison of two pairs' social cooperation skills, NoProblem! application (short vignettes and role-play in different social contexts) on DiamondTouch multi-user table was used. Results: We found impaired affect recognition and ToM skills in patients. Specifically, impaired understanding of intentional lying and sarcasm was revealed. Pairs' behavioural observations showed that patients lacked conversation initiation and spontaneous conversation. Less reciprocal questions and short/improper (off-topic) answers; excessive talk about own views and intentions. Less concordance with other child's answers. Impaired emotion regulation (improper laugh or hypomimia). Less nonverbal communication (avoidance of eye-contact). More mistakes in resolving social situations. Less or no examples for conversation stages: how to initiate, maintain, switch topics and end.Conclusions: It is important to assess children’s skills in social contexts. We found deficits in affect recognition, Theory of Mind, conversation and cooperation skills. Solution is developing social skills rehabilitation designs through multi-user technologies, role-play and therapist guidance.

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Cerebral Palsy
ICNC-0876: Concomitant communication and cognitive problems in two children: girl and boy with severe brain trauma

Objectives: Children with severe traumatic brain injuries (sTBI) may have cognitive and communication impairments. Problems with executive functions could exist already pre-injury. Aim of this pilot study was to identify and compare pre- and post-injury social and behavioural deficits in children with sTBI. Methods: 2 patients with sTBI (4 months post-injury) and 2 healthy controls (boys:12yrs.; girls:10yrs.) participated. Children’s parents completed questionnaires: attention, executive functioning behaviour (BRIEF-P), Social Cognition Questionnaire and Social Skills Rating System. Both pre-and post-injury states were assessed. Results: We found pre-trauma problems in female patient compared to healthy peer: lower attention (score 35 compared to 52), executive functions (177/95), social perception (171/207) and social skills (102/115). No noticeable difference existed between boys pre-injury. Post-injury, both children with sTBI had lower scores in each function compared to pre-injury performance. Attention was 5 points lower post-injury for girl and 13 for boy. Both had increased difficulties with executive behaviour: problem scores higher by 30 points for girl and 48 for boy (207/177 and 158/110, respectively). Social perception worsened 28 points for girl (143/171) and 46 for boy (148/194). Also, performance in social skills lowered 81 points for girl (30/111) and 76 for boy (36/112). Conclusions: Children with sTBI may have pre-existing problems with executive function and social communication. Still, we found noticeably increased problems with executive behaviour, social perception and social skills 4 months post-injury. The girl had lower functions already pre-injury, but the boy had more severe post-injury impairment. Children with sTBI need social skills rehabilitation.

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Cerebral Palsy
ICNC-0320: Clinical factors that predict optimal neurodevelopment in very preterm infants

Objective: Determine neonatal clinical factors that predict above-average neurodevelopmental outcomes in preterm infants at 18 months corrected age. Background: Preterm infants are at greater risk of poor neurodevelopmental outcomes. What leads some infants to perform above average on neurodevelopmental assessment is unknown.
Methods: 232 preterm infants (24-32 weeks gestation) were recruited prospectively from 2006 to 2013 at a tertiary-level NICU. Clinical risk factors were recorded by chart review. Infants underwent MRI early in life and at term-equivalent age. A single neuroradiologist scored brain abnormalities. 180 children (median gestation 29 weeks) were assessed at 18 months corrected age with Bayley-III. 8 infants died before 18 months. Optimal neurodevelopment was defined as scores >1 SD above the mean (>115) for each of the cognitive, language and motor domains. Results: 48, 26 and 11 children scored >115 in the cognitive, language and motor domains respectively. 5 children scored >115 in all 3 domains. In children born >29 weeks, risk factors did not differ significantly between children who scored above or below 115 using univariate analysis. The 23 infants <29 weeks gestation who thrived cognitively had less patent ductus arteriosus (P=0.004), positive culture infection (P=0.01) and chronic lung disease (P=0.045). They also spent fewer days on mechanical ventilation (P=0.02) and were exposed to less morphine postnatally (P=0.001). There were no significant predictors for language, but higher maternal education was associated with above-average motor skills (P=0.02).

Conclusions: Avoiding patent ductus arteriosus, infection and/or chronic lung disease appears to be beneficial to preterm infants <29 weeks.

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Cerebral Palsy

ICNC-0322: The phenotypic and genetic spectrum of SCN cluster deletions

Introduction
The SCN cluster, located at the 2q24.3 region, contains four genes coding for a voltage gated sodium channel (SCN3A, SCN2A, SCN1A, SCN9A). Deletions at this region, especially those involving SCN1A, cause a severe epileptic encephalopathy. The aim of this study is to describe the clinical picture and genotype-phenotype correlation of patients with an SCN cluster deletion. Method
Patients with a deletion of ≥1 genes of the SCN cluster were recruited from different European centers. Borders of the deletion were defined by an array-CGH. Results
Sixteen patients were included, with a de novo deletion averaging a length of 7.276.738 bp (ranging from 1.622.054 – 14.181.695 bp). Two patients were mosaic. Twelve patients had a deletion encompassing the whole SCN cluster. SCN2A was included in the deletion in all patients. SCN1A in 14/16. All patients developed epilepsy. The median time of onset was 4 months (range from 2m till 14years). Preservation of SCN1A and mosaicism predicted a later epilepsy onset but not a better outcome. A, SCN2A, SCN1A, SCN9A). Deletions at this region, especially those involving SCN1A, cause a severe

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Cerebral Palsy

ICNC-0323: Clinical presentation and spectrum of neuro-imaging findings in newborns with incontinentia pigmenti

Background: Incontinentia Pigmenti (IP) is a rare X-linked multisystem disorder with well described and pathognomonic skin manifestations. Neurological manifestations are found in 30% of IP patients and are a major cause of morbidity and mortality though the pathogenesis of the central nervous system (CNS) lesions in IP is still controversial. Aim: To report on the neurological presentation and neuroimaging findings in newborn infants with incontinentia pigmenti (IP).

Methods: The clinical and neurological course including neuroimaging and follow-up data of eight newborn infants with the neurological phenotype of IP, were retrospectively reviewed. Results: While the clinical picture was polymorphic, including mild and fully developed typical skin lesions seen at or soon after birth, the neurological manifestations were defined as encephalopathic and comprised lethargy and seizures in all but one of the infants. Magnetic resonance imaging (MRI) abnormalities were predominantly noted in the white matter. Diffusion-weighted imaging (DWI) was obtained during the acute phase in 7 of the 8 infants, showing restricted diffusion in the deep and subcortical white matter, corpus callosum, basal ganglia, thalami, cerebellum and cerebral peduncles in one infant. Susceptibility weighted imaging (SWI), performed in 5 infants, showed a variable amount of signal loss in lesions considered haemorrhagic on conventional MRI. Neurodevelopmental outcome correlated with the degree of neuroimaging abnormalities. Conclusions: In order to assess the extent of CNS involvement, MRI is recommended in the clinical evaluation of infants with IP. The combination of DWI and SWI allows identification and distinction of haemorrhagic and ischaemic lesions.

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Cerebral Palsy

ICNC-0047: Ambulation status and activities of daily living in non-spastic Cerebral Palsy: 10-year follow-up

Cerebral Palsy (CP) subtype is an important determinant of Ambulation Status (AS) and Activities of Daily Living (ADLs) with Spastic Unilateral and Diplegic Bilateral CP types, achieving considerable independence. Purpose: To longitudinally examine AS and ADLs in predominantly non-spastic CP patients from a hospital-based CP registry. Methods: Review of longitudinal data on AS and ADLs in 43 patients, 5-20 year-old, with Dyskinetic, Ataxic and Unclassifiable CP types. Inclusion criteria included yearly F/U and systematic CP management. AS was scored at 10-year F/U on a 4-point scale (0 = non ambulant to 4 = community ambulant); ADLs, on a 5-point scale (0 = no ADLs to 5 = fully independent). Results: Two subgroups comprised the Dyskinetic group: a. Mainly Dyskinetic: N = 11; GMFCS level II=1, III=5, IV=4, V=1. At 10 year F/U, none was community ambulant, 2 were mostly independent in ADLs. b. Mixed Dyskinetic-Spastic: N = 14; GMFCS level I=4, II=2, IV=5, V=3. At 10 year F/U, 3=community ambulant, 3=mostly independent in ADLs. The Ataxic group: N = 16; GMFCS levels I=1, II=7, III=6, IV=2. At 10 year F/U, 6=community ambulant, 3=mostly independent in ADLs. The Unclassifiable group comprised of 2 hypotonic children, GMFCS level II=1, V=1; of them, one was community ambulant with restrictions and had some ADLs. In total, 10-year F/U was available in 36/43 patients; 10 of them were community ambulant (27.7%) and 8 (22.2%), were mostly independent in ADLs. Conclusion: This case series of predominantly non-spastic CP, at 10 years F/U, demonstrated limited AS and functional abilities, despite provided treatment. Only 27.7% were community ambulant and 22.2% mostly independent in ADLs.

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Cerebral Palsy
ICNC-0048: Risk factors for Cerebral Palsy children in a Rural Hospital of Central India

Introduction: Cerebral palsy (CP) is a chronic motor disorder resulting from a non-progressive static insult to the developing brain, but its etiology is poorly understood. The aim was to evaluate the magnitude of various modifiable and non-modifiable risk factors and associated types of cerebral palsy. Methods: A hospital based observational study was conducted in the Deptt. of Pediatrics, JNMC, Sawangi Meghe, Wardha, Maharashtra during 2012 and 2014. Data was collected through an interviewed questionnaire from the parents of cerebral palsy children. Detailed history regarding risk factors including antenatal, natal and postnatal events was enquired. Results: The mean age of the cerebral palsy children was 7.7±6.8 years. Out of 62 cases, 51 (83%) had spastic type of cerebral palsy, which was further classified as diplegia 25 (49%), quadriplegia 22 (43%) and hemiplegia 4 (8%). Birth asphyxia was found to be present in 12 (20%) of cases and low birth weight accounted for 14 (22%) of cases. Major risk factors identified were home and assisted delivery 42 (67%), consanguinity 28 (45%), infections 19 (30%) and lack of antenatal care 24 (38%). Conclusion: The commonest type of CP was spastic diplegia. Most common risk factors for cerebral palsy were home delivery, consanguinity and infections during pregnancy. Adequate prevention targeting these factors will reduce the incidence of cerebral palsy among children.

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Cerebral Palsy
ICNC-0049: Long term neurodevelopmental outcomes of very low birth weight infants

Introduction: We aimed to evaluate the long term neurodevelopmental outcome and associated risk factors in very low birth weight (VLBW) infants (birth weight <1500g or gestational age <32 weeks). Methods: Very low birth weight infants (n=169) who were hospitalized at neonatal intensive care unit between years 2000-2010 were gathered for this study. Sixty-six cases were recruited and evaluated by neurological examination, cranial MRI and cognitive tests (for children ≤6 years old: Denver II Developmental Screening test (DDST) and for children >6 years WISC-R was performed). Results: Mean age of the patients, birth weight and gestational age were 46.14±19.31 months, 1255±254.2 g and 29.5±1.77 weeks, respectively. Neurological abnormalities were seen in 25.8 % (n=17) of the cases, 9 of them were diagnosed with cerebral palsy. According to DDST 63.6% of the cases showed impairments in their age norms, but all WISC-R results (n=9) were normal. In cranial MRI, lesions in white matter, cortical/subcortical, basal ganglia/thalamus area and other abnormalities were 18.2%, 1.5%, 1.5% and 4.6% respectively. Identified prenatal risk factors for abnormal outcome were history of invitro fertilization, polyhydroamniosis, placenta previa, choioamnionitis, ablatio placenta, urinary tract infection and passive smoking (p<0.05). As neonatal risk factors advanced stage (Stage 3-4) retinopathy of prematurity (ROP), intraventricular hemorrhage (IVH) and periventricular leucomalacia (PVL) were observed (p<0.05). Conclusion: In this study, placentae previa, advanced stage PVL, IVH and ROP are predictors for poor neurodevelopmental outcome of VLBW infants. Key words: very low birth weight, neurodevelopmental outcome cerebral palsy.

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Cerebral Palsy
ICNC-0877: Efficacy of early physio therapy intervention in preterm infant motor development

INTRODUCTION: The increased survival of progressively more premature newborn infants has resulted in a significant number of preterm infants who grow up with neurocognitive abnormalities. Currently, periventricular leukomalacia (PVL) is the principal neurological problem affecting children born extremely premature. Approximately 25% of newborn infants with birth weights below 1,500 g who survive to discharge exhibit moderate to severe permanent motor deficits, such as spastic diplegic. AIM: Report a motor evolution of a premature child with PVL. PARTICIPANT AND METHODS: A single-case study of a male child of 11m chronological age and 08m corrected age, premature, with spastic diplegic referred to the physical therapy clinic of FACULDADE METROCAMPA, a college located in Campinas (São Paulo/Brazil). The physical therapy session begins with a bucket bath (tummy tub) aimed relaxation and adequacy of postural tone. At following the child underwent a neuromotor intervention and at the end of therapy put a functional tape. In the first six weeks put the functional tape in the hands bilaterally by the technical “In Glove” in order to stimulate the sensation of the hands. In the following four weeks was modified the technique for positioning of the thumb in the functional position. 20 sessions of physical therapy were requested up to date. RESULTS: The child stops crying during the sessions establishing a closer contact with the therapist, when the child is relaxed improve the motor globally. In the first weeks of applying the functional tape the child began opening the hands and after the modification of the technique started the pincer movement that allows to pick up objects. The hands to knees; sitting with propped arms and supported standing
with head in line with body. CONCLUSION: These results showed that physiotherapy association with other technics in preterm infants produced greater functionality. This information is of value to physical therapists involved in evaluation and therapeutic intervention programs for high risk infants.

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Cerebral Palsy

ICNC-0878: The use of massage therapy in premature babies of recovery in ICU Neonatal

Abstract: Premature babies have a higher risk of developing social-emotional, behavioral and motor issues, long-term growth, in addition to development and health problems. For over two decades, research has shown that massaging stable premature babies that reside in the neonatal intensive care unit (NICU), leads to greater weight gain and shorter hospital stay. Therapeutic massage has been referred to as an important resource in the care of premature newborns (PN), having a positive impact on the physiological aspects necessary for survival. Objective: This study aimed to investigate the effects of massage therapy in PNs who are in the NICU. Method: It is a traditional review of the literature of papers from the last ten years in PubMed, Medline and PEDro database, using variable interest massage, NICU and prematurity. Results: According to predetermined criteria, eight articles, published since 2009, were contemplated because of the demonstrated effects of massage therapy. Conclusion: A properly applied massage therapy responds in an effective manner, reflecting on the PN’s growth and development, O₂ saturation, immune system, food intolerance, being able to be used as part of care in the NICU. Key words: Neonatal Intensive Care Unit, Premature, Massage Therapy.

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Cerebral Palsy

ICNC-0879: Children’s motor development variability in different environmental settings

Abstract: Objectives: To evaluate, identify possible motor delays and compare the motor development of children in different environmental settings (nurseries and shelters). Methods: Through the use of the Alberta Infant Motor Scale (AIMS) were assessed children from schools and shelters of Campinas, Hortolandia and Braganca Paulista in the state of Sao Paulo (Brazil). Results: 36 children were assessed in different environmental settings: child day care centers (16), orphanages (13) and nurseries (07). Children had mean age of 11.69 (±5.24) months by the time of motor evaluation. Motor delay was observed in 11.1% of the children. We found no significant difference for gender considering the AIMS score (p=0.746). Children attending the day care centers had better motor development when compared to children from orphanages and nurseries (p<0.001). Nevertheless, these day care center children were also the oldest (p<0.001). We also found significant difference when comparing the percentiles of children according to Canadian and Brazilian normative samples (p=0.001). Conclusions: The AIMS when used to evaluate the motor development can be successful, but further studies are needed, with restricted age and other rating scales, in addition to AIMS. The Brazilian’s own normative is important to assess children in Brazil, to the detriment of Canadian normative sample. Key Words: Child Development; Child Day Care Centers; Orphanages; Nurseries; Alberta Infant Motor Scale (AIMS).

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Cerebral Palsy

ICNC-0324: Autism Spectrum Disorder in a population of preterm infants: effects of gestational age, perinatal factors and birth weight

Background: Prematurity is a main risk factor for perinatal morbidity. A still growing population of survivors keeps on living without major motor impairment but showing many difficulties in emotional and social/relational intelligence. Objective: to describe the effects of perinatal factors, gestational age (GA) and birth weight (BW) on brain development and behavioral problems in a population of ex-early preterm children diagnosed for Autism Spectrum Disorder (ASD). Design/Methods: We retrospectively reviewed data about preterm infants born in our Children Hospital from January 2012 to April 2014. Maternal age at conception, obstetrical risk factors, delivery, GA, Apgar, BW, head circumference and days of NICU were collected. Cranial ultrasound (cUS) during hospitalization and brain MRI imaging at term of corrected age (TEA), to screen detectable anatomical brain lesions, were performed. All patients have been followed-up with pediatric, neurological and neurodevelopmental assessment (with GMDS-ER) for a period ranging from 2 to 4 years. Autism Diagnostic Interview Revised (ADI-R) was proposed to parents when ASD was suspected and, when confirmed, further neuropsychological assessments were planned. Results: 161 VLBW preterm babies (with a GA ranging from 26 to 33 weeks) were screened; 42% (68/161) were ELBW. No major anatomical brain lesions at cUS scans or MRI imaging
were found. Nearly 8% (12/161) had a diagnosis of some grade of ASD; prevalence of ASD in ELBW was of 4.5% (3/68). Of interest, preterm babies born with GA between 28 and 33 weeks were the striking majority, with a prevalence of nearly 90% (11/12), suggesting a potential different vulnerability pattern in this population. Conclusions: third trimester of intrauterine life plays an important role in brain development. Even if mortality and motor morbidity in premature babies between 28 and 32 weeks of GA has notably decreased, behavioral problems are a relevant matter of concern in this population. BW between 1000g and 1500g and intermediate-early GA (28-33) could be related also to ASD. Efforts should be taken, inescapably, to better understand premature birth and improve preterm care. References: - Kihara H et al. Early standard development assessment characteristics in very low birth weight infants later classified with autism spectrum disorder. Early Hum Dev. 2015 Jun;91(6):357-9 - Guy A et al. Infants born late/moderately preterm are at increased risk for a positive autism screen at 2 years of age. J Pediatr. 2015 Feb;166(2):269-75.e3 - Lampi KM. Risk of autism spectrum disorders in low birth weight and small for gestational age infants. J Pediatr. 2012 Nov;161(5):830-6

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Cerebral Palsy
ICNC-0050: Neurodevelopmental outcome in patients with typical imaging features of injury as a result of neonatal Hypoglycemia

BACKGROUND: Previous reports described a pattern of hypoglycemia-induced damage predominantly affecting the occipital lobes and posterior parieto-temporal regions. Although associated factors are important with regard to brain injury due to neonatal hypoglycemia, they are not fully understood. This study elaborates on neurological outcomes in children who have experienced neonatal hypoglycemia. METHODS: We retrospectively reviewed the medical records of outpatients who were followed up in our pediatric neurology clinic at a tertiary center from 2007 to 2014. Patients (n=42) with predominately occipital lesions on magnetic resonance imaging (MRI) with the typical pattern of neonatal hypoglycemia were evaluated. Patients with documented hypoglycemia (n=21) were included in this study. RESULTS: All patients had risk factors that were associated with brain hypoglycemia. Eleven patients experienced seizures in the neonatal period. Eighteen patients (85.7%) developed epilepsy during the follow-up. Nine patients (42.9%) manifested microcephaly. Seven patients (33.3%) were diagnosed with cerebral palsy. Of 20 patients with psychometric evaluation, 13 had some degree of cognitive impairment or global developmental delay. Thirteen patients (61.9%) had visual impairment with strabismus and 10 patients (47.6%) had refractory error. The VEP results of all patients evaluated (n=18) were abnormal. CONCLUSION: Neonatal hypoglycemia is still an important health care problem. We believe that most cases of neonatal hypoglycemia are not documented and treated appropriately. Patients at risk and patients with symptoms of hypoglycemia should be vigorously screened.

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Cerebral Palsy
ICNC-0325: Risk factors for neurodevelopmental outcome in infants with neonatal seizures

Prospective study was performed on a cohort of 100 patients who had clinically manifested seizures during the neonatal period. Initial assessment was performed during their hospitalization at Neonatal Intensive Care Unit, while further follow-up was done through regular visits to outpatient facilities of Department of Child Neurology, Pediatric Hospital. Necessity for : resuscitation measures (54%), perinatal asphyxia (52%), mechanical ventilation (54%) - were considered and analyzed as risk factors. Developmental assessment (epilepsy, motoric and neuropsychological assessment ) was performed at the age of one year in patients who had survived the end point of the follow-up. Children who had to be resuscitated and those who needed mechanical ventilation as well as patients with verified asphyxia had a greater chance for establishment the diagnosis of epilepsy and were marked with low scores on motoric assessment (Alberta Infant motoric Scale). In addition, this group of children showed greater discordance with the results expected for age in neuropsychological assessment. Analyzing correlation of examined variables of outcome: epilepsy, motoric assessment and neuropsychological assessment with the variables that correspond to risk factors for neonatal morbidity (resuscitation, mechanical ventilation, asphyxia), the highest correlation was found with the variable of perinatal asphyxia (R=0.39, p<0.01). Prediction model of motoric assessment as a measure of dominant neurodevelopmental disorder showed that asphyxia could predict children with Alberta score below 10th percentile with statistically significant confidence. Children without diagnosis of asphyxia had sevenfold greater chance to have normal motor development.

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Cerebral Palsy

ICNC-0326: Exploring neonatal brain networks using EEG based minimum spanning tree analysis

Background: With age, small-world networks of children’s brains change from random to more ordered configurations. Little is known about the development of these networks in the earliest stages after birth. A new method, suitable to compare network configurations under different conditions, is minimum spanning tree (MST) analysis; representing the most important routes within networks. Aim: To analyse functional brain networks in neonates using MST analysis and compare network configurations of preterm and term born neonates. Methods: MST analysis was used to assess brain network configurations using electroencephalograms from 6 preterm and 22 term born infants. The phase lag index (PLI) was calculated as a measure of overall connectivity. MSTs were constructed, in four frequency bands and several parameters were calculated to characterize network organization. Results: Compared to term born, preterm born infants showed a higher PLI in the delta (p<0.01), theta (p=0.01) and alpha (p=0.03) bands and a higher MST leaf number (p=0.02) and tree hierarchy (p=0.01) in the theta band and a higher MST betweennes centrality (p=0.02) in the alpha band. Conclusion: The differences found in the MST parameters indicate a shift toward more decentralized network configurations in the term born infants, together with a lower overall connectivity. However, cautious interpretation is needed because of the small patient groups and a cross-sectional explorative design. MST seems to be a valuable method to assess functional brain networks, even in these very young infants. A prospective study is being prepared to further investigate brain network development in preterm neonates using MST analysis.

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Cerebral Palsy

ICNC-0051: A case series of patients with cerebral palsy, in a referral pediatric hospital in Colombia.

Background: In Colombia, like in other countries in Latin America, prevalence, demographic, etiological and clinical characteristics of cerebral palsy (CP) are unknown; this hampers the assessment, follow-up and treatment of patients. The study wanted to determine those variables in a population of children with CP, from a referral pediatric hospital. Methods: The study included 112 patients, identified from the medical records of the Rehabilitation clinic from May to October 2014; inclusion criteria were defined according to the American Academy of Neurology practice parameters for CP. Children had a similar male:female ratio, 77% belonged to the public health insurance, suggesting a less favorable family income. 42% of patients were firstborn, 11% of mothers had a previous disease including diabetes, heart disease, hypertension, thyroid disease, thrombophilia, renal failure, mental retardation and substance abuse. Infection during pregnancy appeared in 20.5% of cases, preeclampsia in 10.7%, premature rupture of membranes and hypertension, thyroid disease, thrombophilia, renal failure, mental retardation and substance abuse. Infection during pregnancy appeared in 20.5% of cases, preeclampsia in 10.7%, premature rupture of membranes and chorioamnionitis in 6%. About perinatal conditions, prematurity was found in 55.3% of patients and asphyxia in 9.5%. The most common subtype of cerebral palsy was spastic, and the quadriparesis, the topographic distribution in 60.7% of patients. More than 20% of children didn’t have the Gross Motor scale. Conclusions: The characteristics of children with CP were similar to those described in the literature; prevalence and prospective studies for a formal study of the social impact, etiologic associations, clinic and outcome are necessary.

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Cerebral Palsy

ICNC-0328: Brain imaging and genetic heterogeneity in congenital microcephaly

Introduction: Congenital microcephaly of genetic origin can occur without features of any syndrome. Our aim is to present the brain imaging and genetic diversity in patients with non-syndromic congenital microcephaly. Methods: Ten subjects with severe congenital microcephaly were selected from a cohort of patients. Environmental factors were excluded. Brain MRI was performed by conventional techniques. Array comparative genome hybridization, next generation and Sanger sequencing have been carried out or are in progress. Results: Simplified gyral pattern was found in a patient with trisomy 10 mosaicism. ASPM mutation was associated with bilateral diffuse polymicrogyria, and mutation in WDR62 was identified in a child with bilateral pachygyria. TUBA1A mutation caused agyria-pachygyria, partial corpus callosum agenesis and vermian hypoplasia. Pontocerebellar hypoplasia and simplified gyral pattern were observed in two patients with CASK mutations. The genetic cause is still awaited in a patient with hemispheric asymmetry and unilateral band-like grey matter formation, and another with frontal-parietal polymicrogyria. Genetic cause is likely in further two patients; one who has unilateral hemispheric dysplasia and another one with enlarged extra axial space and smooth brain surface. Discussion: Our findings confirm the highly heterogeneous nature of congenital microcephaly. Genotype-phenotype correlation is very poor, therefore methods testing the whole genome are recommended. Trisomy 10 mosaicism in
association with simplified gyral pattern needs to be further studied. ASPM, WDR62 and TUBA1A proteins interact in cell cycle dynamics as spindle-associated proteins. Nuclear interactions of CASK protein are required for normal brain development. Genetic studies are still under way in four patients.

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Cerebral Palsy

ICNC-0329: Modeling the neural impact of maternal immune activation using human induced pluripotent stem cells

Introduction Maternal infections during pregnancy are well known to increase risk of neurodevelopmental disorders in newborns. Previously, a number of animal studies have shown that maternal cytokine surges, rather than specific pathogens, induce changes in fetal brain development. Among them, prenatal exposure to interleukin-6 (IL-6) are reported to be associated with behavioral and neuropathological abnormalities, though their relevance is unclear in humans. Methods and results We generated neural aggregates from human induced pluripotent stem cells (hiPSCs) using the serum free floating culture of embryoid bodies-like aggregates with quick reaggregation (SFEBq) method, and cultured them in suspension for 50 days. Expression of neural stem cell marker (PAX6), neuronal markers (TUBB3, MAP2) and astrocyte marker (GFAP) suggested that these aggregates mimic in vivo neurogenesis. By exposing these neural aggregates to IL-6 for 24 hours, we examined the early and late effect of IL-6 on neurogenesis. For the early effect, quantitative RT-PCR and western blot analysis revealed that the expression of PAX6 and phospho-STAT3 in neural aggregates cultured with IL-6 were significantly higher than those cultured without IL-6. For the late effect, GFAP expression level was up-regulated after 10 days from IL-6 exposure. Discussion Our results suggest that IL-6 directly promotes the proliferation of neural stem cells by activating JAK-STAT signal pathway which may lead to induce astrogliogenesis. Further histological analyses are needed to clarify the relevance between neural stem cell proliferation and astrogliogenesis.

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Epilepsy

ICNC-0054: Presentation the presence of Autism, Maladaptive Behaviors, and Cognitive Deficits among children with Epilepsy

Introduction: Recognizing social cognitive/behavioral comorbidities among children with epilepsy is important in comprehensive management. This study aims at identifying the frequency and risk factors for autism spectrum disorder (ASD), social behavioral deficits and cognitive deficits among these children. Methods: Prospective study of children with active epilepsy at the pediatric neurology clinic ages 2.5 to 18 years. The social responsive scale (SRS) was administered, demographic data and details of the epilepsy were collected. Parents were asked whether their children had difficulties with academic performance/school attendance. All children are undergoing cognitive assessment utilizing the Wechsler intelligence scale, or the Vineland adaptive behavior scale, and will be undergoing neuropsychiatric assessment for ASD/other behavioral comorbidities by a pediatric psychiatrist blinded for SRS results. Results: Sixty four children have been enrolled so far. Preliminary results show that 14 children (22 %) have moderate/severe deficiencies in reciprocal social behavior typical for ASD on the SRS. Eight of them had not been previously diagnosed with ASD. Twenty five children (39%) had intellectual disability. No statistical evidence was found for the relationship between intellectual disability and increased risk for ASD. Children with high risk for ASD showed significantly higher T scores in DSM compatible subscales for impairment in social communication/interaction and repetitive/restrictive behaviors, (p<0.05). Conclusion: A significant number of children with epilepsy have severe deficiencies in social behavior typical for ASD. A significant number also have intellectual disabilities. The patterns of social impairments and various risk factors will be further analyzed with completion of the study.

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Epilepsy

ICNC-0055: Autonomic seizure experience in a video EEG unit

Introduction: Autonomic seizure can be described as an autonomic disfunction, of any type, at seizure onset, or a seizure in which autonomic manifestations are clinically prominent and distinguished from secondary effects on the autonomic system by the presence of other seizure symptoms. Methods: This study was conducted from January 2011 to December 2015 at Gazi University School of Medicine Department of Pediatric Neurology – Video EEG Unit. In this period 292 patients was admitted to us to separated seizure-pseudoseizure or presurgical evaluation. Only 12 patient of these group had autonomic symptoms during ictal eeg recordings. We collected and investigated demographic features, physical examinations, clinical features, antiepileptic drugs medication, neuroradiological imagings, video eeg recordings of this patients. Result: The study group consisted of 12 patient (9 male) aged 5 to 19 years. (mean 11.6 ± 4.7 years) The minimum age of onset seizure is 20 days old. (age of onset seizure; 20 days to 15 years) While headache was the most common autonomic symptom, 4 nausea-vomiting, 2 tachycardia, 1 dizziness and 1 bradycardia were observed. Temporal lobe epilepsy was the most common epilepsy in this study group. Discussion: Seizure related autonomic changes in children is important to understand the central representation of the autonomic nervous system and the assessment of the epileptogenic focus. Additionally interictal autonomic symptoms may play a role in sudden unexpected death in epilepsy patients. We showed different autonomic seizure in our video EEG unit.

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Epilepsy

ICNC-0056: Long term follow-up of children with West syndrome in a tertiary care centre

Objectives: To study the long term outcome of infants who were diagnosed as West syndrome and treated accordingly. Methods: Fifty four children who satisfied inclusion criteria of West syndrome i.e., infantile spasms, psychomotor retardation and abnormal EEG pattern were followed up for average 4.3 years (minimum 2 years, maximum 10 years). Results: Eighty seven percent of the infants were classified as symptomatic. Mean age of the patients was 10.7 months (maximum 30 months and minimum 3 months). Symptomatic group had history of perinatal asphyxia in 34% cases but it was not significant. In 52% of cases, onset of spasm occurred in 3-6 months age range, 26% of in 6-9 months and 13% in <3 months of age range. Out of this, 96% of the symptomatic group had onset of seizures in 3-6 months age range. Onset in the idiopathic/cryptogenic group was 36% and 33% in the 6-9 and 9-12 months age range respectively. On follow up, 74% of the children had mental retardation, 52% had epilepsy, 46% had cerebral palsy, 7(13%) died. Out of 7
patients who died, 6 (86%) patients were from symptomatic group. Four children were developmentally normal and all of them were from idiopathic group. Twenty eight percent of the children had both epilepsy and cerebral palsy. Conclusion: Outcome in the symptomatic group was worse and onset of seizure was earlier than in the idiopathic/cryptogenic group. Key Words: West syndrome, long term outcome

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Epilepsy ICN-0057: Evaluation of risk factors of drug resistant Epilepsy in childhood
Introduction: Epilepsy is one of the common neurological abnormalities of children affecting quality of life in developing age, 10-20% of all childhood epilepsy have shown inadequate control of seizure in spite of good compliance of antiepileptic drugs, this study aimed to detect both clinical and electroencephalographic factors of drug resistant epilepsy as early predictor. Methodology: This retrospective study was performed from January 2013 to July 2015 at pediatric neurology unit of IPNA (Institute of Pediatric Neurology and Autism), BSMMU, among children with epilepsy in between 6 months to 15 years of age history of taking appropriate antiepileptic drugs for at least 6 months with adequate compliance. We divided the patients in to two groups, group 1 included 50 children with poorly controlled epilepsy, and group 2 included 50 children with well controlled epilepsy. Retrospectively we have compared the clinical and electroencephalographic features of these two groups of patients. Results: In this study, age of onset of seizure below 1 year, mixed type of seizure(22%), epileptic syndrome like West Syndrome (19%), Dravet Syndrome(5%), lennox-gastaut syndrome(4.5%), myoclonic epilepsy(25%), epilepsy secondary to metabolic disorder(15%), symptomatic epilepsy(9.5%) were associated with poor seizure control, initial seizure frequency more than 20 before starting treatment also regarded as a bad prognostic sign in this study. Initial grossly abnormal EEG (P=0.03), burst-suppression pattern (p=0.002), hypsarrhythmia (p=0.001), Continuous Spike Wave in Slow Sleep, CSWS (P=0.002), frequent sharp wave/spike (p=0.003) were electroencephalographic predictors of drug resistant epilepsy. Conclusion: This study has been shown that several clinical factors and EEG abnormalities can predict early about development of drug resistant epilepsy, so that we can pay early attention to these patients regarding initiation of advance modalities of antiepileptic treatment. Key words: Electroencephalogram ( EEG), Drug resistant epilepsy

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Epilepsy ICN-0058: Neuroimaging Findings as a predictor of seizure control in West Syndrome
Introduction: West syndrome (Infantile Spasms; IS) is a severe form of encephalopathy that typically affects young infants ranges from 2.3.5/10,000 live births. Approximately 50% causes of IS associated with a prenatal factors that includes congenital CNS malformations, intrauterine insults, neurocutaneous syndromes such as TSC, genetic syndromes and have poor prognosis. For early identification of underlying etiology a proper neuroimaging is essential it will also help to predict the outcome. For this reason my study aimed to correlate the presence of neuroradiologic abnormalities and its effect on seizure control in the children with West syndrome. Methodology: This retrospective study was carried out in Institute of Pediatric Neurology and Autism (IPNA) in BSMMU. All patients those who were diagnosed as a case of West syndrome in between age of 3 months to 3 years according to ILAE during period of June2013 to May 2015 were included in this study. Results: 41 children with West Syndrome were studied, their mean age of presentation was 17±9.8 months, mean age of onset of seizure was 6.5±3.7 months, 70% of them were male. Patients with normal neuroradiologic findings had early remission of spasms and with anomalies, atrophy and calcification were associated with poor response to drug (p=0.02). ACTH was the most commonly used drug with good seizure remission where neuroimaging finding was normal and in cerebral atrophy as a consequence of perinatal asphyxia (p=0.009). Vigabatrin showed good seizure remission in WS due to Tuberous Sclerosis Complex. Conclusion: Seizure prognosis of West Syndrome differ greatly according to the type of brain lesion so in every suspected cases of West Syndrome early neuroimaging should have to be performed for making proper management protocol. Key words: Neuroimaging, West Syndrome

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**Epilepsy**

**ICNC-0059: A randomized controlled trial of Phenobarbital and Levetiracetam in childhood Epilepsy**

Introduction: Levetiracetam has been introduced for the control of seizures besides phenobarbital as monotherapy in children with epilepsy. But the efficacy has not been assessed in any clinical setting. This study was aimed to compare the effectiveness of these two drugs for the control of seizure. Methods: A double blind randomized controlled trial was conducted in Institute of Pediatric Neurodisorder and Autism (IPNA), BSMMU among children between 1 month to 15 years who were diagnosed as cases of epilepsy (idiopathic focal, generalized, focal with secondary generalization) according to ILAE to see the effect of Levetiracetam (n=50) and Phenobarbital (n=68) from March to August 2015. The children were followed up for 12 months at 3 months interval to compare the seizure remission and side effects of Levetiracetam and Phenobarbital. Two follow ups were completed during last 6 months. Results: 31 (55.4%) patients with levetiracetam achieved satisfactory seizure remission (>50% seizure remission) within 3 months of treatment whereas 25 (44.6%) patients with phenobarbital achieved satisfactory seizure control (p=0.007). Second follow up visit at 6 months period did not show significant improvement in seizure control from 1st visit. Sixteen patients (23.53%) of phenobarbital group shifted to other antiepileptic drug due to nonresponsiveness, whereas only 4 (8.00%) patients of levetiracetam showed nonresponsiveness. 3 patients of phenobarbital group developed behavioral problem and 2 patients of levetiracetam group developed irritability, but no children of both group discontinued treatment due to side effects. Conclusions: Levetiracetam monotherapy is more effective in controlling seizures in focal, generalized and focal with secondary generalization epilepsy compared to phenobarbital with minimum side effects. Key words: Epilepsy, Seizure remission.

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**Epilepsy**

**ICNC-0061: Doose Syndrome: Effective Synergism of Rufinamide and Clobazam. A case report**


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**Epilepsy**

**ICNC-0062: Magnetic resonance imaging of symptomatic epilepsy in children after meningoencephalitis**

Background: Epilepsy is one of the most complex medical and social problem at present time. The high prevalence of the disease in paediatric population of Uzbekistan (10 per 1,000) determines the importance to develop effective measures for early diagnosis, new approaches to correction of treatment and prevention of complications of epilepsy. Objective: to
identify MRI findings of symptomatic epilepsy in children with inflammatory etiology such as meningoencephalitis. Materials and Methods: MRI studies were conducted with 35 children with the diagnosis of symptomatic epilepsy after meningoencephalitis. Children ages ranged from 1 year to 14 years. Results: in our study the main symptoms of epilepsy after meningoencephalitis were multiple lesions of white and gray matter, their predominant bilaterality and symmetry, a clear demarcation from the surrounding tissues. In the study of 35 children who recovered from meningoencephalitis following MRI signs were found, in 5 (14.3%) cases it was midline shift of the brain, in 12 (34.3%) cases it was asymmetry of the lateral ventricles. Subarachnoid perivascular space expansion was found in 22 (62.9%) cases, which often revealed in the fronto-temporal region of the brain. Expansion of the subarachnoid space was revealed in 19 (54.3%) cases, mainly due to atrophy of the brain. Conclusion: Magnetic resonance imaging has an important role in the clinical diagnostics of epilepsy, the use of which in the study of symptomatic epilepsy is one of the important conditions of adequate diagnosis, treatment and prognosis of the disease.

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Epilepsy
ICNC-0064: MRI abnormalities and EEG patterns of symptomatic epilepsy in children with brain anomalies
Relevance. Active introduction modern neuroimaging methods (CT, MRI, EEG) to the practice of child neurologist has greatly advanced our understanding and knowledge about brain anomalies, determination their role in the assessment of neurological status of the child and further prognosis of disease. Objective of this study was to investigate the relationship of MRI, CT and EEG features in children with symptomatic epilepsy with anomalies of the brain. Materials and Methods: MRI studies were performed in 17 children with symptomatic epilepsy against the anomalies of the brain. Age grading was drafted to 14, average age 6.7 ± 1.2 years. Results: In the neonatal period in 15 patients (88.2%) depression syndrome was diagnosed, and 5 patients (29.4%) excitation syndrome, in 2 (11.8%) children various convulsions. In the analysis of EEG studies in 62.5% a specific pattern of EEG - a generalized beta activity of high amplitude was recorded. MRI studies of these children revealed expansion of interhemispheric fissure, subarachnoid space, ventriculomegaly without clinical signs of hydrocephalus. Expansion of interhemispheric fissure and subarachnoid spaces often found in the anterior cortex of brain. In 8 (47.2%) children an abnormality of the brain were various formations of sulcation.
Conclusions: Based on these results it can be suggested that the detection of brain malformations in the earliest possible time of child life cannot be overestimated. Without on time diagnosis of these anomalies paediatric patient are obliged to receive therapy for hypoxic brain damage or intrauterine infection until correct diagnosis of brain anomalies become evident in the later age of child.

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Epilepsy
ICNC-0065: Defining the role of imaging methods in diagnostics symptomatic epilepsy in children
Introduction Defining the role of MRI and CT in the comprehensive assessment of the state of the central nervous system in children with symptomatic epilepsy Subjects and Methods The object of the study were 28 patients with symptomatic epilepsy aged from 1 to 14 years. Debut of seizures observed in a wide range of ages from 1 month to 10 years (mean 6.3 ± 4.9). All patients underwent EEG (electroencephalography) studies, magnetic resonance imaging and computed tomography. Results Structural changes of brain were found in 45.6% of all examined patients in MRI and CT. Pathological changes in the EEG were found in 77.2% of patients. Regional epileptiform activity, represented by a complex-acute or slow waves recorded in 51.9% of cases. Changes on MRI were detected in 44.6% of patients. CT allowed us to determine the state of the ventricular system and subarachnoid spaces. the following MRI signs were found, in 5 (14.3%) cases it was midline shift of the brain, in 12 (34.3%) cases it was asymmetry of the lateral ventricles. Subarachnoid perivascular space expansion was found in 22 (62.9%) cases, which often revealed in the fronto-temporal region of the brain. Conclusion Thus, at present, CT and MRI are the main methods of neuroimaging in the diagnostics of symptomatic epilepsy in children. However, it should be noted that only the focused research, knowledge-based clinics, medical history, EEG findings, MRI and CT scans in total identifies epileptogenic focus.

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Epilepsy
ICNC-0066: The level of intelligence in children with epileptic encephalopathy
Introduction. Clinical manifestations of epilepsy in children are variable and this creates difficulties in diagnosis, especially if there are non-trivial paroxysmal debuts. Epileptic encephalopathy - a condition in which the epileptiform disturbances lead to progressive disorder of brain function that leads to significant social maladjustment. Goal. The study of the state
of intelligence in children with epileptic encephalopathy. Material and Methods: We studied 32 children aged 4 to 14 years with a diagnosis of epileptic encephalopathy, were treated in the department of paediatric neurology clinic TashPMI. Patients were conducted complex clinical neurological and neuropsychological, genealogical research. Results of the study. When a mother's patients complained of enuresis in 13 cases, logoneurosis in 5 cases, and the backlog of psycho-speech development in all cases observations. In 16 patients with hyperactive behaviour was observed, which appeared pugnacity, disinhibition, in all cases, a decrease in school performance. In the study of the intellectual sphere by Wexler, showed a reduction of intelligence - a border zone (70-79 points) was observed in 15 and a mental defect (69 points or less) in 17 patients. In this same figures were reduced by verbal and nonverbal scale. In drawing up the genealogical tree of probands, there was no presence of epileptic manifestations with relatives. The EEG in these patients revealed a stem of high-dysrhythmia and ongoing sharp-slow-wave dysrhythmia. It should be noted that these patients never experienced seizures in a trivial sense. Conclusion Thus, early detection of this disease in children will allow early treatment in these patients, and to prevent their social exclusion.

Dildora Aminova
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Epilepsy
ICNC-0067: Indicators of EEG in epileptic encephalopathy
Relevance. Epilepsy is one of the most urgent problems of paediatric neurology, because of behavioural, mental, neuropsychological impairments, the difficult diagnosis and curable of the disease, especially if there are non-trivial paroxysms. The frequency of childhood epilepsy is on foreign sources of 0.5-0.75% of the child population. International antiepileptic League recently in the classification of epileptic syndromes put term epileptic encephalopathy. Epileptic encephalopathy - a condition in which the epileptiform disturbances lead to progressive disorder of brain function. From a clinical point epileptic encephalopathy divided into 2 types: 1-type - occurs in children with epileptic syndromes, marked by progressive disorders of cognition, intelligence, speech and other cerebral functions. 2-type - is characterized by mental, cognitive, behavioural and social disorders in the absence of seizures. Purpose of the study. Explore electroencephalographic features of the epileptic encephalopathy in children. Material and Methods: We studied 27 children aged 3 to 14 years who were hospitalized in the paediatric neurology clinic TashPMI, with a sharp mental retardation or gross psychomotor retardation. The study patients were divided into 2 groups. Clinical and neurological examination of children in group I - 15 children revealed diffuse focal neurological symptoms, marked an intellectual deficit. The history of these patients had generalized seizures and polymorphic. The EEG data from children revealed a giant amplitude sharply slow wave and spike wave dysrhythmia. Hypsarrhythmia. Clinical and neurological examination of children of group II - 12 children, found no gross localized neurological disorders have been observed hyperactive type of behavior, the backlog in training at the school relative to their peers. In this subgroup of patients did not have a history of epileptic seizures. On the EEG data revealed a high amplitude and a constant stem dysrhythmia sharply slow wave dysrythymia. In addition, these patients have a family history met "small" signs of epilepsy. Children in both groups were appointed by anticonvulsant drugs. The treatment of children have improved somewhat cognitive function. Conclusion. This study demonstrates the importance of neurophysiological research methods for children with retarded mental and psychomotor development in order to eliminate or timely diagnosis and treatment of this disease.

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Epilepsy
ICNC-0069: The features of cognitive functions in children with epileptic encephalopathy type I
Relevance. Epileptic encephalopathy - a condition where the pathological changes electrogenesis brain is the cause of disorders of the brain. In which the epileptic process itself leads to progressive brain damage The purpose of the study. To study cognitive function in children with epileptic encephalopathy type I. Materials and methods. The research is based on data from 16 studied children with epileptic encephalopathy I type. children's age ranged from 2 years to 14 years, the average age was 5.96 ± 0.77 years. The results of the study. In the study of cognitive function in accordance with the Raven Progressive Matrices in children with epileptic encephalopathy type 1 in the comparative aspect we found a high percentage of low-level intelligence in comparison with a group of healthy children. The study showed that in the studied group the high level of intelligence is not registered, the average level was observed only in 11.5% of children (P <0.01), while IQs lower than the average recorded in 65.4% of children (P <0.01), low levels was observed in 23.0% of children with epileptic encephalopathy type I. According to data it can be seen on a low level of non-verbal intelligence, which corresponds to mild dementia. Conclusion. Thus, the reduced level of nonverbal intelligence, ability to visual analysis and synthesis, intellectual exhaustion, low level of voluntary control, difficulties in the distribution of attention and general infantilism are the forefront and most frequent findings in the studied group.
Developmental
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identify the additional genetic and epigenetic factors that determine severity of

as a significant cause of early onset epilepsy. The phenotypic spec

matter bulk, thin corpus callosum and ventri

Three patients presented with autistic features. Non

migrating focal seizures, familial neonatal

cohort, we observed a wide range of electroclinical phenotypes, including Ohtahara syndrome, epilepsy of infancy with

panel, MiSeq sequencing) and (ii) research whole exome sequencing studies with

we studied a cohort of mutation

seizures to severe epilepsy syndromes. In order to better define the electroclinical features and associated genotypes,

Introduction Mutations in SCN2A are reported

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Epilepsy

ICNC-0070: The subcortical band heterotopia/lissencephaly spectrum and epilepsy: phenotypic, molecular, functional, and structural analysis of novel causative DCX and LIS1 variants

Subcortical band heterotopia (SBH), and lissencephaly (LIS) are part of a spectrum of malformations of cortical
development, referred to as the SBH/LIS spectrum. We report the phenotypic, molecular and functional/structural
analysis of novel DCX and LIS1 mutations causing SBH/LIS and epilepsy. Patient 1, a 46-year-old woman, had multiple
seizure types, and severe developmental delay. Brain MRI showed double cortex predominating in the frontal regions.
DCX sequencing showed a c.578delA variant. Using assays with dynamic microtubules, we measured in vitro the ability
of recombinant mutated DCX protein to interact with microtubules. The 578delA variant was found to be defective in its
ability to promote microtubule nucleation and polymerization, and showed impaired cooperative binding to microtubules.
Patient 2, a 28-year-old man, presented, refractory epilepsy, bilateral facial diplegia, pseudobulbar signs and severe
developmental delay. Brain MRI showed a predominantly posterior lissencephaly. LIS1 sequencing showed duplication of
five nucleotides in exon 8 (c.728_732dupATCAA). Bioinformatic analysis of the mutant sequence and mapping onto the
LIS1 structure showed that the change introduces a five residue stretch of altered sequence followed by a premature
stop codon at residue 250, early in the 4th WD repeat of the Lis1 beta propeller. We report two novel pathogenic variants
causing severe SBH/LIS. Our functional analyses show that the DCX variant disrupts microtubule binding as well as the
cooperative interaction between DCX molecules. Our structural interpretation show that the LIS1 protein very likely does
not fold properly, is unable to bind dynein, and is likely targeted for degradation in cells.

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Epilepsy

ICNC-0279: The phenotypic spectrum of SCN2A-related epilepsy

Introduction Mutations in SCN2A are reported in a broad spectrum of epilepsies from benign familial neonatal-infantile
seizures to severe epilepsy syndromes. In order to better define the electroclinical features and associated genotypes,
we studied a cohort of mutation-positive patients. Methods We identified 22 patients from tertiary epilepsy clinics with
mutations in SCN2A. Mutations were identified through (i) diagnostic multiple gene panel testing (SureSelectXT custom
panel, MiSeq sequencing) and (ii) research whole exome sequencing studies with subsequent Sanger confirmation.
Retrospective case note analysis with MRI and EEG review was undertaken. Results: Most patients (20/22) had seizure
onset in the first week of life, though presentation was as late as 3 years of age (median 2 days of age). Within the
cohort, we observed a wide range of electroclinical phenotypes, including Ohtahara syndrome, epilepsy of infancy with
migrating focal seizures, familial neonatal-infantile seizures and non-specific early and later onset epileptic
encephalopathies. Three patients had a severe movement disorder, and the majority had neurodevelopmental delay.
Three patients presented with autistic features. Non-specific features on MR brain imaging included decreased white
matter bulk, thin corpus callosum and ventricular enlargement. Most identified SCN2A mutations were missense variants,
occurring de novo and affecting highly conserved amino acid residues. Conclusions Mutations of SCN2A are emerging
as a significant cause of early onset epilepsy. The phenotypic spectrum of the SCN2A-epilepsies is broad, and therefore
the approach of multiple gene testing via panels or whole exome sequencing is warranted. Further research is required to
identify the additional genetic and epigenetic factors that determine severity of clinical manifestations and outcome.

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Epilepsy

ICNC-0072: Evaluation of treatment lag in infantile spasms and its effect on therapeutic response to adrenocorticotropic hormone/ steroid therapy

INTRODUCTION: Aim of the study was to elucidate the magnitude and determinants of treatment lag in infantile spasms and to evaluate the effect of treatment lag on short term therapeutic response to ACTH/ steroid therapy. METHOD: We conducted a prospective study in a tertiary care hospital in north India during the period 2013-2014. A total of 82 consecutive children with infantile spasms were enrolled. Magnitude and determinants of treatment lag were calculated in all the children. Short term therapeutic response was taken as cessation of spasms within 14 days of therapy and sustained for a period of ≥ 28 days from the last witnessed spasm. To ascertain the effect of treatment lag on therapeutic response, we excluded fifteen children who had either received therapy for less than 2 weeks or had received vigabatrin. We analysed following factors: age of onset of spasms, aetiology, treatment lag and gender for their association with therapeutic response. RESULTS: The median treatment lag duration was 90 days (95% CI: 110-198 days). The significant determinants of treatment lag in our study were: the pre-existing delay of children, educational status of the parents and qualification of the first practitioner visited. Our study showed shorter treatment lag was associated with a better spasm cessation rate (p = 0.011). CONCLUSION: We observed a significant treatment lag in our children. The lead time to treatment emerged as a potential modifiable risk factor for therapeutic response with ACTH/ steroid therapy.

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Epilepsy

ICNC-0235: Evaluating the effectiveness of a pediatric 24/7 Epilepsy hotline

Introduction: The first 24-hour Children’s Epilepsy Hotline (CEH) in Greece began in pilot operation in January 2015 aiming to assure patients immediate access to specialized medical help. The purpose of this study is to present the hotline’s service and to evaluate its effectiveness. Methods: The hotline’s team consists of field experienced personnel. The given directions to patients are based on empirical and literature guidelines and pediatric neurologist's instructions. All calls are recorded and case details are saved in a team-shared database. After 9 months of service, an evaluation questionnaire was filled by 54 caregivers-callers. Results: From January 1 until November 27, 301 calls from 86 different patients were recorded. The number of calls has stabilized at 29 calls/month and includes 8 new callers/month who are often the parents of recently diagnosed patients. 58 of the cases for which transfer to hospital was considered, 44 were successfully handled at home. In the evaluation questionnaire, the 98.3% of caregivers considered CEH necessary, and the 96.6% were satisfied by the received instructions. Discussion: The CEH contributes to a better quality of life and is an important clinical tool in improving the patient's management while avoiding unnecessary hospitalization. Its continued operation can be critical, especially for newly diagnosed cases. The small number of calls may be explained by the fact that the CEH serves only one pediatric neurology unit and by the caregivers’ gradual improvement in managing everyday difficulties. The hotline’s expansion and further publicity is expected to substantially increase its effectiveness.

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Epilepsy

ICNC-0077: Role of the cellular component of immune system in genesis of epilepsy
Purpose: to define the role of immunological changes in infants' epileptogenesis with resistant forms of epilepsy. Material and Methods: The study involved 55 infants aged 0 to 36 months. Study group (I) composed the resistant forms of epilepsy -30 (54,5%), control group (II) included epilepsy with exception of resistance criteria -25 (45,5%). Results: The resistant forms of epilepsy: the West syndrome - 16 (53,3%), the Lennox-Gastaut syndrome - 6 (25%), the Othahara syndrome - 1 (3,3%), and multifocal resistant epilepsy - 7 (23,4%). Control group: 18 (72%) - generalized forms, 7 (28%) - partial forms. I group include 80% (24) - infantile spasms, 20% (6) - generalized tonic-clonic, myoclonic seizures. II group 68% with generalized tonic-clonic, myoclonic seizures; 32% - partial tonic seizures. The EEG: I group -73,3% (22) - hyspsarrhythmia and 26,7% (8) - other types of epileptiform activity. II group - 3 (12%) -hypsarrhythmia and 22 (88%)-other types of epileptiform activity. The indicators of cellular: CD4: I – 0.90±0,33, II – 1,05±0,05; CD8: I – 1,007±0,022, II– 0.75±0,08; CD16: a I – 0,86±0,11, II – 0,55±0,09; CD72: I – 0,88±0,14, II – 0,56±0,04, p<0,05. Decrease of T-helpers, activation of T lymphocyte, growth of NK, B-lymphocytes in study group. Conclusions: the importance of immunological disorders in epileptogenesis plays role in genesis of resistant forms of epilepsy in infants. These data requires further study.

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Epilepsy

ICNC-0078: Cytokine profile of children with resistant forms of epilepsy
Objective: To study the nature of the immunological changes in the genesis of epilepsy in infants. Material and Methods: 41 patients aged 0 to 36 months. The study group -refractory epilepsy - 12 (29.3%), comparative - "epilepsy" with the exception of the resistance criteria - 12 (29.3%), control group - without epilepsy - 17 (41.4%). Results: Resistant forms of epilepsy: West syndrome 6 (50%), Lennox-Gastaut syndrome - 3 (25.1%), syndrome Othahara - 1 (8.3%), multifocal epilepsy resistant - 2 (16.6 %). The study group - 75% form of infantile spasms. In comparison group - no infantile spasms. Pattern "burst-suppression" - 85.7% in study group and 14.3% - comparative group. Cytokine profile (pg / ml): IL-1β: the main group - 7,98 ± 0,60, comparative - 6,31 ± 0,74; TNFα: the main - 6,03 ± 0,29, comparative - 4,18 ± 1,95; IFNγ: the main - 2,49 ± 0,14, comparative - 3,10 ± 0,41; IL-10: the main - 9,54 ± 0,75, comparative - 10,98 ± 0,97. Level of proinflammatory cytokines increased in the main group, anti-inflammatory cytokines - reduced (p <0,05). Conclusion: The greater contribution of immunological disorders in the genesis resistant forms of epilepsy. The results are inconclusive and require further study.

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ICNC-0079: Information is power: An interventional study on parents of children with febrile seizures
Background: Febrile seizure (FS) is a devastating condition for parents due to lack of information, anxiety and feeling of guilt. Family education is crucial in terms of decreasing the anxiety, first aid, and keeping the patient safe in case of a seizure. Aim: In this study, we aimed to investigate the level of information, and the effect of education about FS on approach and anxiety of the parents using objective evaluation methods. Method: We interviewed parents of 113 children who had at least one FS episode and conducted a survey aiming at detailed information on knowledge, attitudes, thoughts and concerns of the families about FS and their approaches to fever and FS. We used Hospital Anxiety and Depression Scale (HADS) and State-Trait Anxiety Inventory (STAI) to determine the levels of anxiety and depression both before and after the education. Conclusions: Parents have misconceptions such as FS damages the brain and causes epilepsy, FS is a life-threatening disease, and electroencephalography (EEG), magnetic resonance imaging (MRI) and computed tomography (CT) scans of the brain are required. After the education, parents’ anxiety levels are significantly reduced and the knowledge about correct interventions during a seizure was significantly higher after the education (p < 0.01 and p < 0.01). Anxiety level of the parents were significantly decreased after the education program (p < 0.01). We conclude that, after proper education, parents will be better in first aid practices and their requests for unnecessary preventive interventions will be reduced.

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There are some differences between male and female patients with early onset epileptic encephalopathy, especially in early infancy. The XCI patterns of female patients were random. Conclusions CDKL5 mutations were mainly found in female patients were random. Conclusions CDKL5 mutations were mainly found in female patients with early onset epileptic encephalopathy, especially in early-onset seizure variants of Rett syndrome. There are some differences between male and female patients in clinical manifestations. XCI pattern may not impact on clinical manifestations. XCI pattern may not impact on clinical manifestations.

ICNC-0060: Cerebral Folate Deficiency: a novel mutation of FOLR1 gene in a Bahraini girl
Introduction: Cerebral folate deficiency is a rare, treatable cause of catastrophic epilepsy that usually manifests during infancy. We present a girl who developed manifestations at later age (four years) with epileptic encephalopathy: intractable seizures, ataxia and cognitive decline. Case: Our patient was a four year old girl, a result of a consanguineous marriage with normal development until the age of two years with past history of a febrile seizure at 18 months. She first presented with symptoms suggestive of pallid spells and six months later she developed polymorphic seizure: unprovoked generalized tonic clonic seizures, myoclonic jerks and drop attacks. Her investigations included a thyroid level, serum lactate, tandem mass spectrometry and urine for organic acids all were unremarkable. Her initial EEG showed generalized spike-and-wave complexes of high amplitude. She continued to have multiple seizure types increasing in frequencies. In view of repeated falls and head injuries she warranted a brain CT/MRI that showed basal ganglia calcification with scattered parenchymal and periventricular calcification as well as right posterior temporal and occipital leucomalacia. Her examination revealed irritability, poor attention span, ataxia with slurred speech and long tract signs. By this time she was tried on multiple anti-epileptics including: Valproate, Topiramate, Levetiracetam, Clonazepam and a short course of Prednisolone but all have failed. A CSF study showed reduced 5-methyltetrahydrofolate level and genetic study revealed exon 3 homozygous mutation in the folate transporter gene FOLR1 (c.242T>G,p.Leu81Arg). Both parents were heterozygous for the same mutation. She was started on Folic acid 2.5 mg/kg and Zonisamide that resulted in remarkable improvement. Conclusion: This case high lights the need to recognize this treatable condition with biochemical studies of CSF 5-methyltetrahydrofolate and the final confirmation by genetic testing.

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ICNC-0080: Malignant migrating partial seizures of infancy: case report
Extremely rare epileptic syndrome, described by G. Coppola et al. Up to date, all of the reports about 50 cases of the disease registered in different parts of world. Malignant migrating partial seizures in 50% of cases occur in the first days of life; the remaining 50% comes from the age of 1-3 months. We have observed 11 months age girl. The first attacks began at 5 months during fever by generalized tonic-clonic seizures with rolling eyes, lasting up to 10 minutes. The frequency of attacks from 5 to 9 months of life was observed once a month, then the seizures became once a week. At the age of 11 months was noted status epilepticus. On EEG there was migration of ictal activity of the brain with the left to the right and back. The seizures were stopped only by prescribing intravenous thiopental sodium titration in conjunction with pulse therapy of steroids for 3 days. Spen therapy: topiramate (5 mg / kg / 24h) + valproic acid (25 mg / kg / 24h) + clonazepam (0.026 mg / kg / 24h). On MRI marked diffuse cortical atrophy, mostly temporal and occipital lobes. We have described the case in many ways different from the previously described in literature: (1) onset of seizures after 3 months of life; (2) onset from febrile seizures; (3) The characteristic EEG and the clinical picture is turned by 11 months; (4) follow-up of a child patient lived for more than one year.

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the clinical phenotype of patients with CDKL5 mutation. Acknowledgements: This study was financially supported by 985 Peking University and Clinical Hospital Cooperation Project.

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Epilepsy

ICNC-0082: Generalized paroxysmal fast activity: Is this found only in Lennox-Gastaut Syndrome?

Introduction: Generalized Paroxysmal Fast Activity (GPFA) is an EEG rhythm mainly associated with Lennox-Gastaut Syndrome (LGS). The GPFA consists of bursts of generalized rhythmic discharges with frontal predominance, frequency of 8-26 Hz, which usually lasts less than 10 seconds and appears most frequently during NREM sleep. Objective: The objective of this study is to verify if other epileptic syndromes may also be present with GPFA. Method: This was a retrospective study conducted at our University Hospital. Data was collected from clinical files and EEG records. EEG records of the last 10 years were reviewed looking for the presence of GPFA. Epilepsy syndromes were classified either as LGS or other according to the clinical picture of the patient. Results: Thirty patients were included: 22 male, mean age 13 years (range: 4 to 51). Eighteen patients (60%) had LGS. Twelve patients (40%) could be classified as having epileptic encephalopathy either with structural lesion (7 patients) or without any structural lesion (5 patients). Conclusion: GPFA, despite being mainly correlated with LGS, may be found in other epileptic syndromes.

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Epilepsy

ICNC-0083: Recovery of the restorative function of sleep in patients with “Encephalopathy with status epilepticus during sleep (ESES)” after remission

Introduction: An important aspect of the restorative function of sleep is its ability to reduce the strength of cortico-cortical synapses. This synaptic downscaling is important for cortical plasticity and can be measured in the electroencephalogram (EEG) as a decrease in the slope of sleep slow waves. We have shown that in patients with ‘Encephalopathy with status epilepticus during sleep’ (ESES) this overnight decrease of the slope of slow waves is significantly reduced. The results suggested a pathophysiological mechanism where the disturbance of the restorative function of sleep is related to the neuropsychological deficits in these patients. Here we tested whether a successful therapy would improve the restorative function of sleep in ESES.

Methods: Retrospective study of EEGs of 4 patients with idiopathic ESES during the active phase and after successful treatment. Calculation of the slope of slow waves (Δ2Hz) in the first and last hour of sleep. Results: We found a more pronounced overnight decrease in the slope of slow waves in all EEGs in remission (active phase: -2.9 ± 2.4%, remission: -7.6 ± 2.3% decrease. In the epileptic focus 3/4 patients showed an increase in the slope across sleep during the active phase (Δ2.9 ± 5.3%). After therapy all patients showed a decrease in the slope (9.2 ± 2.2%, p<0.05). Conclusion: Our preliminary data analysis shows that successful therapy leads to a recovery of the restorative function of sleep as reflected by the reduction of the slope of slow waves in patients suffering from ESES.

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Epilepsy

ICNC-0084: Gain-of-function FHF1 mutation modifies neuronal sodium channel inactivation and causes early-onset epileptic encephalopathy with cerebellar atrophy

Objective: Early-onset epileptic encephalopathies (EOEs) are severe intractable disorders often caused by mutations enhancing excitatory or suppressing inhibitory neuronal activity in the brain. Voltage-gated sodium channel (Nav) encoding genes are among EOEE targets, suggesting that other genes encoding Nav-binding proteins may also play roles in these disorders. Fibroblast growth factor homologous factors (FHF's) are a family of Nav binding proteins, thought to play a broad role in the control of CNS excitability. Methods: To identify additional genes for EOEEs we performed
whole-exome sequencing in a family quintet with two siblings affected by a lethal neurodegenerative disease characterized by EOEE and cerebellar atrophy. The pathogenic nature and functional consequences of the identified sequence alteration were determined by functional electrophysiological studies. Results: A de novo heterozygous missense mutation was identified in the FHF1 gene (FHF1AR114H, FHF1BR52H) in the two affected siblings. The mutant FHF1 proteins had a strong gain-of-function phenotype in transfected Neuro2A cells, enhancing the depolarizing shifts in Nav1.6 voltage-dependent fast inactivation, predicting increased neuronal excitability. Surprisingly, the gain-of-function effect is predicted to result from weaker interaction of mutant FHF1 with the Nav cytoplasmic tail. Transgenic overexpression of mutant FHF1B in zebrafish larvae induced epileptiform discharges. Conclusions: Our data provide the first demonstration of a neurological disorder caused by gain-of-function FHF mutation, and expand the repertoire of genetic causes (FHF1) and mechanisms (Nav fast inactivation gating) underlying EOEE and cerebellar atrophy.

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Epilepsy
ICNC-0085: The risk of developing epilepsy in children in the republic of Moldova
Aim: to establish the risk of developing the disease by the means of associating a number of factors - predictors. Material and methods: 108 children diagnosed with epilepsy hospitalized in the Department of Neurology PMSI BMI between 2009-2012, ages ranging from 1-36 months, were examined. Another 108 healthy children were included in the control group. Risk factors under investigation were perinatal encephalopathy, febrile seizures, hereditary predisposition, maternal hypertension, craniocerebral trauma, CNS infections. By multiple logistic regression, step by step, the interrelation of a number of selected factors was analyzed, such as: hereditary predisposition, evolution of the perinatal period (including childbirth), the presence of CNS infections and trauma brain injury in the postnatal period. Results: The results show that both perinatal and postnatal factors are strongly associated with the development of seizures. Thus, a combination of intrapartum factors (EHIP II emergency caesarean section, vacuum extraction) with some postnatal factors (postnatal CNS infections) generated the following logistic regression coefficients: 3.861, 1.909, 2.377, 4.311, 3.505, proving, thus, a link between these factors and epileptic seizures. Conclusions: These predictive models can be applied in clinical use for the purposes of reducing the risk of developing epilepsy by careful evaluation of these children, particularly in the presence of predictive factors. They also have a practical application in predicting on a case-by – case basis the likelihood of developing the disease and in developing effective measures of primary and secondary prophylaxis.

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Epilepsy
ICNC-0086: Pyridoxine dependent epilepsy. Two case reports
Introduction: Pyridoxine-dependent epilepsy (PDE) may present with early onset seizures and should be suspected in cases of early onset epilepsy without response to anti-epileptic drugs, pyridoxine treatment should be started even without diagnostic confirmation. Methods: presentation of two cases of Pyridoxine-dependent epilepsy Case description: Full-term male and female newborns without prenatal interesting antecedents or incidents during birth. Both were admitted to the intensive care unit, first because of breathlessness presenting in the first five hours sucking and clonic movements of right upper limb; second because of sucking, blinking and clonic movements of left upper limb. Cranial ultrasonography was normal; however the electroencephalography showed slow wave left temporal foci in the first patient and a pattern of cerebral suffering in the second. Both received treatment with phenobarbital with persisting seizures; so, in the first case biotin, pyridoxine and folic acid were added; in the second only pyridoxine with seizures remission. Metabolic study showed high picolalic acid levels in plasma and cerebrospinal fluid so genetic study was requested. First patient had R307X and N273fs mutation; the second one is waiting for results. Both are receiving pyridoxine, the first case with adequate development. Now he is 6 years old; the second without seizures but maintains delayed acquisition of neurodevelopmental items. Discussion: Pyridoxine dependent epilepsy may present with early onset seizures without response to anti-epileptic drugs. Alpha-aminoacidic semialdehyde dehydrogenase enzyme mutation causes accumulation of picolic acid and alpha-aminoacidic semialdehyde which facilitates diagnostic and evaluation of the treatment dose. Nowadays genetic study avoid the need for challenge test.

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Epilepsy

ICNC-0087: Effectiveness and tolerability of perampanel in pediatric population with refractory epilepsy

We aim is to communicate the results of experience in 3 tertiary hospitals in the use of Perampanel (PER) in pediatric patients with refractory epilepsy. We collected data from 49 patients treated with perampanel in our 3 hospitals. We evaluated epidemiological data, dosage and method of titration, drug response, adverse events, and the need for removal or not. Many of the patients was off-label for the age. We record patient with age between 21 months to 17 years (mean 10.8): 35% over 12 years. Very complex patients, with refractory epilepsy and a lot of comorbid diseases. 7 patients with Lennox Gastaut syndrome, 3 with West syndrome, 1 with Dravet. Cerebral malformation 10 (focal dysplasia or midline defect) 43/49 symptomatic. Time of Treatment: 3 months to 16 months. dose range: 2-12 mg / day. Medium dose: 6 mg / dia. Global retention 60%, 85% at least 3 months. Results: Total Respondents 29/49 (%) seizure free. 10% . In 7 allows withdrawal of an AED. Total adverse events (AEs) 16/49 (31%) 8/16 Irritability, Aggressiveness 5/16, Drowsiness 4 / 16, Incontinence Headache 3/16 1 / 16 Aumento crisis 4 / 16. The referred to as temporary or bearable 7 / 16, retired in 5/16, in 1 patient improved by lowering doses. Parents of 9 patients report improved quality of life. No clear relationship with dose AEs. Worse rate if more than 2 EAs associated AEDs. No answer spasms, good response and secondarily generalized partial and generalized tonic. Reflections: PER seems efficient in children and adolescents with drug-resistant epilepsy. The tolerance is acceptable.

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Epilepsy

ICNC-0252: Comparison of the serum cytokine levels before and after adrenocorticotropic hormone (ACTH) therapy in patients with infantile spasm

PURPOSE: Infantile spasm is an age-dependent epileptic syndrome seen in infancy or early childhood. Although studies have been performed concerning the epilepsy-cytokine relationship, there has been insufficient research into the relation between cytokines and infantile spasm. The purpose of this study was to examine the role of cytokines in the pathogenesis of infantile spasm by investigating cytokine levels before and one month after adrenocorticotropic hormone (ACTH) therapy in patients diagnosed with the condition. METHODS: Twenty patients aged between 1 month and 2 years and diagnosed with infantile spasm at the Karadenz Technical University Medical Faculty Department of Child Health and Diseases Pediatric Neurology Clinic, Turkey, and 20 healthy children were included in the study. Patients received 11 doses of ACTH on 2 days a week. Levels of TNF-alpha and IL-2, the main cytokines involved in inflammation and recently associated with infantile spasm, and of IL-1beta, IL-6 and IL-17A, associated with epileptic seizures, and serum levels of the IL-17A activator IL-23 were investigated in all patients at the start of treatment and 1 month after completion of treatment. RESULTS: No statistically significant difference was observed between pre- and post-treatment patient group and control group IL-1beta, IL-2, IL-23 or TNF-alpha levels. Pre-treatment IL-6 and IL-17A levels were significantly higher in the untreated patient group compared to the healthy control group (p=0.00 and p=0.002). CONCLUSION: Our study supports the recent idea that IL-6 and IL-17A are cytokines involved in the pathogenesis of infantile spasm.

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Epilepsy

ICNC-0088: Corpus Callosum and Cerebelum Volumetric MRI changes in epileptic patients

INTRODUCTION: Volumetric changes are described in close areas of epileptic focus, but rarely in remote structures. We aim to describe differences in cerebellar (CV) and corpus callosum volumetries (CCV) of epileptic patients (EP) vs non-epileptic (NEP). PATIENTS AND METHODS: From 2012 to 14, we studied 32 patients from a neuropaediatric outpatient’s clinic (public hospital reference area). A group of 12 EP whose MRI studies were morphologically normal, and another one of 20 with NEP whose MRI were also normal, were submitted to volumetric studies based on XNAT system (Regional prject of the management of medical images). The volumetry (cubic centimetres, cm3) of distant areas of the epileptic focus, such as the CV and CCV were measured. Medians were compared by non-parametric test, and correlation with the decimal age (DA) was obtained with Pearson’s correlation coefficient “r” (SPSS 22.0). Statistical significance was set at p<0.05. RESULTS: The total CV of the EP (Median=141.4 cc, R=112.3-169.5 cc) was significantly...
bigger than the CV of the NEP ones (Median=119.8; R=56.7-152.0) (p=0.001). None of the groups showed significant correlation with the decimal age. The total CCV in the EP group (Median=2.36 cc; R=2-4.5 cc) was slightly smaller than in the NEP one (Median=2.45 cc; R=1.37-4.7cc) without statistical significance. However both groups showed a significant positive correlation. (EP: r=0.578; p=0.049)(NEP: r=0.652; p=0.002). CONCLUSIONS: Epileptic patients showed bigger cerebellar volume than non-epileptic ones, while the volume of the corpus callosum do not differ between groups, although its volume is influenced by the age of the patient.

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Epilepsy
ICNC-0089: Sleep and memory consolidation in children with focal epilepsy
Introduction Cognitive impairment is a major co-morbidity in children with epilepsy. In the past decade, evidence has emerged that the consolidation of declarative memory is promoted by slow-wave sleep (SWS). Previous studies examining the effect of epilepsy on this phenomenon lacked either a control group or a control condition. We investigated sleep-related memory consolidation in children with focal epilepsy compared with healthy children, utilising a within-subject design. Methods Eighteen patients (aged 6–16 years) and 19 healthy, age-matched controls performed tests of memory retention across similar length intervals overnight (sleep condition) and in daytime (wake condition). For each condition, participants learned a list of word pairs for cued recall after the interval. Electroencephalography (EEG) with polysomnography was performed across the sleep condition. Results Memory retention was greater in the sleep than the wake condition (repeated measures ANOVA F=8.16, p=0.007); post hoc tests revealed no significant difference between patients and controls. Across the total sample, gain in memory retention with sleep correlated with proportion of sleep time spent in SWS (R=0.42, p=0.013). Patients had similar amounts of SWS to controls, but did not show the expected developmental decrease in SWS with age (R=−0.46, p=0.047 in controls). Longer duration of epilepsy was associated with worse performance in the Wake (p=0.037) but not the Sleep condition. Conclusion Children with focal epilepsy show benefit to memory consolidation with slow wave sleep similar to that seen in healthy children. The lack of decline in SWS with age in patients, and preservation of sleep-related memory consolidation despite increasing duration of illness suggest that this may be an important compensatory mechanism which could be harnessed to enhance cognitive function. References 1. Reilly C, and Neville BGR. (2011). Academic achievement in children with epilepsy: a review. Epilepsy Res. 97, 112–123. 2. Mölle M, and Born J. (2011). Slow oscillations orchestrating fast oscillations and memory consolidation. Prog. Brain Res. 193, 93–110. 3. Sud S, Sadaka Y, Massicotte C et al. (2014). Memory consolidation in children with epilepsy: does sleep matter? Epilepsy Behav 31: 176–80. 4. Galer S, Urbain C, De Tiège X et al. (2015). Impaired sleep-related consolidation of declarative memories in idiopathic focal epilepsies of childhood. Epilepsy Behav. 2015 Feb;43:16-23.5. Urbain C, Di Vincenzo T, Peigneux P et al. (2011) Is sleep-related consolidation impaired in focal idiopathic epilepsies of childhood? A pilot study. Epilepsy Behav 22: 380–84

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Epilepsy
ICNC-0091: Establishment of isogenic iPSCs from an individual with SCN1A mutation mosaicism as a model for investigating neurocognitive impairment in Dravet syndrome
Introduction: Dravet syndrome (DS) is a severe childhood epilepsy typically caused by de novo dominant mutations in SCN1A. Although patients with DS frequently have neurocognitive abnormalities, the precise neural mechanisms responsible for their expression have not been elucidated. There are wide phenotypic differences among individuals with SCN1A mutations, suggesting that factors other than the SCN1A mutation modify the phenotype. Moreover, since neurocognitive disorders generally have subtle phenotypes in vitro, it is difficult to distinguish disease-relevant phenotypic changes from background variation. Therefore, a well-controlled cellular model system is required to improve our understanding of the mechanisms underlying DS. Methods and Results: We generated induced pluripotent stem cell (iPSC) lines from an individual with SCN1A mutation mosaicism and separately cloned iPSC lines both with and without the SCN1A mutation. These clones theoretically have the same genetic backgrounds, except for the SCN1A gene and should serve as an ideal pair for investigating the pathophysiology caused by SCN1A mutations. We found no prominent difference in the neuronal differentiation propensity between mutant and wild-type cells. Quantitative RT-PCR and western blot analysis revealed higher tyrosine hydroxylase mRNA and protein expression levels in mutant neurons than...
in wild-type neurons. Moreover, dopamine concentrations in media collected from mutant neural cultures were higher than those from wild-type neural cultures. Conclusion: Our findings suggest that SCN1A mutation leads to changes in the dopamine system that may contribute to the behavioral abnormalities in DS. Our isogenic system is well-suited for detecting the subtle cellular phenotype changes causing neurocognitive abnormalities in DS.

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Epilepsy

ICNC-0092: Gender difference of new onset epilepsy over the course of the lifetime: a population-based study
Abstract Introduction Males were thought to have no or marginally increased incidence for epilepsy. However, the gender difference of incident epilepsy over the course of the lifetime has not been addressed. Methods The study aimed to examine the effect of gender on the incidence of epilepsy in 2010 using routinely collected data from National Health Insurance Research Database. The ICD-9-CM code (345) was used for epilepsy case identification. We calculated age- and sex- specific incidence and the 95% confidence intervals (CIs) base on the assumption of a Poisson distribution for the observed number of incident case. Results There were 23,003,863 beneficiaries in at risk cohort, and the total person-years of follow-up were 22,810,967. A total of 15,060 incident cases were identified. The incidence of epilepsy in 2010 was of 0.66 (95% CI, 0.65-0.67) per 1,000 person-years. Men had a higher incidence (0.77 [95% CI, 0.75-0.79]) per 1,000 person-years) than women did (0.55 [95% CI, 0.54-0.57]) per 1,000 person-years). Overall, the incidence of epilepsy was 1.39-fold higher in men than in women. However, the sex difference varies over the course of the lifetime. Men had a marginally higher incidence in children younger than 4 years but this difference disappeared during 5-20 age group and then the man-to-female ratio continues to rise with the most prominent difference in 50-54 age group (Rate Ratio: 1.84). Conclusion Our findings indicate a higher incidence of epilepsy in men than women. The difference was consistent over the lifetime except those aged between 5 to 20 years old.

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Epilepsy

ICNC-0026: Profile of patients with Epileptic Encephalopathy of unknown cause accompanied in one tertiary center
OBJECTIVES The aim of this study was to describe the clinical manifestations of children with epileptic encephalopathy (EE) of unknown cause, defining characteristics, variations and peculiarities, since a considerable number of patients cannot be classified according to the forms described. METHODS We included 51 consecutive patients with clinical diagnosis of EE. Patient’s caregivers were interviewed with semi-structured questionnaire about their medical history, and medical records were reviewed. Data were cataloged and the results presented descriptively. Statistical analysis was performed with SPSS 22.0 program. RESULTS Twenty three percent of patients had their first seizure with fever, 35% had sensitivity to fever, status epilepticus (SE) occurred in 41%, family history of epilepsy was found in 53%; focal seizures occurred in 65%, generalized tonic-clonic in 51%, myoclonic in 55%, tonic in 45%, atonic in 29%, atypical absences in 22% and spasms in 25%. EEG showed focal (90%) and generalized (53%) discharges. AED most used were phenobarbital (55%), valproate (53%) and clobazam (53%). Patients with cognitive impairment had lower age of seizure onset (13 vs. 35 months, Mann-Whitney test, p=0.035). There was no difference in age of seizure onset in patients with or without evidence of regression. Family history of epilepsy was not a predictive factor for the presence of cognitive impairment or regression. CONCLUSIONS Patients with EE of unknown cause show high frequency of sensitivity to fever, SE and family history of epilepsy. Seizures and focal electroencephalographic abnormalities are prevalent. The presence of cognitive impairment is associated with younger age of seizure onset.

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**Epilepsy**

**ICNC-0093: Electrical status epilepticus in sleep: Is this a focal or generalized eletroencephalographic pattern?**

Electrical Status Epilepticus in Sleep: Is this a Focal or Generalized Electroencephalographic Pattern? Raphael R. Almeida, MD; Charlton Cavalanate, MD; Ana Carolina Coan, MD, PhD; Marilisa M. Guerreiro, MD, PhD31PhD Student; 2Assistant Professor of Child Neurology; 3Professor of Child NeurologyChild Neurology Unit - Department of Neurology - FCM - University of Campinas (UNICAMP) -BrazilObjective: Electrical Status Epilepticus in Sleep (ESES) is an electroencephalographic (EEG) finding defined as a pattern of diffuse spike-and-waves (with different degrees of symmetry or even unilateral or focal) occurring in up to 85% of slow sleep. The objective of this study was to evaluate our EEG data trying to verify if the predominant discharges are focal or generalized.Method: This was a retrospective study conducted at our University Hospital. Data was collected from clinical files and EEG records. Inclusion criterion was the diagnosis of ESES. The group was divided into two subgroups according to the predominance of focal or generalized discharges. The two subgroups were further analyzed taking into account the presence of neuroimage abnormalities. Statistical analysis was performed using Fisher Exact Test.Results: Out of a total of 15,983 EEG records, 23 patients presented with ESES (13 boys). Focal EEG pattern was found in 18 patients (78.3%) while generalized pattern was present in 5 (21.7%). Neuroimaging abnormalities were present in 11 patients. Among those patients with focal EEG pattern, 66.7% had normal neuroimaging exams while all patients with generalized pattern had abnormal neuroimaging exam (p=0.0137). Conclusions: Our data showed that focal pattern is more frequent than generalized pattern in EEG tracings with ESES. Patients with focal EEG pattern had mainly normal neuroimaging exams while all patients with generalized pattern had abnormal neuroimaging exam. Our study suggests that there is a significant correlation between certain EEG patterns and brain structural lesions.

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**Epilepsy**

**ICNC-0094: EEG-FMRI in the evaluation of the epileptogenic zone in patients with Pharmacaco-Resistant Epilepsies**

Objectives: Patients with pharmaco-resistant epilepsies can benefit from surgical removal of the epileptogenic zone (EZ). This study aimed to evaluate the use of concomitant electroencephalography and functional magnetic resonance imaging (EEG-FMRI) in the definition of the EZ of children and young adults with pharmaco-resistant epilepsies. Methods: Children and young adults with pharmaco-resistant epilepsies and EEG-FMRI studies were selected. All had been evaluated for epilepsy surgery. They underwent 20-48 minutes echo-planar imaging sequences in a 3T MRI. EEG was acquired using 64 MRI-compatible electrodes. fMRI data was analyzed with SPM8. Spikes were visually identified and used to define associated blood oxygen level dependent (BOLD) changes. Patients with no epileptiform discharges were not selected. Concordant EEG-FMRI maps were defined as the presence of global statistical maximum BOLD activation in the area of surgical resection or of hypometabolism in FDG-PET. Results: Eight patients fulfilled inclusion criteria: four boys, mean age 18 years (range 12 to 22). Five (63%) were submitted to epilepsy surgery and three (36%) became seizure-free after a mean follow-up of 27 months. The remaining three patients had surgical procedure denied due to multifocal EZ (n=2) or in eloquent cortex (n=1). EEG-FMRI was concordant in 2/3 (67%) of patients submitted to surgery that became seizure-free and in none who continued to have seizures. In patients not submitted to surgery, one had a normal FDG-PET and EEG-FMRI was concordant with the hypometabolism in the other two. Conclusion: EEG-FMRI might be able to identify the EZ in children and young adults with pharmaco-resistant epilepsies.

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**Epilepsy**

**ICNC-0096: Intramuscular dexmedetomidine for pediatric electroencephalography sedation**

Objectives: To describe the efficacy and safety of dexmedetomidine given via the intramuscular route for pediatric EEG sedation. Methods: This prospective observational study included 25 patients for electroencephalography who were given a single or repeated dose of 2 mcg/kg intramuscular dexmedetomidine to achieve a minimum Ramsay sedation score of 4. Patient demographics, medical diagnosis, and vital signs were recorded. Outcome measures were as follows: time to sedation, time to recovery, occurrence of adverse events and quality of eeg recordings. Results: All 25 subjects achieved adequate sedation and completed their EEG studies. The mean time to achieve sedation was 14.68 minutes and the mean time to recovery was 24.16 minutes. Four patients (16%) experienced hypotension while 8 (32%) developed bradycardia, though none required intervention and resolved spontaneously. None had respiratory adverse events or experienced emergence agitation. Achievement of sleep and preservation of background was seen in all recordings allowing adequate evaluation. Conclusions: Intramuscular dexmedetomidine is able to produce adequate sedation for electroencephalography while preserving background activity with minimal adverse events. It is a safe and effective alternative to achieve a technically acceptable EEG especially in patients who are uncooperative, agitated or
those with developmental issues in whom completion of EEG studies present a challenge.

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Epilepsy

ICNC-0097: Epilepsy in children and adolescent in Senegal

Introduction Epilepsy is a public health problem in Senegal, with a prevalence of 8.3 to 14/1000. It mainly affects children. The objective of this work is to study the biographical aspects, phenotypic and evolutionary of epilepsy in a cohort of children in Senegal. Patient and methods This is a retrospective chart review of children with epilepsy followed up regularly at Fann University Hospital and Children’s Hospital Albert Royer, July 2003 to December 2010. Inclusion criteria were: epilepsy aged under 16 years, regularly monitored for at least 3 years, with appropriate treatment, effective dose, with good adherence. Results We collected 522 children, aged 3 months to 16 years, with a sex ratio of 1.7 in favor of boys. The epilepsy was idiopathic in 57% of children and non-idiopathic in 43% of patients. Etiological factors were dominated by parental consanguinity, abnormal pregnancy and childbirth, infections of the central nervous system. In the group of idiopathic epilepsies, parental consanguinity and family history of epilepsy were found respectively in 64 children (21.62%) and 20 children (6.75%). Nine children (3%) had isolated language disorder, while only one child (0.33%) had an overall cognitive deficit. In the group of idiopathic epilepsies not, the signs associated with epilepsy were language disorders (15.70%), behavior (15%) and motor deficits (10.32%). 22.41% of school children had learning difficulties sometimes leading to repetition or school exclusion. Conclusion To have a good treatment and good prevision of prognosis we need to characterize epilepsy in children. Keywords: Epilepsy, Epileptic syndrome, Senegal.

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Epilepsy

ICNC-0098: Epileptic encephalopathies of children about 113 cases

Introduction: Epileptic encephalopathies are conditions in which the neurological deterioration is secondary of the epileptic activities. Our aim is to describe epidemiological aspects, associated signs, and the frequency of the various types of encephalopathies. Patients and Methods: We lead a retrospective study from July 2003 to December 2011. 113 folders of children in the neuropaediatric consultation clinical of Fann University Teaching hospital and Albert Royer Children hospital in Dakar were reviewed. Data analysis was made by SPSS.16.0 Results: We collected 113 folders of patients. The average age was 3 years 2 months with a range of 1 month to 14 years, the sex ratio was 2.3 / 1 in favor of males. The mean age of onset was 11 months. Asphyxia was found in 17.7%, parental consanguinity was 15%. Among our patients, 49.5% had only one type of seizures. Partial motor seizures were found in 42.4%. Initial psychomotor development was abnormal in 61.1%. Motor disorder found in 48.6% of all cases, with axial hypotonia in 23.8%. West syndrome was found in 29% of the POCS syndrome in 7.1%, while Dravet syndrome accounted for 4% of our patients. Medical imaging was normal in 18.6%, with 18.6% of cortico subcortical atrophy. Regarding therapy, 73.45% were boarded on VPA, 81% had necessitated a triple therapy which. We noticed drug resistant in 44.2%, while in 31% seizures were controlled. Academic pursuit was disrupted in all our patients. Conclusion: Epileptic encephalopathies present a problem of drug resistance, and poor prognosis. Cognitive, social and motor disorders hence the need of a multidisciplinary approach. Keywords: Epileptic encephalopathies, Drug resistance, Senegal, Children.

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Epilepsy

ICNC-0462: Unique Characteristics of the Photoparoxysmal Response in Patients with Neuronal Ceroid Lipofuscinosis type 2: Can EEG be a Biomarker

Rationale: Neuronal ceroid lipofuscinosis (NCL) is a heterogeneous group of neurodegenerative disorders which are progressive and fatal. Epilepsy is a core feature of NCL. Often electroencephalograms (EEG) will help identify these patients based on a common feature of a photoparoxysmal response to intermittent photic stimulation. We aim to identify unique features of the photoparoxysmal response seen in patients with NCL as compared to patients with a photoparoxysmal response due to other epilepsy syndromes. Methods: The electronic medical record database was searched for patients with NCL type 2 seen at our institution in the last 10 years. Concordantly, EEGs reported to have a photoparoxysmal response during a single year were reviewed. All EEGs were reviewed by two neurophysiologists (DVA
and JV). Results: The search yielded 33 non-NCL EEGs and 35 EEGs from 15 NCL type 2 patients. A photoparoxysmal response was seen in 60% of the patients with NCL type 2. The NCL responses were seen most commonly with low frequency intermittent photic stimulation (76%) which often occurred in a time-locked fashion (63%) and were seen on the patient’s initial EEG (78%). A unique pattern the authors called “sentinel” discharge was identified in 30% of EEGs in patients with NCL. All of the NCL patients had associated sleep abnormalities (100%) and many had waking background abnormalities (84%). This is contrasted to patients without NCL, where the response was most commonly seen during high frequency photic stimulation (91%, p-value <0.0001) and was associated with normal background activity (94%, p-value <0.0001). Conclusions: Photoparoxysmal responses are common in patients with NCL type 2 and have features which are distinguishing from photoparoxysmal responses seen in other epilepsies. In the era of genetic and molecular understanding of NCL, enzyme and gene-targeting therapies are on the horizon. It is now more than ever, critical to identify patients with NCL early in their course when potentially disease-modifying treatments may be feasible

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Epilepsy
ICNC-0101: Safety and tolerability of lacosamide as adjunctive therapy in children with partial-onset seizures
Introduction: This study evaluated the safety and tolerability of adjunctive lacosamide in children with partial-onset seizures (POS). Methods: This multinational, open-label, dose-titration trial (SP0848; NCT00938341) enrolled patients aged 1 month to 17 years with uncontrolled POS to receive lacosamide at 2mg/kg/day and titrated in 2mg/kg/day weekly increments to maximum tolerated or cohort-defined dose. An initial cohort (n=8; 5-11 years) received up to 8mg/kg/day lacosamide, which determined dosing (≤12mg/kg/day; ≤600mg/day) for remaining cohorts (12-17 years; 2-4 years; 5-11 years; 1 month to <2 years). Patients were discontinued if they did not achieve the cohort-defined maximum dose or for other reasons; but could continue in a long-term study (SP0848; NCT00938912). Results: Of 47 enrolled patients (mean age 7.0 years, 51.1% female, mean time since diagnosis 4.3 years, 78.7% taking ≥2 concomitant AEDs), 24 (51.1%) completed; 40 (85.1%) planned to enter the long-term study. Mean lacosamide treatment duration was 40.4 days; 89.4% of patients reported ≥1 treatment-emergent adverse event (TEAE), most frequently vomiting (21.3%), diarrhea (14.9%), somnolence (12.8%), irritability (10.6%), dizziness (10.6%) and pyrexia (10.6%). 20 (42.5%) patients discontinued due to TEAEs, most frequently vomiting (8.5%), gait disturbance (6.4%), dizziness (6.4%) and somnolence (6.4%). 6 (12.8%) patients reported serious TEAEs, most commonly status epilepticus (6.4%). No deaths were reported. Conclusion: This study supports the safety of adjunctive lacosamide in children (aged 1 month to 17 years) with POS. The TEAE profile was generally consistent with that observed in previous lacosamide studies in adults. More flexible titration schemes may improve tolerability. Sponsor: UCB Pharma-sponsored.

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Epilepsy
ICNC-0102: Pure red cell aplasia - a rare hematological side effect of valproic acid
Background: Pure red cell aplasia is a rare hematological side effect of valproic acid. Case characteristics: A 1.5-year-old female child developed pure red cell aplasia within three months of introduction of valproic acid. Outcome: Patient showed improvement in hemoglobin just after discontinuation of valproic acid. Message: Pediatrician neurologists should be aware of such a rare side effect of valproic acid.

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Epilepsy
ICNC-0103: Adverse reactions of anti-epileptic drugs in children and young people
Introduction: This study aims to evaluate the safety and tolerability of antiepileptic drugs (AEDs) in children. Methods: Paediatric Epilepsy Clinic patients ≤18 years, on AEDs were consented and enrolled, September through December 2015. Adverse events (AEs) thought to be possible adverse drug reactions (ADRs) to AEDs in the preceding 3 months were actively elicited from parents and participants using the modified paediatric epilepsy side effect questionnaire. Chi² analysis was used. Results: 97 participants were recruited, mean age 10 years (SD 4.9). 25/97 (26%) had learning disabilities. 15 different AEDs were prescribed either as monotherapy or polytherapy. 43/97 (44%)were taking polytherapy: 30/97 (31%) were on two AEDs, 11 (11%) 3 AEDs and 2 (2%) received 4 AEDs. 45/97 (46%) received levetiracetam, 32/97 (33%) sodium valproate, 17 (17%) carbamazepine, and 14 (14%) lamotrigine. A total of 803 AEs

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were recorded in 86/97 (90%) children. Attention difficulty was the most frequently reported AE with levetiracetam (25/45, 56%), and sodium valproate (20/32, 63%). Bradyphrenia (slow thinking) (11/14, 79%) and fatigue (12/17, 71%) were the most common AEs with lamotrigine and carbamazepine, respectively. Slow thinking was reported significantly more often with lamotrigine than levetiracetam (p=0.02). Increased appetite was more often reported with sodium valproate than with levetiracetam (p=0.04). Conclusion: This is an ongoing study. The preliminary results confirm that neurological problems are the most common AEs associated with AEDs. We will undertake careful analysis for causation, as we suspect this method may be leading to over-reporting of “unrelated AEs” and “possible ADRs”.

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Epilepsy
ICNC-0104: Ketogenic diet in management of Intractable Epilepsy: An Egyptian experience
Intractable or drug-resistant epilepsy constitute around 35% of cases encountered in our Paediatric-Neurology outpatient clinic Ain-Shams University Hospital. Before 2011, ketogenic diet has been used in treatment of drug-resistant epilepsy on very small scales and in sporadic trials in Egypt. In 2011, we started our ketogenic diet clinic by a research work comparing Modified Atkins diet (15 patients) versus classic ketogenic formula (10 patients) in treatment of patients with intractable epilepsy and its effect on anthropometric parameters (weight, length/height, body mass index) as well as lipid profile. We followed-up the frequency and severity of seizures at 3 and 6 months. All our patients (100%) showed improvement on both types of diet with mean reduction of frequency of seizures (57.9% & 70.79%) in patients on ketogenic formula and 40% & 61% in patients on modified Atkins diet. There was no affection of lipid profile along the study, while there was increase in body mass index in both groups. It is worth mentioning that both types of diet were safe, tolerable and effective. In another study, later on, 3 patients with glucose I transporter deficiency and 3 patients with Tuberus sclerosis, similar results were obtained for anthropometric measures; seizures ceases completely after 3 months of therapy. We also studied the effect of ketogenic diet on the quality of life of patients with drug-resistant epilepsy and we demonstrated realised a significant improvement in the quality of life. Regarding side effects of the diet, they were all easy to control in all our patients as constipation, and vomiting. Yet, we detected a risk of renal stone formation, as two patients out of 20 patients developed renal stones after 6 months of start of the diet. To be mentioned, we were not using K citrate as a prophylactic measure before this study, but it is used on regular basis currently. We concluded from our 4-years experience that there is an emergency support for the broad use of different protocols of ketogenic diet as an efficient, safe, tolerable and easy to apply line of therapy for patients with drug-resistant epilepsy. Intractable or drug-resistant epilepsy constitute around 35% of cases encountered in our Paediatric-Neurology outpatient clinic Ain-Shams University Hospital. Before 2011, ketogenic diet has been used in treatment of drug-resistant epilepsy on very small scales and in sporadic trials in Egypt. In 2011, we started our ketogenic diet clinic by a research work comparing Modified Atkins diet (15 patients) versus classic ketogenic formula (10 patients) in treatment of patients with intractable epilepsy and its effect on anthropometric parameters (weight, length/height, body mass index) as well as lipid profile. We followed-up the frequency and severity of seizures at 3 and 6 months. All our patients (100%) showed improvement on both types of diet with mean reduction of frequency of seizures (57.9% & 70.79%) in patients on ketogenic formula and 40% & 61% in patients on modified Atkins diet. There was no affection of lipid profile along the study, while there was increase in body mass index in both groups. It is worth mentioning that both types of diet were safe, tolerable and effective. In another
study, later on, 3 patients with glucose I transporter deficiency and 3 patients with Tuberous sclerosis, similar results were obtained for anthropometric measures; seizures cease completely after 3 months of therapy. We also studied the effect of ketogenic diet on the quality of life of patients with drug-resistant epilepsy and we demonstrated realised a significant improvement in the quality of life. Regarding side effects of the diet, they were all easy to control in all our patients as constipation, and vomiting. Yet, we detected a risk of renal stone formation, as two-patients out of 20 patients developed renal stones after 6 months of start of the diet. To be mentioned, we were not using K citrate as a prophylactic measure before this study, but it is used on regular basis currently. We concluded from our 4-years experience that there is an emergency support for the broad use of different protocols of ketogenic diet as an efficient, safe, tolerable and easy to apply line of therapy for patients with drug-resistant epilepsy.

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Epilepsy

ICNC-0106: Urinary and fecal incontinence during levetiracetam therapy
Introduction: Levetiracetam (LEV), an antiepileptic drug, has become widely used in the treatment of several types of epilepsy. It is used as an adjunctive therapy in the treatment of partial onset, myoclonic and/or primary generalized tonic-clonic seizures. Adverse effects include somnolence, and behavioral changes are usually mild to moderate. We report urinary and fecal incontinence not related to seizures in a child treated with LEV. Case Description: A 11-year-old boy presented with a history of urinary and fecal incontinence since last 10 days to our hospital. On medical history, he had nocturnal isolated seizures, followed by a postictal motor deficit at the right arm since 1 month. LEV had started for his seizures and his seizures were stopped. Three weeks after starting LEV therapy, he experienced daily urinary and fecal incontinence. We thought LEV may be the cause of his complaints and stopped LEV therapy. His urinary and fecal incontinence had completely resolved after discontinuation of LEV. Conclusion: Children treated with LEV should be warned regarding these potential adverse effects, to facilitate early withdrawal of drug.

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Epilepsy

ICNC-0107: ACTH versus Vigabatrin as first line treatment for West syndrome – A prospective study
Abstract: West syndrome represents a seizure disorder with unique clinical and electroencephalographic (hypsarrhythmia) features. The study was done to compare the efficacy of corticotropin (Inj ACTH, deep I/M 3 IU/kg/day) and Vigabatrin (50 mg/kg/day), in suppressing clinical spasms in untreated West syndrome. It was a randomized, prospective study done in 1 year period. Among sixty patients, group A was randomly given inj ACTH and group B was given oral Vigabatrin as per dose schedule. Among the patients 36(60%) were less than 3 months of age, 20(33%) children were in 3 to 6 month of age and 4 cases (7%) were in 6 to 9 month of age. Perinatal asphyxia was the commonest cause in both groups. In both groups abnormal findings of CT scan and MRI of brain were found in 78.3% cases and hypsarrhythmia was the most common EEG finding. 31 patients were treated with ACTH and 29 with vigabatrin(VGB). Cessation of spasms was observed in 12 (41.37%) of the patients randomized to VGB and in 14 (51.61%) of those randomized to ACTH. In ACTH group 32% developed side effects while in VGB group 13 % developed side effects which were statistically significant. (p value < 0.05 ). Conclusion: Our data support that Vigabatrin may be considered as a first line drug giving emphasis to the response and decreased side effects.

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Epilepsy

ICNC-0108: Clinical Spectrum, electrophysiologic profile and medical treatment of children with Nonconvulsive Status Epilepticus
Introduction: Nonconvulsive status epilepticus (NCSE) is a term used to denote a range of conditions in which electrographic seizure activity is prolonged and results in nonconvulsive clinical symptoms. Methodology: This study was done to describe the clinical spectrum, EEG findings and evaluate the efficacy of different therapeutic agents in children with NCSE in 33 patients in 2011 to 2015 period. All patients had EEG before and after treatment. Age range was 6 months to 14 year, 25 were male. Thirty two patients had prior seizure. Regarding development status, 48% had developmental delay, 21% had normal development, 9% had regression and 21% had both developmental delay and regression. The cases were previously diagnosed as epilepsy (29). EEG diagnosis was as follows: Electrical status epilepticus in slow wave sleep (ESES) 16 (48.5%), Generalized NCSE 13(39%). Focal NCSE 3(9%) and Lennox Gastout
syndrome 1 patient (3%) Eighteen patients were treated with Midazolam drip out of which 1 patient had complete remission in EEG, 6 had >80% remission, 5 had >50% remission and 5 patients had minimal or no response. Thirteen patients were treated with methyl prednisolone bolus out of which 2 patients had complete remission, 4 patients had >80% remission while 4 patients had >50% remission and 3 patients showed no response. Conclusion: This study provides clinical criteria and treatment protocol of NCSE and also highlights that intravenous drugs were more effective than oral antiepileptic drugs in remission.

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Epilepsy

ICNC-0109: Three children with coexisting focal and generalized epilepsy: importance of seizure semiology in management
Objective: To review the characteristics of pediatric patients with coexisting idiopathic focal and generalized EEG discharges and its impact on AED selection and seizure control.Method: Chart review of clinical and radiological characteristics of identified children with epilepsy below 15 years of age who had EEGs done in our center between Jan 2011- December 2015 with coexisting focal and generalized epileptiform activity.Result: 3 patients were identified. All had EEG findings of coexisting focal Centro-temporal spikes as well as generalized 3 HZ spike and slow discharges consistent with benign Rolandic epilepsy and generalized absence epilepsy respectively. All had initial semiology of focal Rolandic type seizures; 2 were treated with a sodium channel blocker and 1 was treated with Topiramate. All had emergence of typical absence seizures while on treatment or upon assessment for possible weaning off AED therapy for their focal epilepsy. All patients were successfully switched to absence targeted AED therapy with full control and no relapse of their focal seizures. All had normal neurological exam and brain MRI.Conclusion: Coexistence of primary focal and generalized epilepsies occurs infrequently in people with epilepsy. Children on AED therapy for primary epilepsy who develop seizures after initial control should be evaluated for the possibility of emergence of a new seizure type. The treatment has to be guided by the active seizure type in order to avoid worsening of seizures and potentially pseudo refractoriness.

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Epilepsy

ICNC-0110: Risk factors of vitamin D deficiency in Malaysian children with epilepsy
Introduction: Long-term use of antiepileptic drugs (AEDs) is a significant risk factor for vitamin D deficiency and impaired bone health. The objectives of this cross-sectional study was to: i) determine the prevalence of vitamin D deficiency in children on long-term AEDs in Malaysia, and ii) identify risk factors for vitamin D deficiency in this cohort of patients.Methods: Cross-sectional study of children with epilepsy aged between 4-18years old and on long-term AEDs for >1 year had assessment of their sun exposure behaviour, physical activity, dietary intake, anthropometric measurements and bone health blood tests (including vitamin D levels). Vitamin D deficiency was defined as 25(OH) D levels <37.5nmol/L and insufficiency 37.5-50nmol/L. Results: Total of 250 children (150 males) were recruited. Age ranged 3.7–18.8 years. 25(OH)D levels ranged between 7.5–140.9 nmol/L (mean 58.7 nmol/L). Vitamin D deficiency was identified in 56/250 (22.4%) and an additional 50/250 (20%) had vitamin D insufficiency. Statistically significant multivariate analysis of risk factors P<0.05 identified vitamin D deficiency was more likely to be seen in children on polytherapy on 2 AEDs (OR: 3.14) and >2 AEDs (OR: 3.83); age > 12.7 years (OR 2.59); Indian ethnicity (OR: 5.27); lower sun exposure time / week with Q1 scores (OR:22.66) and Q2 scores (OR: 15.021); and among females (OR 2.952).Conclusion: Despite living in the tropics, a high proportion of Malaysian children with epilepsy risk vitamin D deficiency (22.4%) and insufficiency (20%). Children on long-term AEDs with particular risk factors of polytherapy, female, lower sun exposure time / week and age > 12 years old are at higher risk of vitamin D deficiency. Tailored lifestyle modification and vitamin D supplementation are essential in the management of all children on long-term AEDs in Malaysia. Acknowledgement: This research study received funding from the University of Malaya research grant (P0026/2013A and UMRG 532-13HTM)

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Epilepsy

ICNC-0111: Knowledge, attitude and beliefs about epilepsy among parents attending neurology clinic with their children in a tertiary institution

Background: This study was designed to examine the knowledge, attitude, and beliefs about causes, manifestations, and treatment of epilepsy among parents bringing their children for treatment in a tertiary hospital. Methods: A pre-tested, structured questionnaire was administered to 200 parents in the neurology clinic in University of Port Harcourt Teaching hospital. Results: Majority of the respondents (59.0%) mentioned that epilepsy is manifested by convulsions. Other manifestations of the disorder proffered by the respondents included falling down (36.0%), rolling of eyes (15.3%) and foaming of mouth (10.3%). Up to 40% of respondents did not know the cause of epilepsy. Heredity was identified as a cause of the disorder by (29%), followed by brain injury (19.2%), possession by evil spirits (16.3%) and brain infection (11.7%). Overall (n=52, 26%) of the respondents had good knowledge of epilepsy whereas (n=62, 31%) and (n=86, 43%) had fair and poor knowledge of the disease respectively. Majority of respondents (47.0%) opted for spiritual healing. This was followed by orthodox medical care (34.0%) and the use of traditional herbal medicines (19.0%). Majority of respondents harboured positive attitudes such as tolerance, kindness and sympathy towards epileptics. Literate respondents were more likely to exhibit positive feelings towards epileptics when compared to non-literate subjects (χ² = 31.5 df = 1 P< 0.001). Conclusions: The low level of knowledge and misconceptions demonstrates the need for community educational programmes aimed at demystifying epilepsy with a view to allaying fears and mistrust about the disease as well as lessen stigmatization towards epilepsy.

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Epilepsy

ICNC-0956: Presentation early electroencephalography is useful in epilepsy management

Introduction An early electroencephalography (EEG) to be done within 48 hours is an important diagnostic tool after a first seizure presentation. But it may not be readily available in many settings. In this review, we will review the diagnostic yield of early EEG in a tertiary hospital in Hong Kong. Methods This was a retrospective study. Patients who were admitted from 1 Oct 2014 to 31 Oct 2015 for first seizure/ recurrent seizures without previous history of epilepsy were recruited. The EEGs were performed within 48 hours of seizure. The demographic data, clinical presentation and EEG data were analyzed. Results A total of 42 EEGs were performed in 41 patients. One patient had a normal EEG after first seizure and then another EEG after second seizure, which occurred six months apart. 50% of them showed various abnormalities: focal epileptiform discharges in six, clinical and electrographic evidence of absence epilepsies in two, infantile spasms with clinical seizures in four, typical centro-temporal spikes of rolandic epilepsy in five and focal slowing in four. The EEG information was very useful in management. It allowed prompt and accurate counseling on recurrence risks, diagnosis of specific syndromes and advice on appropriate treatment. Conclusion/ discussion Early EEG demonstrates a high diagnostic yield with useful information. The practicability should be further assessed as it may eventually save money. Acknowledgement The EEG resource was supported by S.K. Yee Medical Foundation

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Epilepsy

ICNC-0112: Clinical feature and gene mutation analysis of 13 cases with Dravet syndrome in china

Introduction: Dravet syndrome is an epilepsy syndrome of infantile onset, frequently caused by SCN1A mutations or deletions. To investigate the clinical characteristics and gene mutations of 13 cases with Dravet syndrome in China. Methods: The clinical data and peripheral blood DNA of DS patients and their parents were collected, and more than 200 epilepsy genes sequencing was performed using next-generation sequencing. The enrichment libraries were sequenced on an Illumina HiSeq 2000 sequencer using paired read 100 bp sequencing. If one’s gene mutations were detected, his parents’ blood would be analyzed by the sanger method to detect the mutation. Result: Among the 13 children, 7 were male and 6 were female. The onset ages ranged from 5 to 11 months. The median onset age of 8 months. First onset of 9 cases had at least one characteristic of complicated febrile seizures (CSF). In the first year after onset: 2 cases had abnormal EEG, 3 cases had abnormal cranioencebral MR, 3 cases had status epilepticus, and 7 cases showed at least three characteristics of CSF. In the three years after onset, 8 cases had abnormal EEG, 3 cases had abnormal cranioencebral MRI, 8 cases had status epilepticus (SE), and 11 cases showed at least three characteristics of CSF. 8 cases of children had SCN1A mutations only, 1 case had SCN1A SCN9A and KCNQ2 mutations, This case than other children with DS has more complex clinical characteristics, 1 cases detected SCN1A and
SLC6A8 mutation, 1 cases detected SCN1A and TSC2 mutations, and 1 family SCN1A mutations were found. Conclusion: DS always onset with CSF, and tended to had SE, while EEG and MRI were always normal. The most common mutation was SCN1A gene mutation, and some accompanied with SCN9A, KCNQ2, SLC6A8, TSC2 gene mutations. The onset of SCN9A may participate in the DS with SCN1A process. Whether other combined mutations of genes have influences on DS need further study. References: 1.Wu YW et al. ANNALS OF NEUROLOGY.2015,78 S155-S155. 2.Rosander C et al.DEVELOPMENTAL MEDICINE AND CHILD NEUROLOGY.2015,57(7):628-633.

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Epilepsy
ICNC-0113: Protocadherin 19 (PCDH19) female limited epilepsy: two case reports
INTRODUCTION: Mutations in PCDH19 on chromosome Xq22.1, cause familial epilepsy and intellectual deficits limited to females or Dravet-like syndrome. PATIENT: CASE 1: 15 months female infant with onset of fever and clustering of generalized seizures. Consciousness was not altered. Head CT, brain MRI, infectious and metabolic screening: normal. EEG: multifocal spikes, predominantly right-sided. Later in evolution persists febrile and afebrile brief seizures with clusters. She was treated with various antiepileptic drugs: Phenytoin, Valproate, Oxcarbazepine, Levetiracetam and Clobazam. Neurological examination revealed mild developmental delay. Molar analysis of the PCDH19 gene identified novel pathogenic mutation: c.707C>T.p. Pro236Leu. CASE 2: 11 month female presented with recurrent focal and generalized seizures. Context of gastroenteritis, afebrile. Head CT, brain MRI, infectious and metabolic screening: normal. EEG: generalized slow spike wave discharges. Seizures were partial controlled with Phenytoin, Valproate, Levetiracetam. After one year without seizures she was hospitalized with recurrent seizures. She was treated with Carbamazepine and Clobazam. Later in her evolution persists seizures, especially focal, often with fearful screaming. She presented motor and speech delay, hyperactive and impulsive behavior. Molecular analysis of the PCDH19 gene revealed one heterozygous variant without classification c.703_705delAAP; p. (Asn235del). CONCLUSIONS: In infantile female the pattern of seizure clusters, which are reminiscent of a type of organic encephalitis, may be a key feature that suggests the presence of PCDH-19 epilepsy, and genetic analysis should be considered in such cases. Early diagnosis may help avoid excessive treatments and provide better clinical management.

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Epilepsy
ICNC-0073: The “know-how” of starting a Ketogenic diet program in a developing country
Currently our country has limited treatment options for patients with intractable epilepsy. Implementation of a ketogenic diet (KD) program is important particularly in the area of provision of choice to patients as well as the kindling of research interest in the diet. Methods: The establishment of a KD program requires a considerable amount of organization such as team building, development of treatment protocols, educational materials, as well as surveys to evaluate the response to therapy. Clinical outcomes like: seizure control, adherence to medications and dietary preferences of 59 patients with intractable epilepsy were evaluated. Twelve of 59 children were selected as candidates for a trial of classic KD. Results: A KD program was designed and received ILAE Comission on Medical Therapies recognition. This initiative is the first dietary program of such kind in the region. KD program implementation included training and site visits with experienced international teams from UK, South Africa, Canada and USA. Our team has attended Fourth Biannual Ketogenic Dietary Therapy Global Symposium in Liverpool, UK. A pediatrician knowledgeable about the KD was designated as team leader. Core team members are nutritionist, nurses and social workers. Groundwork work was performed to import and register KD nutritional supplements in the country. Conclusions: If effectively implemented, as intended, our program has the potential to facilitate a substantial reduction in the epilepsy treatment gap and improve the quality of epilepsy care in resource-limited settings. Local recipes could be identified and, possibly, formulations unique to the region also developed.

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Epilepsy

ICNC-0280: Epilepsy with phantom absences: long-term follow-up
Introduction. Generalized epilepsy with phantom absences is an unrecognized syndrome characterized by absences that are inconspicuous and never appreciated prior to the onset of GTCS which is commonly the first overt clinical manifestation usually starting in adulthood as well as frequent absence status epilepticus. Phantom absences fulfill the criteria of typical absences with more than 2.5-Hz generalized spike and wave discharges. There are suggestions that phantom absences may be a separate syndrome within the wide spectrum of genetic generalized epilepsies. Case report. We report the girl who was diagnosed with idiopathic generalized epilepsy at the age of 3 years in 1999 because of single event characterized by confusional state lasting about 20 minutes followed by short tonic seizure and frequent, spontaneous and hyperventilation-induced generalized 3.5-4 Hz spike/multiple spikes and slow waves discharges of 1-4 sec duration. Treatment with valproic acid was started and continued for 8 years. During treatment period video-EEG recordings were performed yearly (til 2007) with the same constant findings. Clinically nobody observed absences although instructed, her development was normal. Patient was invited for follow-up visit at the age of 20: she continued to be seizure free, neurological examination was normal except mild positional tremor. Video-EEG recorded hyperventilation-induced generalized 4.5-5 Hz spike and slow wave discharges 1-2 sec duration without photosensitivity. Conclusion. Epilepsy with phantom absences may start in early childhood and persist during adulthood. Long-term follow up reporting may help define new syndromes and allow of better understanding of management needs and prognosis.

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Epilepsy

ICNC-0114: From Somatosensory Reflex Epilepsy to Dravet Syndrome: Different clinical features due to novel SCN1A mutations of the p.Q422P amino-acid
Introduction: Dravet syndrome (DS, also known as Severe Myoclonic Epilepsy of Infancy) is a severe epileptic encephalopathy of the early childhood. Patients with Dravet syndrome have multiple seizure types during the course of the disease. Seizures often provoked by fever; less frequent precipitating factors are flashes of light, physical exercise, emotions and other individual stimuli. We report a case of a 10-month-old girl presented with reflex epileptic seizures provoked by somatosensory stimuli with a novel de novo mutation of SCN1A gene. Case: A 10-month-old female patient was admitted to hospital with eye deviation, unresponsiveness, that occurred several times daily over a period of 20 days. Her psychomotor development was delayed. Video-electroencephalography (EEG) revealed generalized spike-and-wave patterns. Her seizures were temporally controlled by the administration of valproate. After a while, she had febrile and afebrile epileptic seizures. At 16 months old, she had an unprovoked prolonged episode of right hemispheric status epilepticus. Interictal EEG showed sharp waves in left occipital area with a normal background. We found a de novo heterozygote mutation in SCN1A gene, c.1337A>C (p.Q422P). To our knowledge, this mutation has not been previously described and also this is the first report of Dravet syndrome as a presenting with reflex epilepsy of somatosensory stimuli. Conclusion: Dravet syndrome is an intractable epileptic encephalopathy that can present with different seizure types including reflex seizures provoked by somatosensory stimuli. We describe a case of Dravet syndrome presenting with reflex seizures. Reflex epilepsy have been reported in one patient with Dravet syndrome provoked by music, but to our knowledge this has not been described seizures trigged by somatosensory stimuli.

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Epilepsy

ICNC-0314: Approach to a child with the first unprovoked seizure
The approach to a child who has experienced a first unprovoked generalized tonic-clonic seizure is challenging and at the same time controversial. The approach to a child who has experienced a first unprovoked generalized tonaclonic seizure is an important endeavor in daily clinical pediatric neurology practice. If occurrence of an ictal event is established, the main question is whether treatment by Anti Epileptic Drugs (AED) should be initiated or not? The main reason for prescribing AED is to prevent further seizure. Thus such therapy is justified when there is reasonable chance seizure will recur. Deciding to initiate treatment requires balancing the risk of drug side effects against the psychosocial consequences of future convulsions. Knowing that treatment does not ensure that seizure will not recur and that it merely lowers the probability of recurrence, it behooves us to think twice about initiating AED therapy. As we discuss the subject of first unprovoked seizure (FUS) it is necessary to have a clear-cut understanding of FUS How to establish the diagnosis, ways and means of investigation and whether treatment is appropriate, are different aspects of this subject. In this writing the above mentioned matters are discussed.
Epilepsy

ICNC-0115: Early onset epileptic encephalopathy: importance of genetic diagnosis in the management, single center experience

Introduction: we describe clinical presentation, genetic analysis, therapeutic response and outcome of 87 patients with early onset epileptic encephalopathy seen at our Institution from October 2014 to December 2015. Methods: patients were studied with videoEEG, clinical and MRI follow-up, genetics investigations as array CGH and genetic panel for epileptic encephalopathies (including 19 pathogenetic genes). Results: 14/87 patients had the onset and were seen for the first time last year, the others came for follow up visits. 26/87 were diagnosed with Dravet Syndrome (16 SCN1A, 1 SCN1A + SCN2A mutations, 3 with Array CGH alterations), 33/87 presented with West Syndrome: 13/33 symptomatic (21 trisomy, tuberous sclerosis, ATRX syndrome, focal lesions, post-hemorrhagic or hypoxic-ischemic damage), 20/33 with unknown etiology; 6 performed genetic panel, 1 with SCN2A variant, 5 are in progress. 28/87 were classified as other form of EE. 4 have CDKL5, 2 variant TBC1D24, 2 KCNQ2, 1 ATRX, 1 KCNT1, 1 SCN8A, 1 Angelman, 1 Smith Magenis, 1 Williams Syndrome, 1 mitochondrial pathology, 3 have cerebral malformations, 1 SPTAN, 1 tuberous sclerosis, 3 with negative genetic panel. Conclusion: in many cases electroclinic characteristics of early onset EE do not permit specific syndrome diagnosis. Moreover, the same genetic defect can be related to different clinical pictures. The etiologic diagnosis is essential for clinical and therapeutic management. The diagnostic pathway requires not just neuroimaging, biochemical, metabolic but also wide genetic investigations.

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Epilepsy

ICNC-0117: ACTH x vigabatrin: a comparative study on the treatment of infantile spasms

Introduction: Infantile spasms (IS) are an epileptic encephalopathy of infancy characterized by epileptic spasms, developmental delay and often hypsarrhythmia. The patients do not respond to conventional antiepileptic drugs, requiring the use of ACTH, prednisolone or vigabatrin (VGB). We aim to compare the effectiveness of ACTH and VGB in the treatment of IS. Methods: retrospective analysis of 37 medical records of patients with new onset IS was performed. Twenty-four patients received VGB, and 13 were treated with ACTH. The patients were matched for age of onset of seizures, elapsed time from onset and treatment, and etiology. Both groups were compared according to the time of response, seizures control in the first 14 days of treatment, and seizure control within the first 12 months. Categorical and continuous variables were assessed using the chi square test and Student t test, respectively. Results: Our analysis did not highlighted differences between the ACTH/VGB groups in any of parameters studied. The control of short-term spasms (14 days) and long term responses (12 months), were similar between the two groups. Short-term control was achieved by 91.6% ACTH and 70.8% VGB group (p=0.16). Long-term control was achieved respectively by 87.5% and 65.2% (p=0.23). Time elapsed between the introduction of treatment and seizure-freedom was similar (4.3 days ACTH group and 2.7 days VGB group, p=0.067). Conclusions: The effectiveness of ACTH and VGB are similar in the treatment of infantile spasms.

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Epilepsy

ICNC-0184: Efficacy of Nitrazepam in children with infantile spasms

Objective: ACTH, prednisolone and vigabatrin are considered the mainstream treatment for Infantile Spasms (IS). However, some patients present refractory spasms and other antiepileptic drugs should be considered as second line therapy. Nitrazepam is an antiepileptic drug used in several types of epilepsy, including IS. The objective of this study was to evaluate the efficacy of nitrazepam as add on therapy in children with IS. Method: This was a retrospective study conducted at our University Hospital. Data was collected from clinical files and follow up visits. Inclusion criteria were: age younger than 18 years-old, diagnosis of IS, and current use of nitrazepam. The data was compared with a disease
control group of epileptic patients without current use of any benzodiazepine. Results: Eighteen patients were included (11 boys, age between 6 months and 6 years-old, mean = 2.5 years-old). Improvement in seizure control was present in 15/18 (83.3%) patients. The improvement rate ranged from 0 to 50% in 3 patients (20%), from 50 to 75% in one patient (6.7%), and from 75% to 100% in nine patients (60%). Two patients (13.3%) presented complete seizure control after introduction of nitrazepam. Conclusion: Nitrazepam is highly effective in children with IS and should be considered as add on therapy in patients with refractory spasms.

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Epilepsy
ICNC-0118: Effect on serum vitamin D levels and bone mineral density in children aged 3 to 14 years with newly diagnosed epilepsy on 6 months of Valproate monotherapy - a longitudinal study
Introduction The prevalence of hypovitaminosis D (<21ng/ml) varies between 25% and 75% in children with epilepsy with varying degrees of ambulation, nutrition, duration of epilepsy and number of antiepileptic drugs. Studies evaluating effect of valproate monotherapy on vitamin D levels and bone mineral metabolism are few and with heterogeneous results. Methods The study was conducted in a tertiary care teaching hospital in North India. Total body bone mineral density (BMD) measured using DEXA scan (Dual Energy X-ray Absorptiometry) and analysis of serum 25 hydroxy (OH) vitamin D, parathormone, calcium, phosphate and alkaline phosphatase were done at baseline and at 6 months follow up in 52 children, aged 3-14 years, with newly diagnosed epilepsy on valproate monotherapy. Results The decline of mean serum levels of 25 OH vitamin D at 6 months compared to baseline was by 28.8% (p= 0.0053). Hypovitaminosis D (<20ng/mL) was seen in 76% of study subjects at baseline compared to 92% at 6 months follow up (p=0.028). However the difference between mean BMD z score at baseline (0.64 + 1.73) and at 6 months follow up (0.62 + 1.76) was statistically not significant (p =0.73). Correlation between mean serum vitamin D levels and mean trough serum valproate levels at 6 months follow up was statistically not significant (P Value = 0.29). Conclusion Valproate monotherapy in children with epilepsy is possibly associated with impaired bone mineral metabolism. However changes in BMD z score will be appreciable only in studies with longer follow up.

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Epilepsy
ICNC-0120: Cardiological problems in children admitted to the Video-EEG monitoring
Introduction: The interaction of the heart and brain in patients with epilepsy has been widely studied. On the other hand nonepileptiform paroxysmal events owing to cardiac pathology may be misdiagnosed as seizures. Methods: We retrospectively reviewed the patients who were admitted to the video-EEG monitoring unit and were consulted by cardiologist during the admission. Results: We studied 75 patients who were admitted between January 2006- May 2014. The median age was 9 years (3 months- 17 years); 18 patients (%24) had non-epileptiform paroxysmal events, 57 (%76) had epilepsy. The majority of causes leading to cardiac consultation were ictal/interictal dysrhythmias in 28 patients (%37.3), syncope in 13 patients (%17.3). Seven of 56 echocardiogram studies revealed abnormal findings. Continuous ambulatory Holter ECG monitoring was obtained in 43 patients and 16 were abnormal. Ten of 16 had mild abnormalities with unclear clinical significance. The remaining 6 had more severe findings including frequent ventricular extrasystole (VES), frequent VES with ventricular tachycardia, frequent VES with aberrant supraventricular tachycardia, frequent VES with frequent supraventricular extrasystole, and long QT syndrome. These patients also had a diagnosis of epilepsy and subsequently underwent close cardiological follow up due to the underlying dysrhythmia. Two patients with known epilepsy were found to have cardiac dysrhythmia, and one patient with known cardiac dysrhythmia was diagnosed to have epileptic seizures during admission. Conclusion: The detection of cardiac problems is crucial in patients who are referred for video-EEG monitoring for correct management of the underlying disease.
Epilepsy
ICNC-0122: Efficacy and safety of oral Lacosamide in drug resistant seizures in children

INTRODUCTION: To evaluate efficacy and safety of oral lacosamide treatment on children with intractable epilepsy

METHOD: Nineteen children, under 16-year-old, with partial and secondary generalized seizures resistant to conventional anti-epileptic agents were enrolled between May 2014 and February 2015. Efficacy of lacosamide observed retrospectively. RESULTS: 19 patients were included with a mean age of 9.1 (range, 1 and 16). 11 patients (57.9%) were female, whereas 8 (42.1%) were males. The changes in seizure frequency were complete response in 4 (21%), more than 50% reduction in 6 (31.6%), less than 50% reduction in 6 (31.6%) patients and no response in 1 (5.2%) patient. Those patients with focal seizures demonstrated the highest decrease in the frequency of the seizures. Dizziness and sleepiness (2 patients, 10.5%), loss of appetite (one patient, 5.2%) and increase in the frequency of seizures (2 patients, 10.5%) were accepted as possible side effects. CONCLUSION: Lacosamide is a well-tolerated and effective anti-epileptic drug in partial and secondary generalized seizures in children. Multicentric studies are needed to further support the effect of lacosamide in partial, secondary generalized seizures in childhood.

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Epilepsy
ICNC-0123: Pyridoxine dependent epilepsy: Clinical and genetic findings of five Turkish children

Objective: Pyridoxine-dependent epilepsy is a rare autosomal recessive epilepsy, caused by mutations in the ALDH7A1 gene. In the classical form, it is characterized by intractable neonatal seizures responsive to high doses of pyridoxine. Early diagnosis and appropriate treatment is essential for seizure control and neurodevelopmental outcome. Here we present clinical features of five pyridoxine-dependent epilepsy patients from three families. Methods: The medical records were reviewed for seizure type, treatment, magnetic resonans imaging, electroencephalography and genetic findings. Results: Five patients, (3 girls, 2 boys; aged 7 months-15 years), from three families were included. All patients had seizures during the neonatal period between 2-12 days. Four patients from two families had the same mutation in ALDH7A1 gene [c.1597delG (p.A533PfsX18)]. One patient had compound heterozygous mutation (SS47/T192M), not reported before. Severe cognitive impairment was present in one patient whom diagnosis was made at the age of nine, after her newborn sister was diagnosed with pyridoxine dependent epilepsy. Conclusion: Pyridoxine trial is important in neonatal seizures, and intractable seizures in children. Molecular genetic analysis is now becoming widely employed, and confirms the diagnosis of pyridoxine dependent epilepsies.

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Epilepsy
ICNC-0124: Prevalence of sleep disturbances and its effect on health-related quality of life in schoolaged children with and without epilepsy

Purpose: To explore the prevalence of sleep disturbances in school-aged children with partial epilepsy compared to normal children and to find the relation between sleep disturbances and health related quality of life (HRQoL).Methods: In this study, in children with and without epilepsy, the questionnaires SleepDisturbances Scale for Children (SDSC), Medical Outcomes Study-Sleep Scale (MOS-SS), Groninger Sleep Quality Scale (GSQS) and Kidscreen-27 were used to measure respectively sleep (over several time units) and quality of life. The Hague Scales were used to measure the severity of epilepsy. The returned questionnaires of 130 children, 4-10 years of age, treated in the outpatient clinics, and of 161 normal children, of the same age were compared. Additional a comparison of HRQoL was performed in children with and without sleep disturbances, this in both study groups. Results: The sleep was scored worse in children with than without epilepsy. Pathological scores of SDSC (past half year) (T≥70) were seen 12 times more often in children with epilepsy (36.92% vs. 3.01%, p<0.001). HRQoL was scored significantly lower in children with than without epilepsy. Comparison of HRQoL in subgroups children with and without sleep disturbances, resulted in scores below norm in those with epilepsy and also sleep disturbances, significantly lower than those without sleep disturbances. Conclusion: This study confirms the high prevalence of sleep disturbances in children with partial epilepsy compared to children without epilepsy. Quality of life is already lower in children with than without epilepsy, sleep disturbances lead to further worsening.

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ICNC-0125: The effect of carbamazepin and valproic acid on liver enzymes

Introduction: In the countries with limited resources, carbamazepin (CBZ) and valproic acid (VPA) have been first line antiepileptic drugs till now. Aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gama-glytamyl transferase (GGT) could be elevated due to CBZ and VPA hepatotoxicity. The aim of the study has been to evaluate the effect of CBZ and VPA on serum liver enzymes.

Material and methods: The study has included 100 patients, who were treated with CBZ or VPA for at least 12 months. Patients with liver lesion or patients who were treated with other drugs that can induce elevation of liver enzymes have been excluded from the study. The initial serum level of enzymes (AST, ALT, GGT) and after 12 months of treatment have been compared.

Results: 100 patients (57 boys, 43 girls), with the age range 0-15 years, have been treated with CBZ (53/100) and VPA (47/100). One year after treatment, AST was elevated at 9/47 (19.15%) VPA patients and 4/53 (7.5%) CBZ patients (χ²-test = 3.965, p < 0.05). There is statistically significant AST elevation in the VPA group. One year after treatment, ALT was elevated at 9/47 (19.15%) VPA patients and 5/53 (9.4%) CBZ patients (χ²-test = 6.953, p < 0.05). There is statistically significant AST elevation in the VPA group. One year after treatment, GGT was elevated at 7/47 (14.9%) VPA patients and 18/53 (34%) CBZ patients (χ²-test = 4.831, p < 0.05). There is statistically significant GGT elevation in the CBZ group.

Conclusion: There is statistically significant elevation of AST and ALT in VPA group and GGT in CBZ group.

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ICNC-0126: Infantile spasms in patient with neurofibromatosis type

Introduction: Neurofibromatosis type 1 (NF1) is the most common neurocutaneous disease with prevalence of 1 in 4,000 individuals in general population. Infantile spasms occurs in NF1 with a frequency (0.2-0.3%) ten to fifteen-folds higher than reported in general population (0.02-0.05%). We report clinical data and follow-up findings in patient in whom infantile spasms (IS) were associated with NF1. Case presentation: He is a 6 months old male infant of related parents (mother). He was born as 37 weeks of gestation; his birth weight was 3360g. On the skin 25 café-au-lait spots with diameter ranging from few millimeters to 2.5cm were noted. His initial development and growth were normal. He started presenting clusters of sudden, brief, bilateral tonic contractions of the axial and limb muscles 2-3 times a day. Brain magnetic resonance imaging showed no structural brain anomalies. Laboratory examination had no abnormalities. Electroencephalogram at 6 months of age on presentation demonstrated hypsarrhythmia before treatment and remission of hypsarrhythmia occurred 8 weeks after treatment with pulse methylprednisolone. A pulse dose of 25mg/kg intravenous methylprednisolone on each of 3 successive days, followed by 1.5 months oral prednisolone taper. Treatment led to rapid remission of IS within 5 days. Relapse after an initial remission of IS was not occurred and his development was not delayed until 11 months old. A. Pretreatment 6 months old B. Posttreatment 8 weeks after treatment

Conclusion: Initial treatment with intravenous methylprednisolone and oral corticosteroids is a effective approach to IS with NF1 and it can lead favorable neurologic outcomes.

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ICNC-0127: Biomarkers of mesial temporal lobe epilepsy

Mesial temporal lobe epilepsy associated with hippocampal sclerosis is the most common form of partial epilepsy. The aim of this work is to find asuitable biomarker that can help with the diagnosis and prognosis of this intractable form of epilepsy. To achieve this aim, 15 children diagnosed with complex partial seizures and 15 controls with ages from 4-18 years were subjected to a battery of laboratory analysis including: S100B protein, MatrixMetalloproteinase 9, C-Reactive protein, prolactin, together with neuropsychological, radiological and psychometric assessments.

Results: A significant elevation was found in all the biomarkers between the cases and the controls. The performance of the epileptic patients in psychometric assessments were below average. MRI showed typical findings of MTS, EEG showed anterior temporal spikes. A significant negative correlation was found between MMP9 and psychometric test. Another significant negative correlation between seizure severity and biomarkers was found.

Conclusion: Serum biomarkers for neuronal injury are elevated with mesial temporal lobe epilepsy. Cognitive deficits are associated with mesial temporal lobe epilepsy.

KEYWORDS: Mesial temporal lobe epilepsy, Hippocampal sclerosis, S100B, MMP9, CRP, Prolactin, psychometric assessments
Epilepsy

ICNC-0128: Glycosylphosphatidylinositol (gpi) anchor proteins and their role in Epilepsy

Over the last years, disease causing mutations have been described in 12 genes involved in the biosynthesis of the glycosylphosphatidylinositol (GPI) anchor. These constitute a new subclass of congenital disorders of glycosylation, and although each differs in its distinct phenotype they all share central hypotonia, intellectual disability (ID) and epilepsy. We report here a series of seven patients of four families with novel or rare mutations in four different genes involved in GPI-anchor biosynthesis. Patient 1 presented with neonatal seizures followed by infantile spasms, severe ID, hypotonia, cortical blindness, cardiomyopathy and hydronephrosis. Whole exome sequencing (WES) revealed a novel missense PIGN mutation. Patients 2-4, are siblings that presented with mild-moderate ID, portal vein thrombosis and atypical absence epilepsy. Direct sequencing revealed a hypomorph mutation in the PIGM gene promoter that has so far been reported only once. Patients 5-6, are brothers that presented with infantile myoclonic seizures, severe ID, stereotypies, microcephaly, dysmorphism, central hypotonia and peripheral spasticity. WES revealed a novel PIGA missense mutation. Patient 7 presented with severe ID, cataract, stereotypies, microcephaly, dysmorphism, peripheral spasticity and tonic-clonic seizures. WES revealed a novel PGAP1 missense mutation and flow cytometry demonstrated reduced granulocytes CD59 expression. Although all patients featured significant epilepsy, none of them exhibited primary developmental cortical malformation, suggesting their epilepsy is a consequence of the GPI-anchor defect. We hypothesize that decreased activity of the GPI-anchored alkaline phosphatase which causes reduced neuronal levels of the Glutamate decarboxylase co-factor pyridoxal phosphate, might serve as a common epileptic mechanism of these diseases.

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Epilepsy

ICNC-0129: ADCK3 mutations with childhood onset epilepsy, stroke-like episodes and progressive cerebellar ataxia

Introduction: The major functions of CoQ10 include electron transport, from respiratory chain complexes I and II to complex III, and pyrimidine nucleoside biosynthesis. It is involved in modulating apoptosis. Defects of CoQ10 metabolism cause a variety of disorders ranging from isolated myopathy to multisystem involvement. Mutations in ADCK3, one of several genes associated with CoQ10 deficiency, can present with progressive cerebellar ataxia, epilepsy, and migraine. Diagnosis is challenging due to the wide clinical spectrum and overlap with other mitochondrial disorders. Methods: We provide a detailed description of three new and one previously reported patients with mutations in the ADCK3 gene focussing on the epileptic semiology. In the three patients, we used exome sequencing to identify the ADCK3 mutation and in two measurement of skeletal muscle CoQ10 was performed. Results: The phenotype of our patients is compatible with earlier reports with all having a slowly progressive cerebellar ataxia with cerebellar atrophy. Additionally, our patients had epilepsy complicated by episodes of status epilepticus and evidence of stroke-like episodes affecting the posterior brain. Three patients had epilepsy partialis continua. EEG showed focal epileptic activity in the occipital and temporal lobes. Genetic investigation revealed ADCK3 mutations in all patients. Conclusion: ADCK3 mutations cause a combination of progressive ataxia and acute epileptic encephalopathy with stroke-like episodes. The clinical, radiological and electrophysiological features overlap with the phenotype of polymerase gamma (POLG) related encephalopathy. We suggest that ADCK3 mutations should be considered in the differential diagnosis of mitochondrial encephalopathy with POLG-like features.

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Epilepsy

ICNC-0130: A comparison of ILAE 2010 and semiological seizure classification in children with epilepsy

OBJECTIVE: This study aimed to evaluate both ILAE (International League Against Epilepsy) 2010 and semiological seizure classification (SSC) in terms of applicability and utility for seizure classification and to predict epileptogenic zone in children with epilepsy. METHODS: Data from a total of 138 children were collected from the Pediatric Video EEG Monitoring Unit at Gazi University School of Medicine over the last two years. Both ILAE 2010 and SSC which is a part of
five dimensional classification were performed for each patient. After the assessment of the seizures types and etiologies, data were also compared to evaluate for correlation between epileptogenic zone and seizure subtypes in both ILAE 2010 and SSC. RESULTS: ILAE 2010 indicated that 66.7% of the patients had focal seizures, 15.9% had generalized seizures, and 14.4% had seizures of unknown origin. The SSC revealed that 39.9% of the patients had dialeptic seizures, 56.5% had simple seizures, and 46.4% had complex motor seizures. When ILAE 2010 and SSC were compared to predict epileptogenic zone, SSC was found to be more specific than ILAE, as more of the SSC subgroups were related to the subgroups of epileptogenic zone (p<0.05). Furthermore, the relationship between epileptogenic zone and etiology was remarkable in the five dimensional classification. DISCUSSION: During seizure classification, there is a fine line between recording unnecessary details and having enough information to understand the disease. Therefore, in some patients, a one dimensional classification may not be detailed enough to understand the nature of the seizures. Both ILAE 2010 and SSC have weak and strong points. The SSC is more informative in terms of identifying the epileptogenic zone which may be important in specific occasions like pre-surgical work up, while ILAE is simple and easier method that can be used for defining seizures and their characteristics in daily practice.

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Epilepsy
ICNC-0131: Rufinamide for Lennox-Gastaut Syndrome: More than drop attacks?

AIM: To determine the efficacy of rufinamide for drop attacks and other epileptic seizures in the Lennox-Gastaut syndrome, an epileptic encephalopathy of childhood with intractable epilepsy, global developmental cognitive impairment, psychomotor retardation and pharmacoresistance to AEDs. METHODS: From a database of 10,000 patients in a community-based neurological clinic of suburban Toronto, evenly divided into pediatric (<18 years) and adult (>18 years) cases, ten subjects were identified by clinical, EEG and neuroimaging findings to meet the ILAE criteria for the Lennox-Gastaut syndrome: multiple seizure types pharmacoresistant to major AEDs including valproate, clobazam and others in the therapeutic ranges, intellectual cognitive impairment and global developmental disability. Five were started on rufinamide (Banzel, TM Eisai) at 100-400mg daily while other AEDs were continued. Five continued on original AEDs without the addition of rufinamide. All were followed by the same team: study coordinator, RN, RET doing their EEGs in the same laboratory, read by the same EEGer blinded to their therapy. The blind was maintained by the pharmacist filling their prescriptions at arms’ length. Follow-up varied from 6 months to 24 months at regular intervals of 4 months regardless of therapy group. Two outlier cases were identified that might have impacted on outcome assessment by seizure diary: one adolescent had partial callosotomy prior to rufinamide treatment, the other in the untreated group was found to have Glut-1 deficiency and had a trial of the classical ketogenic diet. RESULTS: After a minimal period of six months of rufinamide, the treated group had fewer drop attacks than the untreated group, were more alert by caregiver observation, and had less drug interactions with other AEDs. There was some amelioration in the EEGs of the treated more than the untreated group, but the changes were quite variable and could not be quantified. Overall an improved quality of life was found with the rufinamide treatment, leading to continuation of the new drug past the study period. CONCLUSION: This preliminary study in a single community-based neurology clinic in a retrospective case-cohort study of Lennox-Gastaut syndrome showed the efficacy of rufinamide in decreasing drop seizures in an otherwise refractory epileptic encephalopathy of childhood, but may also decrease other seizure types such as atypical absences and myoclonic seizures, leading to an improved quality of life.

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Epilepsy
ICNC-0133: Reflex seizures triggered by diaper change in Dravet Syndrome

Dravet syndrome (DS) is a severe epilepsy syndrome characterized by early onset of multiple types of seizures. We report the first case of reflex seizures triggered by diaper change in a 2-year and 9 months-old girl with a mutation in the SCN1A gene causing DS. Reflex seizures have been reported in patients with DS provoked by increased body temperature or visual stimulation. The case we report widens the spectrum of triggers causing reflex seizures in children with DS. Cortical hyperexcitability resulting from the genetic defect explains the tendency to experience such reflex seizures.

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Epilepsy

ICNC-0134: Mother's knowledge of and behavior during acute seizures

Background: Maternal knowledge during acute seizures is influenced by their knowledge and experience. Our objectives were to study maternal knowledge of and behavior during acute seizures. Methods: A cross sectional study included consecutive mothers from September 15, 2013 until January 15, 2014 through the pediatric neurology clinics of King Abdulaziz University hospital, Jeddah, Saudi Arabia. A structured 30-item questionnaire was designed to examine their demographics, knowledge, and behavior. Results: A total of 92 mothers were interviewed and 41% witnessed at least one acute seizure in their affected child (range 1-15, mean 4.5). Up to 26% felt not knowledgeable at all about the acute care and management. Mothers with higher education (college or university degree) were more likely to feel very knowledgeable (19% vs 11%, p=0.02). Only 10% were aware of an antiepileptic drug that could be used at home to stop prolonged seizures and 35% mentioned that they would wait for 15 minutes before taking the child to the emergency department. Most mothers (93%) wanted more information. Those who felt strongly about that (66%), were more likely to be younger (<27 years) and have at least 3 out of 7 mismanagement decisions (p=0.01 and 0.003, respectively). Conclusions: Maternal level of knowledge and behavior during acute seizures needs improvement. Many mothers have significant misinformation, negative behavior, and poor management practices. Increased awareness and educational programs are needed.

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Epilepsy

ICNC-0281: Challenges in international multicenter trials in rare diseases

Background Results from well-designed randomized clinical trials allow for a definitive and unbiased assessment of the clinical benefit of one of the treatments under evaluation. International multicenter trials have the advantage of being able to recruit many patients within a relatively short period. This is particularly useful for rare diseases. Methods To study the most effective treatment in patients with epileptic encephalopathy with electrical status epilepticus in sleep (ESES), the so-called RESCUE ESES trial, was designed. This is a European, multicenter, randomized, controlled, clinical trial with blinded outcome assessment in 130 children aged 2 to 12 years with ESES, to compare the effects of treatment with corticosteroids and clobazam, for a period of six months. The primary outcome measure is cognitive functioning at six months after start of treatment. Results Several challenges had to be overcome to ensure optimal trial conduct and coordinate trial sites working under different regulations and technical and cultural conditions. We experienced different approaches between investigators and clinical trial units. Against expectation patients insurance was not covered in many centers. Although in clinical care readily available, the study drugs were not allowed as part of the trial and had to be imported by most study sites. Finally, approval of the study protocol and documents, but especially agreeing of the clinical trial agreements between the sponsor and the participating centers, proved to be very time consuming. Significance The lessons learned are considered of great importance to all centers taking part in international multicenter studies. Highlights and recommendations are presented. Acknowledgement This trial is funded by the ‘Nationale Epilepsie Fonds NL’, ‘Stichting WKZ fonds NL’ and ‘ECRIN-IA WP7 Fr.’

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Epilepsy

ICNC-0135: Improving post-discharge follow-up and management of neonatal seizures in Lusaka, Zambia: A quality improvement project

Rationale: There is a large gap in treatment of epilepsy in developing countries. Data shows the gap is especially large in the perinatal period where neonatal seizures can result in significant morbidity and mortality. The purpose of this quality improvement intervention was to improve early life outcomes, by increasing education amongst providers in the neonatal intensive care unit (NICU) on identification of seizures, appropriate discharge antiepileptic drug (AED) regimes, and neurology follow-up. Methods: In collaboration with the University Teaching Hospital (UTH) NICU in Lusaka, Zambia, we designed an educational intervention focused on teaching of basic concepts of neonatal seizures and implementation of a treatment algorithm based on the WHO neonatal seizure algorithm. Providers included nurses, post-graduate officers, and physicians. Tests assessing provider knowledge were administered before and after the intervention and compared as our initial outcome measure. Results: A total of 12 participants were present. All 12 took the pretest and 11 took the post-test, with one drop out due to clinical duties. The participants demonstrated an improvement in their recognition of the rarity of GTCs in neonates, the need to maintain patients on AEDs after discharge (42% to 73%), and that prompt neurology follow-up post-discharge is essential. Conclusion: The intervention was an important first step in a structured educational collaboration with the aim of recognition and treatment of neonatal seizures. In addition to raising awareness, our intervention fostered a weekly multidisciplinary clinic with NICU and neurology physicians, and future studies will assess direct clinical outcomes.
Introduction: Measles is the second most common vaccine preventable cause of death under five years in low and middle income countries. Logistical and financial challenges preclude adequate vaccination coverage. Between 2009 and 2011 measles outbreaks were reported across Africa and Europe. Method: Six children (n=3 male; median age 4y5m (range 4y3m - 6y2m) were diagnosed with Subacute Sclerosing Panencephalitis (SSPE) between 2014-2015 at one centre. Four of their clinical phenotypes have been published (Kija et al.SAMJ 2015; 105(9): 713-718). Two were HIV infected and two were HIV exposed. All were infected with measles in the first year of life, before vaccination. They presented with rapid onset myoclonic jerks, atonic head nods, and cognitive regression. All had raised measles antibody titres on CSF. This study delineates their sequential electrophysiological (EEG) findings. Results: Between 2014 and 2015, 26 EEGs were performed (3-6 studies per child). EEGs performed within 1 month of symptom onset, were encephalopathic. In four children, generalized polyspike/ slow spike and wave activity, with independent foci were recorded without EEG correlation with abnormal movements. By a median of 2.5 months post disease onset, (range 2-5 months), four children
had EEG correlation associated with myoclonic jerks. There were no differences between the EEGs of the HIV infected/exposed compared with non-infected children. Conclusion: The EEG changes in patients with SSPE are well documented in established disease, but studies at the onset of disease do not always show characteristic changes. Children with regression and movement disorders should have SSPE included in the differential diagnosis.

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Epilepsy
ICNC-0139: Reduced sodium currents in GABAergic interneurons from Dravet Syndrome patient-derived induced pluripotent stem cells
Introduction: Dravet syndrome (DS) is a devastating infantile-onset epilepsy syndrome. In more than 70% of patients, DS is caused by de novo mutations in the SCN1A gene which encodes a subunit of the neuronal voltage-gated sodium channel Nav1.1. In this study, we established induced pluripotent stem cell (iPSC) lines from one DS patient and aimed to determine how mutant SCN1A affects human neurons. Methods and Results: We generated iPSCs from a DS patient with a missense mutation of c.4261G>T substitution [p.Gly1421Trp] in SCN1A. Neural precursors from DS and human control iPSCs displayed a forebrain identity and differentiated into bipolar- and pyramidal-shaped neurons. Neurons derived from these iPSCs were primarily GABAergic (>80%). DS patient-derived glutaminergic neurons showed increased sodium currents but GABAergic neurons showed reduced sodium currents. Conclusions and Discussion: Our results demonstrate that GABAergic neuron from DS patient-derived iPSCs exhibited a functional decline. Here, DS patient iPSC-derived neurons could recapitulate the neuronal pathophysiology and offer a platform for screening new antiepileptic therapies. Acknowledgements: This research was supported by National Research Foundation of Korea(NRF) funded by the Ministry of Education, Science and Technology (2013R1A2A2A01014108).

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Epilepsy
ICNC-0140: Public awareness, knowledge on practice relating to epilepsy among adults in Konya
Introduction: This study aimed to determine the familiarity with, knowledge of, misunderstandings, and attitudes toward epilepsy among a group of Turkish adults living in Konya, an urban city in central Turkey. Methods: By using an established familiarity-knowledge-attitudes practice questionnaire, 500 randomly selected adult residents of Konya were interviewed face-to-face. Demographic and sociocultural factors that predicted negative attitudes were determined. Results: More than half of all participants (68.4%) reported hearing or reading about epilepsy, 44% knew someone with epilepsy, and 42.2% had witnessed a seizure. The primary source of knowledge was via relatives and friends; Negative attitudes were present concerning marriage and inability to live alone. The primary reason for negative attitudes was female gender, lower educational status, living in a rural area. Conclusion: Negative attitudes regarding the marital status of epileptic patients still exist. These may stem from misconceptions about the cause and treatability of epilepsy.

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Epilepsy
ICNC-0141: Knowledge of, perceptions of, and attitudes toward epilepsy among medical students in Turkey
Purpose: The aim of this cross-sectional study was to assess the current level of knowledge about epilepsy, treatment together with their attitudes and perception to person with epilepsy among medical students in Turkey Method: The study was conducted using a structured questionnaire to assess professional experience with epilepsy, knowledge and awareness about epilepsy among medical students at the Selcuk University. Results: Eight hundred fifty subjects were interviewed, and 68.8% reported their awareness about epilepsy. Of these, 31.8% knew someone who had epilepsy, 59.3% had witnessed an epileptic seizure, 39.5% believed that epilepsy is a hereditary disease. Eighty-seven percent considered epilepsy as a dangerous disease, and most of them (82.7) thought that epilepsy is a lifelong condition. 50.1% indicated that putting an object into the patient’s mouth to prevent tongue biting during a seizure is appropriate, and 91.6% stated that drug therapy was the only treatment available for epilepsy. The most common negative attitudes toward PWE were that the students would refuse to marry someone with epilepsy (60.2%) and that children with epilepsy must join schools for persons with disabilities (18.2%). In conclusion, many students have misconceptions about the causes, treatment, and nature of epilepsy, and students have moderate negative attitudes toward patients with epilepsy.
Epilepsy

ICNC-0143: Use of Anakinra in a patient with Febrile Illness-Related Epilepsy Syndrome (FIRES)

INTRODUCTION: Febrile illness-related epilepsy syndrome (FIRES) is a rare, poorly understood, pediatric epileptic encephalopathy characterized by a preceding febrile illness, and multifocal, often refractory, status epilepticus. Response to treatment is generally poor, with high mortality in the acute phase, and profound neurological sequelae, including refractory epilepsy chronically. Interleukin 1 (IL-1) is a proinflammatory cytokine, implicated in a variety of autoinflammatory disorders. Anakinra is a recombinant human IL-1 receptor antagonist, with proven efficacy in animal seizure models and pediatric patients with autoinflammatory disease. CASE DESCRIPTION: We report a developmentally normal 2-year-old patient with FIRES and super-refractory status epilepticus. Brain imaging, CSF analysis (including autoimmune epilepsy panel and neurotransmitters), an extensive metabolic screen and a comprehensive epilepsy genetics panel were normal. Anakinra was initiated on day 5 of presentation (5 mg/kg subcutaneous b.i.d.), with a significant decline in her mean daily seizure frequency (5.8 seizures/day (day 1-6) vs. 1.2 seizures/day (day 7-31); p = 0.02). Nineteen days after the anakinra was stopped, the patient’s seizures relapsed. Reintroduction of anakinra was associated with substantially improved seizure control (from an average of 7.4 to 0.4 seizures/day; p = 0.036). Six months after presentation, she remains on anakinra, her motor and verbal skills are age appropriate, and her seizures remain well-controlled. DISCUSSION: This is the first report of an IL-1 antagonist in the treatment of FIRES. While these results must be interpreted with caution, anakinra has been well-tolerated and associated with an excellent clinical outcome. Further study of anti-IL-1 therapy in the treatment of FIRES is warranted.

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Epilepsy

ICNC-0144: Electrical status epilepticus during slow sleep in children with various forms of epilepsy

The purpose of the study is to analyze the specific characteristics of seizures in children which had electric status epilepticus during sleep. Materials and methods: 1600 EEGmonitoring was carried out for three years in neurophysiological laboratory of neurology department (inpatient and outpatient), EEG was performed for 3 hours and more. 690 (43%) children of them had not seizures, complained about the delay in development and different paroxysmal states. Other children (910-56%) had convulsions of different types. 560 (35%) children have been severe epilepsy. Research data: The analysis of bioelectric activity in 75 (5%) of children in the EEG showed signs of ESES-electrical status epilepticus during sleep. Clinical examination of these children showed that almost all children have delayed development, seizures in history. 25 children had more frequent attacks at the time of the examination, and 11 children not had seizure at the moment of examination. Most of the children had severe developmental delay. There is an interesting fact - girls 10 years old, who had only 2 tonic-clonic seizure in history, not had development and mental delay, a good student at school, but had ESES on EEG. On her EEG was found regional continuous epileptic activity. Seizures in children had different types - regional and secondary generalized tonic-clonic seizures in 15% children, myoclonic seizures -8%, absences -3%, in the majority of children -74% recorded polymorphic attack- tonic spasms with tonic-clonic seizures, atypical absences with myoclonia, atonic seizures. Children with ESES on EEG had the following diagnoses: syndrome pseudo-Lennox, Landau Kleffner syndrome, consequence of acute stroke, epilepsy with electrical status epilepticus during slow sleep, Lennox Gastaut syndrome.

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Epilepsy

ICNC-0145: The clinical profile and outcome of children with West Syndrome: a 10 year retrospective review

Introduction: West Syndrome (WS) is an epileptic encephalopathy characterized by epileptic spasms, hypsarrhythmia on electroencephalography and developmental delay in infancy (1). There is a paucity of published literature knowledge on WS in Africa. We aimed to describe the clinical spectrum, course and outcome of children with WS in South Africa.Methods: We performed a retrospective chart review of patients diagnosed with WS over a 10 year period from January 2005–August 2015. Results: We identified 8 children (Males-7, African-6, Asian-2) with WS out 2206 admitted with epilepsy. The mean age was 7.5 months (range 1-9 month). The average time between onset of epileptic spasms and diagnosis was 3.1 months. The mean number of clusters per day was 5. Six patients had abnormal neuroimaging (Atrophy-2, Corpus Callosum Agenesis-2, Tubercous Sclerosis-1, Focal Dysplasia-1). Drug management included Sodium Valproate (n=8) with Topiramate (n=7) and Levetiracetam (n=3). Subsequent definitive treatment was
Adrenocorticotrophic hormone - ACTH (n=3), Vigabatrin (n=2) and Prednisone (n=4). Four (50%) patients had complete seizure remission (Neuroimaginatory Disorder-2, Tuberous Sclerosis-1, Idiopathic-1) and partial remission in 4 (Neonatal complications-3, Idiopathic-1). Hypsarrhythmia on EEG resolved in 4 (50%). 7 patients had global developmental delay.


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Epilepsy

ICNC-0282: Bone metabolism abnormalities in South African children with Epilepsy

Introduction: In Africa over 50% of people with epilepsy are children and 69% of the convulsive seizures begin in childhood. Studies on bone metabolism and antiepileptic drugs (AEDs) in America and Europe revealed inconsistent findings with Phenobarbitone and Carbamazepine most implicated. Data on bone metabolism in children with epilepsy in Africa is lacking. As such there is no evidence to suggest if this group are Vitamin D deficient and require supplementation with vitamin D and calcium. Methods: A hospital based case control study was undertaken on children recruited from an Epilepsy clinic from February-June 2015. Blood and urinesamples were taken for the assessment of markers of bone metabolism. A control group was from a day surgical ward. Results: Seventy-five cases (male to female ratio 1:1; median 9 years) and 75 controls (median 3 years) were recruited. 28 (37.3%) children were on 2 AEDs and 19 (25.3%) on more than 2. Four (5.3%) were on Phenobarbitone, 20 (27.4%) on Carbamazepine and 59 (78.7%) on Valproic Acid. Mean phosphate levels was 1.76±0.03mmol/L cases versus 1.38mmol/L±0.09 controls (p value<0.001). Mean corrected serum calcium was 2.34±0.01mmol/L cases versus 2.32±0.01mmol/L controls (p=0.55). Data analysis will complete January 2016. Conclusion: From the preliminary data, children in this cohort are more likely to receive AEDs which could affect their BMD. Whilst bone fractures were not identified, the final outcomes from the completed study should provide more comprehensive data on their bone metabolism. Acknowledgement: This study is part-funded by the International ChildNeurology Association (ICNA) Global Burden of Disease Seed Grants.

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Epilepsy

ICNC-0148: Serum IL-1β and IL-1ra levels in children with febrile seizures

Introduction: Pro-inflammatory cytokines induce fever during infection, and may trigger the development of febrile seizures. To estimate whether active inflammation occurs during febrile seizures, we compared levels of IL-1β and IL-1ra in children with febrile seizures, febrile illnesses without seizures and epilepsy. Methods: Twenty-six febrile seizure patients who visited the emergency department of Konyang University Hospital from October 2013 to May 2014 were included in this study. Blood was obtained from the patients within 30 minutes of the time of the seizures. Control samples were collected from children with febrile illness without seizures (n=17) and afibrile seizures (n=12). Results: Serum IL-1β levels were significantly lower in febrile seizure group than in febrile illnesses without seizure group (19.1±85.8pg/mL vs. 171.6±222.0pg/mL, p=0.019). Serum IL-1β levels were also lower in epilepsy group than febrile illness without seizure group (39.5±130.2pg/mL vs. 171.6±222.0pg/mL, p=0.166). Serum IL-1ra levels were not significantly different among three groups. In febrile seizure group, there was no significant difference in serum IL-1β levels between first febrile seizure subgroup and recurrent febrile seizure subgroup (30.6±106.5pg/mL vs. 0.8±1.2pg/mL, p=0.391), between febrile seizure under 10mins of duration and prolonged febrile seizure over 10mins of duration (7.7±17.4pg/mL vs. 23.3±97.9pg/mL, p=0.692). In epilepsy group, the serum IL-1β and IL-1ra levels were not significantly different between under 10mins of duration and prolonged seizure over 10mins of duration. Conclusion: IL-1β levels were significantly lower in febrile seizure patients. Our data suggest that increased level of serum IL-1β might be more related to fever itself than febrile seizure or epilepsy.

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Epilepsy

ICNC-0149: Preliminary outcomes of a proposed treatment strategy for childhood Absence Epilepsy

Purpose: Childhood absence epilepsy (CAE) is the most common pediatric epilepsy syndrome and attentional deficits are the most important marker of cognitive dysfunction and related with duration of absence seizures. The success of treatment depends on fast remission of clinical seizures. We are determined preliminary outcome in children with CAE who were treatment with temporary combination therapy of valproic acid and lamotrigine. Method: We retrospectively reviewed the medical charts of children receiving temporary combination treatment of valproate and lamotrigine until March 2015. The temporary combination treatment consists of intravenous valproate rescue (loading dose) and oral valproate maintenance with slow titration of lamotrigine. Eventually, patients receive a monotherapy of lamotrigine after taper-off valproate. Time to seizure-freedom, time to normalized EEG, duration of follow up and clinical characteristics were recorded. Results: Four patients (all girls) aged 9.7 ± 1.3 (range, 8.0~11.1) years were identified. Mean duration of follow up was 10.2 ± 4.1 months. They took time about 1 or 2 years to treatment from symptom onset. All patients had seizure freedom within 2 weeks after treatment and parents reported improvement of patient’s attention. EEG findings at 4 months were normal in 3 of them. All patients tapered off oral valproate by 4 months and maintained monotherapy of lamotrigine (dose range 4.4 ~ 5.4 mg/kg/day). No adverse events occurred during and after combination treatment. Conclusion: Using strength of valproate’s faster onset of action and delayed effect of lamotrigine with cognitive advantages, the valproate-lamotrigine temporary combination treatment is a considerable alternative in CAE. Keywords: Childhood absence epilepsy, Combination treatment, Valproate, Lamotrigine

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Epilepsy

ICNC-0150: Ohtahara Syndrome

Introduction: Ohtahara Syndrome commonly occurs in neonates, within the first 3 months of life. It is characterized with frequently recurring tonic spasms on an isolated or cluster basis and exhibits a suppression-burst pattern on electroencephalography. Here, we present a 12-month boy, who had his first seizure when he was 3 days old and exhibited a suppression-burst pattern on EEG. Case Report: The 12-month-old patient, was referred for refractory seizures. The patient was using an anti-epileptic agent, was detected to have a poor overall condition, no consciousness, irregular respiration and spasticity on all extremities, and had generalized tonic-clonic seizures. Laboratory investigations revealed normal whole blood count and biochemical results, blood-urine aminoacids and urinary organic acid levels. Cranial computerized tomography detected cavaum septum pellicidum and EEG showed suppression-burst pattern. Although the patient received phenobarbital, phenytoin and levatiracetam, his seizures persisted and thus he was given midazolam infusion. The patient, with continued seizures, was put on IVig, ACTH and ketogenic diet. Despite all treatments, his focal motor seizures, refractory tonic spasms persisted and his EEG revealed cortical multifocal epileptiform abnormality; he is currently under follow-up with the diagnosis of Ohtahara Syndrome. Discussion: The Ohtahara Syndrome, is one of the epileptic encephalopathies that occur at the youngest age. The cases commonly manifest with severe mental and motor developmental retardation or neurologic disorders and the prognosis is poor. Ohtahara syndrome should be considered in patients for diagnosis, who have an onset of disease within the first months of life, are resistant to treatment and have refractory seizures.

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Epilepsy

ICNC-0154: Cognitive function in Nigerian children with newly diagnosed epilepsy: a preliminary report

Aim: The purpose of the study was to evaluate cognitive function in a cohort of Nigerian children with newly-diagnosed epilepsy and to determine the correlates of impaired cognitive dysfunction. Methods: New cases of epilepsy seen at a pediatric neurology clinic were evaluated for any evidence of cognitive impairment. Intelligence quotient (IQ) of the participants was measured using the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV). Scores on cognitive subtests and Full Scale IQ (FSIQ) were computed and association between the subsets scores and seizure variables were calculated. Results: 40 children, aged 6 to 16 years with a mean of 10.8 (SD=3.0) years, were enrolled. Global intellectual functioning as measured by the WISC-IV was in the normal range (FSIQ scores < 85) for 21 (52.5%) and 47.5% children scored between the borderline and severe category for intellectual disability. The strongest correlation was between ‘caregiver’s assessment of school performance’ and FSIQ, (r = 0.70; p < 0.001). Age at onset of epilepsy and seizure type had no significant association with the WISC-IV composite scores. Conclusion: There is a high prevalence of significant cognitive dysfunction in Nigerian children with epilepsy, even in the absence of any known brain insult. Caregivers’ assessment of child’s performance and child having repeated a class showed significant correlations.
with the IQ rating. In the setting of limited resources, children with epilepsy whose caregivers' express dissatisfaction with their academic performance should be given a high priority for IQ assessment in order to allow for early intervention and improved outcomes.

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Epilepsy
ICNC-0283: Choice of anti-epileptic drugs in the management of childhood epilepsy in a tertiary centre in Nigeria: the current trends

Background: Epilepsy is the leading neurological disorder worldwide. Children in the developing world are disproportionately affected and outcomes are hampered by stigma, a wide treatment gap and lack of access to appropriate anti-epileptic drug (AED) therapy.

Aim: We audited our paediatric epilepsy service over a 6-month period in order to evaluate the pattern of AED prescription and to document seizure outcomes in a period of improved access to the use of newer AEDs.

Methods: Consecutive cases of paediatric epilepsy who had been under our care for a minimum period of 6 months were enrolled. Details of seizure history, diagnosis, treatment and seizure outcomes were evaluated.

Results: 114 children, 74 males and 40 females were enrolled. Duration of treatment ranged from 6 months to 14 years, median 23.5 months. Epilepsy was generalised in 68 (59.6%) and localisation-related in 46 (40.4%). Epilepsy was idiopathic in 70 (61.4%) and remote symptomatic in 44 (38.6%). 67 had associated co-morbidities and the most frequent was intellectual disability (31.8%). Carbamazepine (43.4%) and sodium valproate (41.3%) represent the most frequently prescribed AED in our practice. There has been a drastic reduction in the use of phenobarbitone, in use in 11 (8.7%) of the cases. By the end of the first 6 and 12 months of initiation of AED therapy, 26.3% and 34.2% respectively had required a change in AED.

77 (67.5%) children were on monotherapy. Use of newer AEDs was employed in 20 (17.5%) and levetiracetam is the most frequently prescribed second line AED. Children with co-morbidities were more likely to be on a second line AED.

Conclusion:

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Epilepsy
ICNC-0155: Presentation prognosis of antiepileptic drug withdrawal in seizure free patients: combining predictors in a meta-analysis of individual patient data

Background: Seizure free people with epilepsy may consider stopping antiepileptic drug (AED) treatment. The literature on predictors of the outcome of AED withdrawal is far from conclusive. The aim of this study is to identify independent predictors of seizure recurrence and long-term seizure outcome in a meta-analysis of individual participant data.

Methods: Systematic review of literature was conducted to identify candidate predictor variables and articles eligible for inclusion. Authors of eligible articles were contacted with the proposal to collaborate by sharing anonymous individual participant data. Random effects proportional hazards regression was used for analysis. Candidate predictor variables were studied uni- and multivariably for two outcome parameters: seizure recurrence and seizure outcome at final follow-up visit.

Results: Data from seven research groups (1294 patients, 51% children) were gathered at the time of writing this abstract, whilst awaiting the last results from collaborators. Preliminary analysis on 401 pediatric patients (median follow-up 7 years) resulted in six significant independent predictors of seizure recurrence and two of long-term seizure outcome.

Predictors were related to structural deficits to the brain and epilepsies which are difficult to treat. Analyses on the full cohort will be presented. Discussion: Through collaboration, this study provides new estimates how to predict the outcome of AED withdrawal for the individual patient. Predicting long-term outcome might be as valuable as predicting seizure recurrence; both will be possible with the outcomes of this study.

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Epilepsy

ICNC-0156: Favorable efficacy of zonisamide as add-on therapy in intractable epileptic children

Introduction: The aim of present study was to evaluate the efficacy and safety of zonisamide as add-on therapy in intractable epileptic children. Factors influencing drug responses were analyzed. Methods: We retrospectively reviewed intractable epileptic children (age < 18 years old) who used zonisamide as add-on therapy during a 2-year period in a tertiary medical center. Results: 38 patients were enrolled, including 20 boys and 18 girls. Age at onset of epilepsy ranged from 1 month to 17 years (mean, 4.1 years). 22 (57.9%) were generalized seizures, 5 (13.2%) focal seizures, and 11 (28.9%) unknown seizures. The mean number of prior anti-epileptic drugs was 3.5. The follow-up period was more than 6 months. Among these patients, 13 children (34.2%) had good responses (seizure reduction rate> 50%) at 3-month including 3(7.9%) seizure free, while 14 children (36.8%) had good responses at 6-month and 6 (15.8%) seizure free. The drug retention rate was 89.4% and 81.6% at 3 month and 6 month, respectively. Only 2 cases (5.3%) had side effects. 16 cases (66.7%) in poor-response group had abnormal brain MRI findings, comparing to 4 cases (28.6%) in good-response group (P=0.042). There was no difference in the factors of age at seizure onset, seizure patterns and number of prior anti-epileptic drugs. Conclusion: Zonisamide is an effective and safe drug as add-on therapy in intractable epileptic children. Negative brain MRI finding may be a favorable factor.

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Epilepsy

ICNC-0158: Evaluating localizing value of generalised paroxysmal fast activity using connectivity analysis in Lennox–Gastaut syndrome

Lennox-Gastaut syndrome (LGS) is one of the most severe childhood-onset epilepsies. It is characterized by multiple types of seizures, electroencephalographic (EEG) characteristics, such as generalized slow sharp and wave discharges and generalized paroxysmal fast activities, and progressive mental retardation. Resective surgery can be an effective treatment and patients can be freed of seizure by removing the epileptogenic zone. It is critical to accurately localize the epileptogenic zone for successful resective surgery. Recently, functional brain connectivity analysis such as Granger causality methods has been proposed to better explain causality and directionality of epileptic network. This analysis method can also be used to identify the source of the abnormal electrical signals. Many studies have analyzed generalized sharp and wave discharges (GSW) to locate the source of epileptiform discharges. On the other hand, localizing value of generalized paroxysmal fast activity (GPFA) using this method has not been well evaluated. We analyzed GPFA from preoperative EEG using direct directed transfer function (dDTF) of 11 LGS patients. The brain areas identified from the analysis were compared with the actual resected area, which resulted in favorable surgical outcomes. We found that the regions identified by the dDTF analysis were included in 5 patients and there was no patient with complete matches of the resected areas without other foci. We believe that this mismatch arises that the generation of GPFA is more involved in the diffuse network that includes association cortices and the involvement of subcortical structures which causes simultaneous cortical activation of other brain regions.

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Epilepsy

ICNC-0035: Longitudinal change of Thyroid hormone levels in children with epilepsy on ketogenic diet

Background: To evaluate the prevalence of hypothyroidism and the change of thyroid hormone level in the children with epilepsy on ketogenic diet (KD). Methods: The level of serum free throxine (FT4) and thyroid-stimulation hormone (TSH) were measured at the start of KD and at 6-12 months intervals in children with intractable epilepsy. Hypothyroidism was defined as FT4 level <0.8 ng/dL and TSH level >7.0 uIU/mL. Results: A total of 21 children (13 boys, 8 girls) were enrolled in the study. Mean age of onset of seizure was 1.4±1.5 years, mean age of start of KD was 3.4±2.5 years and mean duration of KD was 2.1±1.5 years. The patients of hypothyroidism with only decrease of FT4 at baseline levels were 2 (9.5%) and at last follow-up were 2 (9.5%). Overall, there was no significant longitudinal change of the mean FT4
Epilepsy

ICNC-0160: SCN1A gene mutations associated to severe clinical phenotype in Dravet Syndrome children

Background: Approximately 40%-80% of patients with Dravet syndrome (DS) carry mutations in SCN1A. There are few studies to compare the clinical phenotype of SCN1A mutations positive to SCN1A mutation negative. Methods: Twenty-four DS patients (10 males, 14 females, mean age at 3.2 years old) were retrospectively studied. The clinical records were collected and all patients were performed with SCN1A genitic test. Cognitive assessment and electroencephalograph were analysed for all patients. Results: Analysis revealed SCN1A mutations comprising with missense, nonsense, splicing and frame shift mutations in 14 patients and no mutation in 10 patients. The clinical features of mutation positive patients were characterized by earlier seizure onset, higher frequency of seizures per month before one year old and higher ratio of status epilepticus (SE) at seizure onset. The percentage of patients with moderate or mild mental retardation increased with increasing age. Patients in SCN1A+ group were more likely to have a diffuse background slowing of electroencephalograph. Conclusions: These findings confirm that the DS patients in SCN1A mutation positive group manifested more severe clinical symptoms such as the early onset of seizures in previously healthy children, the long duration of the first seizure and frequent episodes before first year. Mental retardation or regression in DS children is dependent by age. Key Words: Epilepsy; SCN1A gene mutations; Dravet syndrome

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Epilepsy

ICNC-0161: Prediction the effectiveness of Antiepileptic Drugs by analyzing EEG features in children with Epilepsy

Introduction: Epilepsy is a common chronic disorder in pediatric neurology. Nowadays, a variety of antiepileptic drugs are available in the treatment of epilepsy. However, there is lack of scientific method for predicting the effectiveness of antiepileptic drugs. In this study, we try to use QEEG analysis as a biomarker to predict therapeutic effectiveness. Method: 20 epileptic children, aged from 5y1m to 17y11m, were enrolled in this study. Participants were classified as effective if they had achieved a reduction in seizure frequency over 50% compared with baseline following AED treatment for six months. On the contrast, ineffective was defined a reduction in seizure frequency less than 50%. 11 of them were classified into effective group. The remaining 9 patients were ineffective group. EEG segments before and after 1 to 3 months of antiepileptic drugs start/change were analyzed and compared by quantitative EEG. Results: There were seven crucial EEG feature descriptors selected for classification. Significantly increased RelPowAlpha_avg_AVG, SampEntropy_snr_AVG, HjorthM_snr_AVG, SpectrEdgeFreq_snr_AVG, and RelPowBeta_snr_AVG values were found in the effective group as compared to the ineffective group. On the contrary, there were significantly decreased in Wavelet_db4_EnergyBand_6_std_AVG and RelPowTheta_std_STD values in the effective group as compared to the ineffective group. The analyses yielded a precision rate of 91.5%. Conclusion: The developed method is a useful tool in prediction the effectiveness of the antiepileptic drugs. It may assist pediatric neurologist in selecting adequate antiepileptic drugs when they handle the patients with epilepsy.

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Epilepsy

ICNC-0162: EEF1A2 (eukaryotic elongation factor 1, alfa-2) related early infantile epileptic encephalopathy

Objective: Description of the first Israeli patient identified a heterozygous de novo EEF1A2 (eukaryotic translation elongation factor 1, alfa-2) mutation and definition of the EEF1A2 related early infantile epileptic encephalopathy (EIIEE) based on the current literature. Methods: Whole exome sequencing was performed in a patient with early infantile epileptic encephalopathy. Case report: A one year old female infant born to non-consanguineous Jewish parents presented at 3 months with apneic seizures, progressing to EIIEE. Her seizures consisted of focal, dyscognitive, tonic and myoclonic seizures. EEG demonstrated multifocal discharges. Imaging and an extensive metabolic work-up were uninformative. Multiple antiepileptic drugs failed to control her seizures. Phenytoin and the ketogenic diet worsened her seizures while a combination of leviracetam, valproic acid and phenobarbital had a mild transient positive response. Medical cannabis (CBD 20% -24mg/kg/d CBD ; 1:18 mg/kg/d THC) seemed to ameliorate the seizure burden- specifically the myoclonic seizures. At 12 mo she has intractable epilepsy, profound intellectual disability (ID), postnatal microcephaly, hypotonia and mild facial dysmorphism. A novel de novo EEF1A2 mutation [NM_001958.3:c.374C>A:p.Ala125Glu] was found. The mutation is predicted to be damaging. Discussion: The EEF1A2 protein is involved in protein synthesis, suppression of apoptosis and regulation of actin function and cytoskeletal structure. It is expressed in the CNS, muscles (myocardium & skeletal muscles), endocrine and exocrine systems. The clinical spectrum in all cases consists of severe ID, motor developmental delay, neonatal hypotonia, epilepsy, autistic features with aggressive behavior and postnatal microcephaly with mild facial dysmorphism. Conclusion: De novo EEF1A2 mutations cause a new neurological syndrome consisting of epileptic encephalopathy, postnatal microcephaly, profound ID, hypotonia and mild dysmorphism. Our patient is the youngest diagnosed patient. She is also the first patient with an EEF1A2 mutation to be treated with medical cannabis, possibly ameliorating her myoclonic seizures.

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Epilepsy

ICNC-0163: Early onset Epileptic Encephalopathy – Role of clinical Exome sequencing and long term outcome

Introduction: Early onset epileptic encephalopathy of cryptogenic nature as a challenging group to find etiologic diagnosis and counsel. Aims and objectives: To analyse the diagnostic yield of clinical exome sequencing in epileptic encephalopathy. Study period - Jan 2014 to Oct 2015, Rainbow Children’s Hospital Hyderabad, India Methods: infants with epileptic encephalopathy; without a etiologic diagnosis after clinical/ metabolic and structural imaging were evaluated with clinical exome sequencing. 9/14 clinical exome sequencing demonstrated pathogenic abnormality on the on Illumina sequencing platform With mean>80-100X coverage. Data was collected prospectively and analysed Results: Total 14 children were tested. Age at onset was birth to 6 months Mf.:9:5. Epileptic spasms in 7, 6/7 had normal MRI, one had cerebellar and white matter signal changes. MECP2 -1.DOCK7 -1 KCNQ2 (-)-1, PLCB1 – 1, RARS2 -1 and normal in 2. One child with RARS2 mutation and cerebellar changes died at 4 years. Except in child with MECP2 mutation most had mild to moderate reduction in the seizure frequency on follow up of 1.8 to 4 years. Two had Malignant migrating partial epilepsy of infancy with normal MRI, one had KCNT1 mutation with persistent seizures at 1.4 years, another child without any mutation had poor motor outcome with seizure control at 5 years. One infant with myoclonic and GTCS along with tremors had KCTD7 mutation with regression of motor and cognitive milestones. Seizures with Apneas was noted in one family with previous sib death due to similar history had heterozygous mutation in KCNT1. An infant with complex partial epilepsy phenotype and severe autistic features had normal clinical exome. Multifocal onset seizure as predominant clinical phenotype was noted in 2, one had mutation in STBXP1 and normal in another child. Conclusion: The clinical phenotype correlated with genetic information in 7/9 tested infants. Most of these infants had poor seizure and cognitive outcome. Genetic testing helped to counsel about natural history and risks of recurrence

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Epilepsy

ICNC-0164: Super refractory status epilepticus: Case series from tertiary care pediatric hospital in India

Aims and objectives: To study the etiological spectrum, short and long term outcome in children with super refractory status epilepticus. Study design: Retrospective data from May 2012 to Nov 2015 data collection and follow up information was analyzed. Results: Fifteen children -four months to 14 years were included. Eleven boys and four girls. Five had Probable viral encephalitis, one SSPE, five presumed autoimmune encephalitis, three structural etiology and one
suspected mitochondrial cytopathy. 13/15 managed in PICU with mean of 18 days. Fourteen had convulsive and NCSE. Eleven required ventilation with mean 13 ventilator days. Four required tracheostomy and three required gastrostomy. Infusions used-Midazolam -14(48-576hrs)/ketamine -9(12-120hrs)/thiopentone -8(15-58hrs)/Isoflurane-2(48-96hrs). Methylprednisolone used in eleven, IVIG in five and Rituximab in four as immunomodulator. Mean duration of status 244 hours and Maximum duration 576 hours. CSF analysis including viral PCR done in 13, was normal in all. CSF autoantibodies done in 8/15 and were negative in all. Three died during treatment. Follow up 5 to 40 months (Mean 18 months). 6/12 survivors had complete seizure control, twelve complete motor recovery, eleven normal vision and only one had normal cognition on long term follow up. Conclusion- Long term seizure outcome is good in more than 50% of children with super refractory status with normal motor outcome in all survivors.

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Epilepsy
ICNC-0165: Initial Monotherapy of newly diagnosed pediatric Epilepsy: Expert opinion in China
Objective: To compile expert consensus opinion in initial monotherapy of newly diagnosed pediatric epilepsy in China.
Method: A questionnaire on monotherapy of pediatric epilepsy by the Delphi Method was sent to some pediatric neurologists of the tertiary hospital in the field of epilepsy. The experts were asked to rate options using the modified 5-point scale for medical appropriateness. Consensus was defined as a non-random distribution of scores by the mean, standard deviation, and 95% confidence interval, with ratings used to assign a categorical rank (initial, first-line, second-line and not recommended drugs) to each option. Result: Among the 58 experts to whom the survey was sent, 53 (91.4%) replied the questionnaire effectively. The results showed that oxcarbazepine and carbamazepine were the first choice in the initial monotherapy for partial seizures and secondarily generalized seizures. Valproate was initial treatment of choice for generalized seizures, epileptic spasms, multi-type seizures and unclassified epileptic seizures. As initial therapy for Lennox-Gastaut syndrome, Doose syndrome, Landau-Kleffner syndrome, epilepsy with continuous spike-waves during slow-wave sleep and juvenile myoclonic epilepsy, valproate was initial treatment of choice. For childhood absence epilepsy, ethosuximide and Valproate were initial treatment of choice. For benign childhood epilepsy with centro-temporal spikes, oxcarbazepine was initial monotherapy of choice. As initial therapy for infantile spasms, adrenocorticotropic hormome (ACTH) was treatment of choice. Conclusion: These results concisely summarizes clinical experience of pediatric epilepsy experts in China, and this opinion may be helpful in initial monotherapy of newly diagnosed common pediatric epilepsy types and epileptic syndromes.

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Epilepsy
ICNC-0170: Top-down-bottom-up outreach pediatric neurology clinics in remote poor community
Background: In countries with scarce pediatric neurology specialist, patients are usually referred. The other alternative has been mobilizing specialists, clinical specialist outreach. This study examines whether clinical specialist outreach is a cost effective way of using scarce health expertise to provide specialist care as compared to provision of such services through referral system in outreach areas in Pakistan. Objectives: To assess the cost effectiveness of pediatric neurology outreach clinic in a remote poor community. Methods: This is a single day snap shot survey of outreach pediatric neurology outreach clinic. Its cost effectiveness, cost, cost savings and patient satisfaction. We compared the cost by the outreach project and cost saved of the patients by refraining their referral to the central hospitals. Results: A total of 110 children and adolescents attended the clinic on single day. There were slightly more boys (56%) than girls (44%). The mean age of patients was 6.5±3.5 years, the youngest being 1months and the oldest being 18 years. On the single day outpatient clinic by spending 53000 Pak. Rupees by the organizing group, 572000 Pak. Rupees of the patients were saved by refraining their referral, in addition to high satisfaction among these patients. Conclusion: Clinical specialist outreach is a cost effective and cost saving way of spending clinical specialists’ time as compared to provision of similar services through referral system. It is highly convenient and patients are satisfied. Adopting such outreach clinics revolutionary health facilities can be produced at footsteps of remote communities at very economical cost.

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Epilepsy

ICNC-0948: Semiologica features in frontal lobe epilepsy in children

Mazur

ICNC-0171: Risk factors of intractable epilepsy patients below 3 years of age with focal epilepsy

Maria

Epilepsy

ICNC-0173: Milestones and myoclonic epilepsy- the metabolic link

Ismael
Epilepsy

ICNC-0174: Vigabatrin and Zonisamide Combination: new promising treatment option for the patients with CDKL5 Mutation?

Mutations in the CDKL5 gene are associated with early onset seizures, epileptic encephalopathy, severe developmental delay and Rett-like symptoms. In the majority of cases, epilepsy is refractory to the conventional anti-epileptic drugs (AED), therefore there is a need to develop new pharmacological strategies. Here we report two female patients with CDKL5 mutations successfully treated with VGB and ZNS combination. Patient 1 (c.1733_1737dup): 19 months old girl with history of unilateral seizures starting from two months evolving into infantile spasms, refractory to conventional AEDs, partial response (>50%) to VGB. ZNS was added to VGB with cessation of the spasms. EEG has never shown hypersynchrony, but few frontal spikes and slowing of the background. Patient has now been seizure-free for 11 months. Patient 2 (c.578A>T): 3 years and 8 months old girl with onset of epilepsy at 4 weeks. Seizures were refractory to conventional AEDs; partial (>50%) response to ketogenic diet, corticosteroids and ZNS. VGB was added to ZNS, seizures stopped at the day 4 of VGB introduction. Patient has been seizure free for 3 months now. Hypersynchrony replaced with diffuse slowing, mixed with occasional SW discharges. Conclusion: Little is known about effective antiepileptic treatment of epilepsy caused by CDKL5 gene mutation. Combination of VGB+ZNS fully controlled seizures and resulted in marked EEG improvement in one patient and keep stable in the other. Given the limitation of our observation due to rarity of the patients with CDKL5 mutations, a large prospective multicenter study needs to be performed to confirm these promising results.

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Epilepsy

ICNC-0175: Differeent faces of GRIN2A mutations in epilepsy-aphasia syndromes

Background: Epileptic encephalopathies (EA) are a group of severe disorders characterized by seizures and abundant epileptiform activity that leads to cognitive and behavioral impairment, as they comprise a range of electroclinical syndromes with characteristic ages of onset and clinical and EEG manifestations. Two syndromes with overlapping manifestations have a notable EEG signature of continuous spike and wave during slow-wave sleep (CSWS) and Landau-Kleffner syndrome (LKS). GRIN2A codes for NR2A, a subunit of the NMDA receptor. These are postsynaptic glutamate receptors that allow for the influx of sodium and calcium and are essential for transmission of neuronal activity. NMDA receptors are crucial for synaptic plasticity, the molecular mechanism that underlies learning and memory. Recent research demonstrated GRIN2A mutations occur in 9-20% cases of EA. Proposal: We intend to describe the clinical course of a family, in which the child developed well until the age of 3 years and then developed language delay and mild generalized seizures that were well controlled, but later a global regression, with severe behavior, motor impairment, oral dyspraxia and auditory agnosia developed. His EEGs initially presented as benign centrottemporal spikes evolved to almost continuous bilaterally synchronous pattern of CSWS, that was resistant to different medical treatment. GRIN2A gene found to be positive for the same gene mutation (c.1007+1G>A) in the child and his father, suggesting an autosomal dominant inheritance with variable manifestations. These results highlight that GRIN2A diagnostic testing is warranted in individuals with epilepsy-aphasia spectrum disorders and may enhance prognostic and genetic counseling for families.

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Epilepsy

ICNC-0177: Magnetic Resonance Imaging (MRI) and early Electroencephalographic (EEG) findings in children with Complex Febrile Seizures

Introduction The role of MRI and early EEG in evaluation of children with Complex Febrile Seizures (CFS) is unclear. This study was carried out to describe the findings of MRI and early EEG (EEG done within first 7 days of seizure) abnormalities in previously neurologically normal children with CFS and also to find out their association with different complex features of the CFS. Material and methods Forty children between 6 months – 5 years age with CFS admitted as inpatients or coming to the OPD in a tertiary care hospital were subjected to an MRI brain and EEG within 7 days of the seizure. Children with pre-existing neurological deficit, known epilepsy or afebrile seizures, or in whom the EEG or MRI could not be done for any reason were excluded. The types of abnormalities were noted. The association between MRI or EEG positivity and each of complex feature was evaluated by Chi square test. If the cell size was small then Fisher’s exact test was applied. Results 7 out of 40 children (17.5%) with CFS were found to have abnormal EEG (Epileptiform in 3 and non epileptiform in 2 cases). There was no correlation between EEG abnormalities and any of complex features by Fisher’s exact test with P< 0.05. Only 4 Children (10%) were found have MRI abnormalities, two cases being chronic insult, one being structural abnormality and one case neurocysticercosis. MRI abnormalities were higher in children with focal features & this was statistically significant by Fisher’s exact test with P= 0.022. Conclusion EEG: None of EEGs were indicative of any epileptic syndrome which would require institution of antiepileptic therapy. Therefore the further management of children remains unchanged despite EEG abnormalities found. There is no correlation between any complex feature and the EEG abnormality. MRI: MRI abnormalities are higher in children focal seizures. One child was found to have Neurocysticercosis, where appropriate treatment, including AED had to be instituted. Thus MRI would be useful in children with CFS who have focal features.

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Epilepsy

ICNC-0178: EEG profile & yield in evaluation of first non-febrile seizures in children-epidemiological observation & review of literature

Abstract Introduction: Seizures are among the most common neurological disorders in the pediatric age group. Up to 10% of children might experience at least one episode suggestive of seizure activity in their life. It is thought that 5% of all medical attendances to emergency department are related to seizures. Whether the first non-febrile seizure is the kick start of long term epilepsy is always a question that physicians & families encounter. Ordering Electroencephalogram (EEG) for children with first non-febrile seizure is a subject of continuous debate. Objectives: To collect demographic background data for children (1 month to 14 years) who presented with the first non-febrile seizure, To determine the prevalence & pattern of EEG abnormalities in Children (1 month to 14 years) with first non-febrile seizure, To estimate the possible yield of EEG in first non-febrile seizure as possible predictor of seizure recurrence or future epilepsy, and To collect possible evidence sufficient to make a recommendation for the use versus abandoning use of routine EEG in children with first episode of non-febrile seizure. Methods: In a retrospective observational study around (400) children who were admitted with first non-febrile seizure to the Pediatric Emergency Centers (PECs) and their seizure were defined using the international league against epilepsy (ILAE) between January 2012 to December 2013 were studied. EEG was requested for 76 patients. Their EEG were reviewed and interpreted by pediatric neurology consultants. Patients’ demographic data and EEG records are then analyzed. Results & Conclusion: Epileptic seizure should be diagnosed clinically and EEG is just a helpful tool. Utility of EEG is debatable in childhood first non-febrile seizure. EEG is helpful but interpretation should be individualized. EEG alone is not very good predictors of seizure recurrence or overall prognosis. Larger scale studies with longer follow up are needed. Key Words: Non-febrile seizure, Electroencephalogram, epileptiform activity.

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Epilepsy

ICNC-0179: Prolonged seizures in children in Sub-Saharan Africa clinical : aspects and management

Prolonged Seizures in Children in Sub-Saharan Africa Clinical : Aspects and Management. MUKEBA KAHAMBA Daniel Lord1, Ndahindwa V2, Kaputu-Kalala-Malu C3 Université de Kinshasa Service de Neurologie Pédiatrique, Département de neurologie, Centre Neuro Psycho Pathologique, Faculté de Médecine, Université de Kinshasa, RDC. 2University of Rwanda - College of Medicine and Health Sciences, School of Public Health, Kigali, Rwanda. 3Service Universitaire de Pédiatrie-Neuropédiatrie, CHR-CHU Sart-Tilman, Université de Liège, 4000 Liège, Belgique. INTRODUCTION There is a paucity of epidemiologic studies of prolonged seizures (persisting for more than 5 minutes) in the Democratic Republic of
Congo (DRC) and in Rwanda. AIM We sought to analyze the clinical presentation, causes, pharmacologic management, and short-term course of these seizures. METHODS We enrolled 436 children, aged five months to ten years, who presented with prolonged seizures at the pediatric emergency departments of nine hospitals. RESULTS Overall, 57.8% of the children were younger than three years; 7% had pre-existing psychomotor delay. Although 21% had had previous seizures, only 13% were receiving antiepileptic therapy. On presentation, 63.5% of the patients had fever and 26% were in status epilepticus. The seizures were focal in 21% of the cases. Malaria was the most common cause, involving 63% of the cases. The recurrence rate was 38% and the mortality rate 4%. CONCLUSION Prolonged seizures in DRC and Rwanda are frequently associated with fever, most commonly caused by malaria. The immediate use of long-acting antiepileptic drug could improve their outcomes. KEYWORDS: children; prolonged seizures; sub-Saharan Africa

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Epilepsy

ICNC-0182: De novo SCN1A mutations in Genetic Epilepsy with Febrile Seizures Plus

Objective: Genetic epilepsy with febrile seizures plus (GEFS+) is a familial epilepsy syndrome characterised by heterogeneous phenotypes ranging from mild disorders such as febrile seizures to epileptic encephalopathies such as Dravet syndrome (DS). While DS often occurs with de novo SCN1A mutations, milder GEFS+ spectrum phenotypes are associated with inherited mutations. Here we determine if sporadic cases with mild GEFS+ phenotypes arise due to de novo mutations in SCN1A. Methods: Over a 15 year period, we recruited probands with GEFS+ phenotypes other than DS, and screened SCN1A for mutations. Results: Seven cases of mild GEFS+ with de novo SCN1A mutations were identified, including a pair of monozygotic twins. Febrile seizures plus (FS+) occurred in six cases, five of which occurred with additional seizure types. The remaining case had childhood-onset temporal lobe epilepsy without febrile seizures. Development was within normal limits for all cases, with the exception of the twin girls, who had significant language impairment and deficits in working memory. All cases had SCN1A mutations which were not detected in either parent. One mutation had been previously reported in a case of DS, and the remainder were novel. Conclusions: SCN1A-associated GEFS+ is traditionally thought to follow a pattern of autosomal dominant inheritance. Our finding of de novo mutations in mild GEFS+ phenotypes suggests that GEFS+ is not always inherited. SCN1A screening should be considered in patients with GEFS+ phenotypes as identification of mutations will influence antiepileptic therapy, prognostic and genetic counseling.

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Epilepsy

ICNC-0185: Landau Kleffner Syndrome – Clinical features and molecular genetic findings in a cohort of 50 patients

Introduction: Landau Kleffner syndrome (LKS) is a rare epileptic encephalopathy, with an estimated incidence of 1 in 978,0001. It presents in the 3-10 year age range with language regression and characteristic abnormalities on electroencephalogram2. Recently, mutations in the gene encoding the glutamate receptor, ionotropic, N-Methyl-D-Aspartate, subunit 2A (GRIN2A), have been reported in 8-20% of individuals with LKS and related focal epilepsies with aphasia3,4,5. Methods: In this study, we (i) delineate the clinical features of our cohort (including response to treatment and long-term outcome through retrospective case note review) and (ii) determine the frequency of GRIN2A mutations using direct Sanger Sequencing and multiplex ligation probe amplification (MLPA) techniques. Results: Fifty patients were identified. 88% had clinical seizures. The mean age of regression was 4.6 years (S.D. 2.0). Duration of follow up ranged from 1 to 20 years. Approximately 35% are now adults. Preliminary data suggests that in adulthood, approximately 35% remain dependent (unable to gain employment/in residential care), 35% are fully independent with no/minimal difficulties, and 30% are independent but have significant residual impairment of speech and language or continue to have seizures or neuropsychiatric symptoms. Approximately 15% of the cohort are positive for GRIN2A mutations. Mutations include indels, frameshifts and missense mutations. Conclusion: This is one of the largest reported cohorts of children with LKS with long term follow up data, providing valuable information for prognostication. The frequency of GRIN2A mutations in this cohort is in keeping with previous studies confirming that LKS is likely to be

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Epilepsy
ICNC-0186: Clinico-etiological profile of infants with first seizure: An observational study from a developing country (India)

Introduction: The risk of seizures is the highest in infancy but there is not much data from this region on infants with first seizure. Methods: We studied 75 (61.3% males) consecutive infants (28 weeks-1 year) presenting with their first seizure to the pediatric emergency. Seizures were classified as per ILAE Classification, 1981. Seizure semiology was determined based on eye-witness account (77.3%), or direct observation. Routine biochemical studies, inter-ictal EEG, and developmental assessment were done in all infants. Neuroimaging was done selectively. Results: Mean age was 5.8±3.4 month and 42.7% had seizures as their only complaint; fever was the most common co-morbidity. 57 (76%) patients presented with a first seizure. 93.3% infants had short-lasting (<15 min) and generalized (72%) seizures. Biochemical studies were abnormal in 27 (36%), with hypocalcemia in 26. 12 CT scans and 10 MRI studies were done in 20 patients. In unprovoked seizures, only 31% of these provided any diagnostic information. Majority of the infants had provoked seizures (68%), 1/3rd of which were due to hypocalcemia. 29.3% had neuroinfections (pyomeningitis, 21.3%). Eight (10.7%) infants had febrile seizures and 5 had Benign infantile convulsions. Thirteen (17.3%) infants had developmental delay, with majority having moderate delay. Nine (12%) infants died during the duration of the study, 2 during the course of a seizure. Conclusion: Metabolic derangements and neuro-infections were the commonest etiology. Existing management guidelines for infants with an initial seizure need to be modified for our region.

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Epilepsy
ICNC-0187: Teenage talks and a teenage tailored booklet for enhancing self-management of epilepsy

Introduction: Teenagers with Epilepsy require knowledge to enhance their self-management skills and confidence prior to transition to adult services. Methods: Teenagers aged 14 and 18 were given: (1) A semi structured individual session (Teenage Talk) with clinical nurse specialist (CNS) covering lifestyle and safety issues for young people with epilepsy. (2) The teenager was then given a booklet developed by the CNS and epilepsy team covering these topics. A telephone questionnaire was used to obtain the teenagers’ views about this approach. Results: 30 teenagers had the Teenage Talk and the information booklet. 30 said they would be ‘extremely likely’ to recommend the CNS Teenage Talk to a friend with epilepsy. The majority had not previously had information about the following prior to the Teenage Talk: Contraception (77%), Cigarettes, alcohol and drugs (77%), enjoying yourself and keeping safe when out and about (83%), how can my friends help? (80%), SUDEP (73%) and feeling positive (70%). Teenagers said they would like information on managing their epilepsy at school, sport, bullying, living independently when they are older and group workshops. Prior to having this service, only 10% felt they had always had enough opportunity to ask questions in clinic, 51% mostly and 31% sometimes. 15/30 teenagers provided additional comments showing what they valued about the Teenage Talk. Conclusions: This audit evidences the value of a CNS routine in providing information to teenagers with epilepsy, utilising a semi structured approach with additional written information. Topics covered should be also be informed by the teenagers.

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Epilepsy
ICNC-0188: Epilepsy onset features in puberty period

Purpose: to study epilepsy onset features in puberty period in girls Material and methods: Research was part of prospective observational uncontrolled comparative study of the antiepileptic drugs reproductive side effects. The age of epilepsy onset were studied at 155 female patients. Patients were divided into three groups according WHO classification of puberty age (1997): 1gr. - before puberty- 1-9y.o., 2gr. – puberty- 10-18, 3g. – after puberty- older 18. Frequency of epilepsy onsetand menarche was studied in 4 subgroups of puberty period. STATISTICA for Windows system (version
5.5) was used Results: there were 23 patients (15%) in 1 gr, 92 (59%) – in 2gr, 40 (26%) – in 3 gr. Differences in the epilepsy onset in the comparison groups were statistically significant above in puberty (p <0.001). Epilepsy began in childhood (until 18 y.o) in 75%. Epilepsy onset in 4 subgroups of puberty period according phases of maturing of hypothalamo-hypophysial system: 10-11y.o- beginning of hypothalamo-hypophysial hormones secretion, 12-13-beginning menses, 14-15- becoming of ovulatory peak, 17-18- establishment of a constant rhythm of hormones secretion. There were — 18 patients (20%) into 1 subgroup, subgroup 2 — 35 (38%), subgroup 3 — 24 (26%), subgroup of 4 — 15 (16%). Prevalence of epilepsy onset in the integrated age range of 12-16 years was statistically reliable (p<0.001). The direct connection of epilepsy onset with menarche was revealed at 13%. It was increased risk of catamential and resistant epilepsy. Conclusion: Thus, hormonal changes during the puberty period often provoked epilepsy onset. The epilepsy onset occurred during periods of the beginning oestradiol production and its ovulatory peaks. It confirms proconvulsive effect by estrogens. Relation epilepsy onset with menarche was increased risk resistant epilepsy due to catamential pattern. The reported study was funded by RHSF according to the research project № 15-06-10816

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Epilepsy
ICNC-0169: Quantitative EEG analysis in acute encephalopathy during acute phase
Introduction: Acute encephalopathy (AE) in children is associated with considerable mortality and/or severe neurological sequelae. Electroencephalogram is routinely used for diagnosis and assessment of AE. However, it is not easy to predict the prognosis of AE with visual assessment of EEG in acute phase. The aim of this study was to examine whether qualitative analysis of EEGs was able to predict the prognosis. Methods: Patients were grouped into those with normal outcome (n = 54), with mild-moderate (n = 4), severe (n = 5), and most severe (n = 5) sequelae. EEGs were recorded within 120 hours and representative EEG epochs were selected for analysis. Furthermore, data from unfavorable outcome (severe and most severe groups, n = 6) and favorable outcome (normal, n = 38) for whom EEG was recorded within 24 hours were also compared. Results: Although the milder and the most severe grades of EEG correlated with neurological outcome, the outcome of moderate EEG severity group was variable and was not predictable from usual inspection. Frequency band analysis revealed that the mild-moderate group showed the highest power value in the delta band. In EEGs within 24 hours from onset, alpha band powers were significantly lower in the unfavorable outcome group than the favorable outcome group in frontal and occipital areas. Conclusion: Sequential EEG recording up to 24 hours from onset appear to be helpful for distinction of the severe and most severe groups from the favorable outcome groups.

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Epilepsy
ICNC-0190: Evaluation of effectiveness of ketogenic diet in treatment of refractory Epilepsy in children
Introduction: Refractory epilepsy means inadequate seizure control despite appropriately used 2 AEDs for 18 – 24 months. This prospective study aimed to evaluate efficacy of the ketogenic diet in children with medically refractory epilepsy. Methods: The study included two groups of children with symptomatic intractable epilepsy. Group “A” with 22 patients with age range 3.5-7 years and given classic ketogenic diet and group “B” with 20 patients with age range 3.5-8 years and started 3rd antiepileptic drug. Results: eighty percent of patients of group A showed tolerance of ketogenic diet. There was a significant increase in mean z score of anthropometric measurements at 3 and 6 months. There was, no significant difference in serum cholesterol triglycerides LDL levels in group A. Regarding intractability and severity, there was a significant reduction in seizure frequency comparing group A to group B at 3 and 6 months. Also, the seizure frequency in group A at 0, 3, 6 months was significantly reduced after 3months and after 6months. Regarding the severity of seizures, group A had a lower Chalfont seizure severity score compared to group B after 3months and 6months. Also, seizure severity was significantly decreased in group A at 3 and 6 months. Conclusion: The study proved that the ketogenic diet could be a tolerable, safe and effective adjuvant therapy for intractable childhood epilepsy with no apparent adverse effects changes occurring regarding anthropometric measurements and lipid profile.

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Epilepsy

ICNC-0191: Clinical profile and treatment outcome of febrile infection-related epilepsy syndrome in South Indian children

Purpose: To describe clinical features and outcome of Febrile infection related epilepsy syndrome (FIRES), a catastrophic epileptic encephalopathy in a cohort of South Indian children. Methods: We conducted a retrospective chart review of a cohort of children with previously normal development who presented with status epilepticus or encephalopathy with recurrent seizures followed by nonspecific febrile illness during the period between January 2007 and January 2012. They were divided into two groups: super refractory status epilepticus (SRSE) and refractory status epilepticus (RSE) depending on the duration and severity of the seizures. Key Findings: 15 children met the inclusion and exclusion criteria and were included for final analysis. The age at presentation, ranged from 3 to 15 years (median 6.3 years). All the children presented with prolonged or recurrent seizures occurring 1 to 12 days (median 4 days) after the onset of fever. Eight children had super refractory status epilepticus while seven children had refractory seizures with encephalopathy. CSF analysis was done in all the children in the acute phase and the cell count ranged from 0-12 cells/ul (median 2 cells/ul) with normal sugars and protein. Initial neuroimaging (MRI in 10 and CT in 5) was normal in 13 children. Treatment modalities included multiple antiepileptic drugs (4-9 AED; median 5 drugs). Midazolam infusion was administered in seven patients. Eight patients required barbiturate coma to suppress the seizure activity. Duration of barbiturate coma ranged from 2 to 90 days (median three days). Steroids were used in 14 children and intravenous immunoglobulin (2 gm/kg) in seven children. Three children died in the acute phase. All children were maintained on multiple AED till the last follow up, the number of AEDs ranging from 1 to 6 (median 5 AEDs). Patients with super refractory status in the acute phase were more severely disabled on follow up, the median score on the Glasgow Outcome Scale being 2 compared to 5 in the RSE group. Significance: This study reports one of the largest cohort of FIRES from a single center from south India, with an adverse long term developmental and seizure outcome. The duration and severity of seizures in the acute period correlated well with the short term and long term clinical outcome. There is an urgent need for developing new effective therapeutic strategies in this acute catastrophic epileptic syndrome.

Key Words: Status epilepticus, Encephalopathy, Febrile infection

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Epilepsy

ICNC-0198: An open-access web-based EEG platform for remote reading, teaching, and data exchange - Towards crowd sourcing in clinical neurophysiology

Introduction: The widespread use of commercial EEG reading software is limited by restrictive licenses, local access only, and vendor-specific tools. Additionally, current EEG software and atlases for teaching are cost-prohibitive and require local installation of applications. Finally, in resource-limited settings, both clinical care and research in epilepsy are limited by availability of clinical neurophysiology expertise. We aimed to overcome these obstacles by building an open-access web-based EEG platform. Methods: We created a web-based platform, to display EEG data in European Data Format (EDF) files using C, C++, Python and PHP to generate a graphical representation of the EEG data in real-time when requested by the user. The web front-end running on the user’s computer is implemented using Ajax (asynchronous JavaScript and XML) in order to display the EEG data asynchronously, loading one page at a time. Results: A prototype was implemented on a secure web server. Without installing custom software, users can view and read EEG recordings in any standard web browser that displays HTML, JavaScript, and SVG files. Users can switch montages, change sensitivities, add notch filters and simultaneously view files. During development, 31 pediatric EEGs were successfully uploaded from Zambia, and accessed for interpretation in Boston, MA, USA. Conclusions: Our web-based EEG platform lifts many of the limitations of current EEG software. Uploaded data is available almost instantaneously, and can be browsed and read from any web browser. Remote reading, teaching, and both national and international EEG data exchange will enable access to expertise across borders, and allow for peer consultations and crowd-sourcing of neurophysiological expertise. Our site: http://blazeeeg.com/ Source of Funding: World Federation of Neurology, Boston Children’s Hospital MSO Innovated Research Award

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Epilepsy

ICNC-0192: Cornelia de Lange syndrome and epileptic encephalopathy: an uncommon association

Introduction: Cornelia de Lange syndrome is characterized by multiple congenital anomalies and mental retardation. Epilepsy is a clinical feature found in about 20% of cases, and focal epilepsy is the most common type of epilepsy in these patients. A recent clinical series reported several Italian patients with easy-to-treat epilepsy in monotherapy with a favourable outcome. In about 65% of cases is caused by mutations in three known different genes: NIBPL, SMC1A and SMC3. This case report refers to the unusual association Cornelia de Lange syndrome and difficult-totreat epileptic seizures. Clinical Case: A seven years old boy with a mutation in the NIBPL gene has attended Neuropediatrics Outpatient Clinic since the age of four years because of with myoclonic, frontal hypermotor and postural tonic seizures. An aggravation of seizures occurred with several daily seizures, namely tonic. Video-EEG showed extensive epileptiform activity (spike and wave and polyspikes) with marked sleep increase, and a few tonic seizures were recorded. No structural lesion was found on MRI. An association of antiepileptic drugs was tried, first with little benefit (valproic acid, levetiracetam and zonisamide), with a significant improvement with the association of rufinamide. Discussion: Contrary to the most frequent situation in Cornelia de Lange epileptic patients, this patient evolved to a pharmacoresistant epileptic encephalopathy. This case report pretends to alert to the possibility of more severe forms of epilepsy in patients with Cornelia de Lange syndrome, with so that this can be recognised early and adequate polytherapy be established.

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Epilepsy

ICNC-0194: Predictors of poor seizure control in children managed at a tertiary care hospital of eastern Nepal

Introduction: Various factors have been claimed to predict outcome of afebrile seizures in children. This study aims to find out the predictors of poor seizure control in children at a resource limited setting. Methods: This was a prospective study done from July 1st 2009 to January 31st 2012 at B.P. Koirala Institute of Health Sciences, Nepal. Children (1 month-20 years) with afebrile seizures presenting to pediatric neurology clinic were studied. Significant predictors on bivariate analysis were further analyzed with binary logistic model to find out the true predictors. Positive predictive values (PPVs) and negative predictive values (NPVs) for the true predictors were calculated. Results: Out of 256 cases (male: female ratio 3:2) with afebrile seizures followed up for median duration of 27 (IQR 12-50) months, seizure was poorly controlled in 20% cases. Three factors predicted poor seizure control. They were frequent (≥1 per month) seizures at onset (p = 0.022, OR 12.76, 95% CI 1.44-112.73, PPV 25%, NPV 98%); remote symptomatic etiology (p = 0.043, OR 3.56, 95% CI 1.04-12.17, PPV 36%, NPV 92%); and need of more than one anticonvulsant drug (polytherapy) (p = 0.000, OR 12.83, 95% CI 5.50-29.9, PPV 56%, NPV 96%). The strongest predictor was need of polytherapy. When all three factors were present, PPV and NPV for prediction of poor seizure control were 70% and 90% respectively. Conclusion: Frequent seizures at onset, remote symptomatic etiology of seizure and need of polytherapy were associated with poor seizure control in children with afebrile seizures.

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Epilepsy

ICNC-0195: Case report: treatment of pharmacological resistant form of Lennox-Gastaut Syndrome in the two-year child

Introduction: The problems of development of infants’ brain are known to be complex and urgent because the success of solving these problems increases quality of life in childhood and adolescence. One of these problems is epileptic encephalopathy (EE) in infants. There is a wide variety of this syndrome, what makes the diagnostics very difficult (West, Lennox-Gastaut syndrome (LGS) etc.). The main role in establishing of diagnosis plays EEG with video monitoring that shows hypsarrhythmia of the waves. However, the clinical course in combination with hi-tech examination are strongly recommended. The aim of investigation was optimization of methods of treatment of pharmacological resistant forms of epilepsy that can be illustrated by the case of the two-year boy with symptomatic Lennox-Gastaut syndrome. Materials and methods: The diagnosis was based on the routine examination and clinical manifestations (seizures, appeared with different periodicity). The child was ill since birth and treated with different combinations of antiepileptic drugs (AED). The treatment was unsuccessful, what forced us to find another approach. Tablets of hydrocortisone we dose up to 2 mg. The treatment was carried out during five months. EEG with video monitoring was carried out during 8 hours in active and passive wake, night sleeping and after awaking. Results: First EEG examination provided, when child was 1 year old, showed “sharp slow wave”, “spike-, polyspike-and-waves” complexes in the right parieto-temporal area. In the left one were registered “sharp slow wave” and “spike-and-wave” complexes with reverse of phase under the electrodes P3 and T5. Physiological patterns of sleeping were weakly manifested and periodically were substituted by epileptiform activity. In the middle of therapeutic course the child became seizure-free and considerable more active and...
some life skills developed. During the one-year follow-up period was not revealed any seizures, though the child did not take AED or hormones. EEG registered just single complexes “sharp slow wave” with amplitude up to 100mcV in left temporal area of the brain with reverse of phase under the electrodes T3, T5. There were not any pathological movements during the sleeping. As result of a treatment was also observed obvious development of child’s brain, which was manifested in physical and mental activity. Conclusion: Thus, we can conclude that early beginning of individually selected therapy in infants with EE and LGS gives the possibility for the normal development of their brain that may be seen in the normalization of physical and mental development.

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Epilepsy

ICNC-0196: Epilepsy Syndromes in Children Attending Child Neurology Clinic: A Descriptive Study at Eastern Nepal

Introduction: Recognition of epileptic syndromes allows an accurate diagnosis and management of seizure disorders. This study aims to study the common epilepsy syndromes in a resource-limited setting. Methods: This was a prospective hospital-based study from 1st July 2009 to 31st July 2015. Patients (1 month-20 years age) with afebrile unprovoked seizure were studied. Epilepsy syndromes were diagnosed electroclinically. Results: Epilepsy syndromes were diagnosed in 88 (15.5%) out of 568 cases. Epilepsy with Generalized Tonic Clonic Seizure Alone (36.4%), West Syndrome (22.7%), Rolandic Epilepsy (11.4%), Childhood Absence Epilepsy (CAE, 11.4%), Lennox Gastaut Syndrome (LGS, 8.0%), Self Limited Familial Infantile Epilepsy (SLFIE, 3.4%), Febrile Seizure Plus (FS+, 2.3%) and Juvenile Myoclonic Epilepsy (JME, 2.3%), were common Epilepsy Syndromes. Age of onset, clinical feature and response to therapy were unique for each syndrome. Most common causes of West syndrome were birth asphyxia and meningocencephalitis (50% and 35%) and that of LGS was birth asphyxia (57%). Response to monotherapy was 100% for CAE, JME and FS+. For LGS and West Syndrome, response rates to monotherapy were low (15% and 20%) whereas pharmacoresistance rates were high (40% and 35% respectively). Status epilepticus was common (42%) feature in LGS. Positive family history of seizure was present in all cases with SLFIE. Conclusion: In a resource limited setting, syndromic diagnosis of epilepsy is possible in majority of children using proper clinical data and simple tools like electroencephalogram and CT scan. Birth asphyxia and brain infections are the common causes of epileptic encephalopathies and they respond poorly to antiepileptic drugs.

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Epilepsy

ICNC-0197: Sex disparity in children with West syndrome: Evidence from Indian data

Introduction: West syndrome is a distinct age-dependent epileptic encephalopathy, characterized by constellation of clustered spasms and hypersrrhythyma pattern on EEG. There is preliminary data from Indian studies which suggests male preponderance in children with West syndrome. The objective of the present study was to investigate this gender disparity and its relationship with short-term or long-term outcome if any. Methods: We investigated this association via systematic review of published studies from India. We used a systematic review strategy as there is no national population-based registry for West syndrome. We searched in PubMed, EMBASE, Scopus and Web of Science database for publications in English language from January 2001 to November 2015 using key terms: West Syndrome OR Infantile Spasms and India. Data on gender distribution and its effect on outcome were extracted from all the sources and incorporated in our study. Results: We identified seven eligible published studies. Male preponderance was observed in two-third of study population. There is also significant interregional variation in gender ratio. However, there is insufficient evidence to suggest its relation with short or long-term outcome. Conclusion: Our study clearly demonstrated significant high male prevalence in children with West syndrome in India. There is a clear need of prospective studies to confirm this observation and assess its implications on outcome.

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Epilepsy

ICNC-0959: Myoclonic manifestations associated with typical absences in children: an observational study

Background: The myoclonic manifestations are frequently associated with absence seizures in children. We report the spectrum of myoclonic manifestations associated with typical absences in children. Methods: The clinical records of children presenting with absences at two tertiary care referral centres in North India from June 2013 to December 2014 were reviewed. The results were summarized and reported. Ethical approval was taken from the Institutes’ Ethics committee. Results: Twenty-four children with absences were seen during the study period. There were 15 boys and 9...
Epilepsy

ICNC-0199: Search for behavioural and learning difficulties in children with childhood absence epilepsy

Background
ADHD is more frequent in children with epilepsy (20%) compared to general paediatric population (3-7%). Children with epilepsy, particularly CAE, suffer attention and executive function problems between seizures which often persist post treatment. Aim
A retrospective study reviewed the comorbidity of ADHD in children diagnosed with CAE from an epilepsy clinic in South Africa (between 2005-2015). Methods The neurology service database was searched for all children with CAE based on clinical and EEG features; documentation of associated features of ADHD or other comorbidities were recorded. Results Of the 177 identified patients data was available from 65; median age of onset 5 years (range 2-12 years). 41 children had typical clinical seizure presentation with typical EEG features, 24 had atypical EEG changes. All received sodium valproate, 7 with poor seizure control received additional lamotrigine. 39 (60%) had learning difficulties; 16 (24.5%) children had behavioural issues (hyperactivity and inattention). Of the 16 children with ADHD, 6 received methylphenidate without exacerbation in their CAE. Conclusion
Whilst ethosuximide is the drug of first choice for CAE, access is limited in South Africa, hence the use of valproate and lamotrigine. Prevalence of ADHD may be underestimated, as in a busy clinical setting the management focus tends to target epilepsy control and features of ADHD would need to be actively screened for. Inattention and hyperactive symptoms are part of the CAE, and ongoing service delivery will include tools to monitor for this co-morbidity.

Tandokazi Quvile, Jo Wilmshurst

Epilepsy

ICNC-0200: Ethosuximide in the treatment of typical absence seizure

Ethosuximide (ESM) is a "classic" antiepileptic drug in use since the 50s of the last century. ESM is a chiral molecule, with high bioavailability, low protein binding, metabolized in the liver and excreted by the kidneys. Elimination half-life is long, between 40 and 60 hours in adults, 30 and 40 hours in children. Side effects include abdominal pain, nausea, vomiting, hiccups, sedation, and serious side effects, although rare are bone marrow suppression, lupus erythematosus and Stevens-Johnson syndrome. ESM was the first choice drug for epileptic absence type seizures, but the advent of new antiepileptic drugs such as valproate and lamotrigine, its use becomes exceptional. Latest research re-emphasizes its clinical importance given the risk-benefit ratio in a real indication. Complete absence remission is frequent after treatment with ESM compared to VPA, which is consistent with results in animal models and the hypothesis of a potential disease-modifying effect of ESM in absence seizures. Over a period of five years and 9 months (01.01.2010-01.09.2015,) at the Division of Pediatric Neurology, Department of Paediatrics, University Hospital Center Rijeka, ESM were introduced in 24 children for typical absence seizure, who were resistant to treatment with VPA and/or LTG. Majority of patients (90%) were seizure free. It is necessary to take into account new information and new guidelines which again points to the fact that the ESM is effective and useful drug, which becomes again the first choice in the treatment of typical absence seizures.

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Epilepsy

ICNC-0201: Clinical features and outcome of treatment in West Syndrome Patients-study in a tertiary care hospital

Introduction: This study describes the clinical features and treatment outcome with vigabatrine, prednisolone and ACTH among patients with West Syndrome in a tertiary care hospital. Methods: A cross sectional descriptive study was carried out over a period from 2013-2015. Inclusion criteria were clinical symptoms of infantile spasms and hypsarrhythmia/modified hypsarrhythmia on EEG. Either vigabatrine, prednisolone or ACTH were used. In case of Tuberous sclerosis vigabatrine, in hospitalized cases ACTH at home prednisolone were given first. In unresponsive cases other drugs were tried. Results: Total 100 patients were included. Mean age of onset of seizure was 4.97±SD3.94 months and age of first treatment was 5.03±SD 3.80 months. Sixty six percent were male. Focal neurological deficit were present in 4% of patients. Motor delay 56%, speech delay 42% and cognitive impairment in 28% patients. Abnormal neuroimaging found in 73% patients among them cerebral atrophy was found in 45% patients. Thirty nine, 34 and 27 children got vigabatrine, prednisolone and ACTH respectively. Complete remission occurred in 23, 21 and 16 patients from each group respectively (p=0.86)(Anova test). Structural defect were in 67% patients. Conclusion: Motor and speech delay were common. There was no significant difference in the initial treatment response among the drugs.

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Epilepsy

ICNC-0202: Thyroid function in children with epilepsy treated with sodium valproate monotherapy

Introduction: This study was done to observe the thyroid function in children with epilepsy treated with sodium valproate. Methods: A prospective interventional study was done in a tertiary care hospital, during 2013 to 2014. A blood sample was obtained after 12-hours of fasting in early morning. Free thyroxine (FT4), triiodothyronine (T3) and thyroid stimulating hormone (TSH) were determined in serum by immunoassay. Pretreatment and six months after treatment serum FT4, T3, and TSH status were analysed. Result: Male to female ratio was 2.8:1. The mean weight was19.56 kg, the mean dosage was 21.39 mg/kg per day and the mean age of onset of seizure 5.16 years. Absence seizure was in 11(36.7%), simple partial in 6(20.0%) and complex partial in 13(43.3%) patients. The mean FT4 was 1.98ng/dl in pretreatment and 1.76 ng/dl 6th months after treatment. Mean T3 was 1.5mg/dl in pretreatment and 1.57 ng/dl post treatment at 6th month. Mean TSH was 3.36 micro IU/ml in pretreatment and 3.70 micro IU/ml in post treatment after 6 months. Mean serum valproate level 57.95microgram / dl. TSH level was significantly (p<0.05) higher after 6th months of treatment. Conclusion: Valproate monotherapy may cause high TSH in children with epilepsy.

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ICNC-0203: Prehospital treatment of status epilepticus in children and adolescents in central part of Slovenia

AIM To determine the practice of prehospital management of prolonged seizures-status epilepticus (SE) in pediatric age: which drug and when after the seizure onset? METHODS All patients aged from 1 month to 18 years, admitted to our hospital from 1.1.2011 to 1.5.2015, due to prolonged seizure (>5 minutes duration) were included in the study. Medical data were collected retrospectively: age, seizure type, seizure duration, drugs during prehospital treatment. Statistical analysis was done using chi-square test, Fisher’s exact test, Mann-Whitney U test and descriptive statistics. RESULTS Among 113 patients with 184 seizure episodes, 174 episodes fulfilled all inclusion criteria. In 71 (41%) patients it was their first seizure. Median age at SE was 2.7y. Etiology was most often prolonged febrile seizures in 64 cases (35%), remote symptomatic in 42 cases (24%), acute on remote symptomatic in 37 pts (21%). Prehospital treatment was given in 129 episodes (74% of all episodes). Rectal diazepam was used in 91% of all episodes in the age group <3 years, in comparison to 71% of episodes in patients older than 3 years. If an appropriate 1.dose was given later than 10 minutes after the seizure onset, it was still efficient in 17% of cases. CONCLUSIONS The majority of children with prolonged epileptic seizure/SE received the first line treatment in the prehospital setting. The most commonly used drug was rectal diazepam. Treatment later than 10 minutes after the onset of the seizure may still be efficient for termination of prolonged epileptic seizures or SE.

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Epilepsy

ICNC-0208: Valproate induced reversible brain "Pseudo-Atrophy"
Introduction: Reversible cerebral atrophy with cognitive decline due to valproate is a rarely described entity. Valproate remains the drug of choice in treating a wide spectrum of epileptic disorders. We describe an interesting case of a child being treated with valproate developing cerebral atrophy and cognitive decline. Subsequently, valproate was stopped resulting in the reversal of cerebral atrophy and improvement in cognition. We describe the clinical and radiological phenotype of our case (with images). Case A previously well girl with an unremarkable peri-natal and developmental history presented with generalised tonic-clonic, myoclonic and absence seizures at the age of 7 years and MRI was normal. She was then started on Valproate and noted to have cognitive decline with loss of skills and worsening epilepsy with a deterioration of epileptiform discharges on EEG. Follow up MRI revealed significant cerebral atrophy. Extensive workup looking for progressive disorders did not reveal a cause. Valproate was postulated as the possible cause and was replaced by levetiracetam. Repeat MRI at 8 months showed reversal of the cerebral atrophy alongside improvement in her clinical seizures as well as her EEG. She has better cognitive skills, activities of daily living and school performance. Discussion: Our case demonstrates that valproate can induce cognitive deterioration along with a reversible brain “pseudo”-atrophy. It is important to consider valproate as a cause whilst investigating for an aetiology in children with progressive deterioration in epilepsy and cognition. In the absence of any other aetiology, stopping valproate and follow up neuro-imaging must be considered.

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Epilepsy

ICNC-0209: Impact of Caregiver Burden in paediatric epilepsy
INTRODUCTION In paediatric chronic health conditions such as epilepsy, the impact of the disease and its treatment on the caregivers and their family functioning is an important consideration given the role of the family in child adaptation to the disease. Therefore, there is need for periodic evaluation of effects of caregiver burden and its implication on the family using systematic measures of their subjective experiences and perceptions. METHODS 109 eligible primary caregivers of children with epilepsy attending our paediatric epilepsy clinic completed questionnaires providing information on their sociodemographic and epilepsy-related variables as well as Paediatric Quality of life family impact module. RESULTS The median health-related quality of life score of the caregivers was 46.3 (IQR = 31.3, 67.5), ranging from 1.9 to 95. While the median family functioning score was 46.9 (IQR = 31.3, 71.9), with a range of 3.1 to 100. There was a strong correlation between family functioning score and caregivers HRQL score (p=0.78, p<0.001). On regression analysis, lower caregiver education level and a higher number of seizures per month were associated with a low total functioning score of the caregivers after adjusting for age of the caregivers and the number of AEDs taken. CONCLUSION Paediatric epilepsy is associated with a high impact of caregiver burden (poor functioning) in a quarter of our subjects. It is associated with lower caregiver education level and poor seizure control.

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Epilepsy

ICNC-0210: Clinical Features of the Patients with PCDH19 Mutation
Protocadherin 19 (PCDH19) related epilepsy is a novel epileptic syndrome, characterized by the presence of epilepsy in female patients, associated with mental retardation and autistic features in most cases. PCDH19 encodes protocadherin 19 and is located on chromosome Xq22.1. Clinical features and seizure semiology have been described as heterogeneous. The main characteristics of seizures, making clusters of brief seizures, frequently associated with fever. Intellectual disability might be present, ranging from mild to severe. Behavioral and psychiatric problems are a common feature of the disorder, such as aggressiveness, depressed mood, and psychotic traits. We present four girls, aged between 7 and 18 years, who have PCDH19 mutations. All patients manifested mostly fever induced seizure clusters, but initial seizures were afebril in all patients. The onset of seizures were ranged between 7 and 16 months. One patient showed an atypical presentation, who had a late- onset (16 months) seizure, no history of status epilepticus and intellectual disability. Her seizures were controlled with valproate monotherapy and she is seizure free since 5 years. Other patients had normal development until the onset of seizures, but showed intellectual disability and/or behavioral...
abnormalities during follow-up. The seizures of these patients could not be controlled despite combined antiepileptic therapy. Molecular diagnosis is essential to plan antiepileptic treatment and predicting prognosis of genetic epileptic syndromes. Therefore, PCDH19 mutation should be considered in female patients who presented with cluster of seizures with or without fever and mental and/or behavioral abnormalities.

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ICNC-0211: The clinical spectrum of febrile infection-related epilepsy syndrome
Introduction Febrile infection-related epilepsy syndrome (FIRES), also known as acute encephalitis with refractory, repetitive partial seizures (AERRPS), is a seizure disorder characterized by refractory focal seizures and poor neurological outcome. Its clinical phenotype has not been fully understood due to the very low incidence of this condition. Aim To summarize clinical features of newly identified patients with FIRES. Methods A prospective nationwide survey between 2010 and 2014 in Japan. Results Among 28 registered patients, 26 patients (19 males) fulfilled the diagnostic criteria of AERRPS and were enrolled. Age at onset was between 2 and 12 (mean 7.5) years old. The onset was preceded by infection or vaccination in 25 of 26 patients with average latent period of 4.5 days. Cerebrospinal fluid from 20 patients (76%) showed mild to moderate pleocytosis. Magnetic resonance imaging abnormalities were present in 17 patients (65%) and mainly involved hippocampus, amygdala, basal ganglia, cerebral cortex, or thalamus. All patients received immunomodulatory treatments including corticosteroid and/or intravenous immunoglobulin. Twenty-four patients (92%) were treated by high-dose Intravenous barbiturates (duration: 26.5 ± 27.7 days, dosage: 9.1 ± 4.1 mg/kg/h). Prognosis was good in 9 (35%), moderate in 11 (42%), and poor in 6 (23%). Compared to our historical cohort, the present cohort showed shorter duration but higher dosage of barbiturate anesthesia, more frequent use of immunomodulatory treatments, and better prognosis. Conclusion These data suggest possible harmfulness of excessive barbiturate anesthesia and the favorable effect of immunomodulation on the long-term outcome of FIRES.

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Introduction Psychogenic non epileptic events (PNEE) are paroxysmal events with absence of clinical or electrophysiological evidence of epilepsy. This study aimed to identify the variables that are associated with PNEE, develop a PNEE score card and to test the diagnostic accuracy of the developed score card. Methods Retrospective chart review of 101 consecutive children and adolescents aged 3-18 years with a diagnosis of PNEE and a control group of 75 children with epilepsy were carried out. Children with breath holding spells, self-stimulatory behaviour, tics, chorea were excluded. Results In the sample of 101 children and adolescents with PNEE, there was a mild preponderance of girls (54.5%). Mean (SD) age of the whole sample was 11.30 (3.11) years. Age of onset and presentation, gestational age, neonatal encephalopathy, developmental delay, family history, aura, semiology, amnesia for event, post ictal phenomena, recurrence, duration, neurological deficit and neurocutaneous markers were statistically significantly associated with PNEE either as protective or risk factor. The age of onset more than 6 years was 17 fold, presence of somatic aura was 13 times, long event duration was 14 times, absence of post-ictal phenomenon was 170 times and school absenteeism was 16 times more among the PNEE patients. Score card based on these predictive factors has a specificity of 95% and sensitivity of 85% for a cut-off score of ≥ 45. Conclusion Our PNEE score card can be used to screen children and adolescent for PNEE in resource limited countries with high burden of epilepsy and PNEE.

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Epilepsy

**ICNC-0214: Modeling the cellular phenotype of STXBP1-related epileptic encephalopathy using iPSC**

【Objective】Syntaxin-binding protein 1 (STXBP1) is essential for synaptic vesicle exocytosis. Mutations of its encoding gene, STXBP1, are among the most frequent genetic causes of epileptic encephalopathies. However, the precise pathophysiology of STXBP1 haploinsufficiency has not been elucidated. Using patient-derived pluripotent stem cells (iPSCs), we aimed to establish a neuronal model for STXBP1 haploinsufficiency and determine the pathophysiologic basis for STXBP1 encephalopathy. 【Methods】We generated iPSC lines from a patient with Ohtahara syndrome (OS) harboring a heterozygous nonsense mutation of STXBP1 (c.1099C>T; p.R367X) and performed neuronal differentiation. Biochemical and morphological analyses were conducted on iPSC-derived neurons with STXBP1 mutation. 【Results】Both STXBP1 mRNA and STXBP1 protein expression levels of OS-derived neurons were approximately 50% lower than that of control-derived neurons, proving that OS-derived neurons are a suitable model for elucidating the pathophysiology of STXBP1 haploinsufficiency. Through western blot and immunocytochemistry assays, we found that OS-derived neurons show reduced levels and mislocalization of syntaxin-1, a component of soluble N-ethylmaleimide-sensitive factor attachment protein receptor (SNARE) proteins. In addition, OS-derived neurons have impaired neurite outgrowth. 【Conclusions】This model enables us to investigate the neurobiology of STXBP1 encephalopathy throughout the stages of neurodevelopment. Reduced expression of STXBP1 leads to changes in the expression and localization of syntaxin-1 that may contribute to the devastating phenotype of STXBP1 encephalopathy.

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Epilepsy

**ICNC-0215: Economic and Psychosocial Burden in Pediatric Epilepsy**

Background: Pediatric epilepsy (PE) has a substantial impact on quality of life (QOL) of patients & caregivers & can be more disabling than epilepsy itself in developing countries. Objective: To study and compare various domains affecting the QOL in lower socioeconomic (LSE) versus higher socioeconomic (HSE) group. Methodology: The sample included 107 patients (78LSE, 29 HSE) aged 3-15 years on antiepileptic drug (AED) for at least 12 months. QOL was measured by Quality of life in childhood epilepsy (QOLCE) questionnaire which was modified for our study. The Fisher’s t-test was used to compare the mean QOL scores. The domains assessed were psychosocial, economic, medical, behavioral, cognition & education. Results: The factors affecting the QOL are age, socioeconomic status, literacy, family support, seizure type, frequency & number of antiepileptic drugs. Our study showed a significant difference with high prevalence of adverse social impact (42% vs 34%), economic burden (71% versus 17%), cognition and education (60% versus 17%), mood and behavior (67% versus 24%) in LSE versus HSE. Medical side effects were reported more in the HSE (21%) versus LSE (8%). On statistical analysis, economic burden was found to be significant in LSE (p value < 0.0001; CI - 95%). The social impact was significant in LSE (p value - 0.0649; CI - 95%). AED side effects were more in HSE (p value - 0.0558; CI - 95%), although both variables were not clearly statistically significant. All other domains studied were statistically insignificant. Conclusion: This ongoing study in small number of children has revealed interesting results while comparing LSE versus HSE groups & extending this study further by including large numbers would help us in reducing the impact of PE on QOL.

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Epilepsy

**ICNC-0216: Early onset epileptic encephalopathy caused by SCN8A mutation**

Objective: Since 2012, over 60 mutations of SCN8A have been identified in early infantile epileptic encephalopathy (EIEE) 13. In order to refine this syndrome phenotype, we performed a review of patient records reported to date, adding a new personal case. Methods: Whole exom sequencing was performed on our proband patient. We performed a review of the clinical picture of other patients reported to date. Results: A de novo mutation in the SCN8A gene (c.2641G>T (p.V881L)) was detected in our 4 year old male patient presented by 8 month with global developmental delay and infantile spasms. He was treated with ACTH with partial impact. He was then treated with numerous anti epileptic agents and ketogenic diet with no influence on his intractable seizures. Following syndrome diagnosis, he was treated with carbamazepine reported as efficient. The seizure number decreased but he suffered from irritability. He is now treated with cannabis. Mutations in SCN8A account for about 1% of EIEE. Most patients have generalized tonic-clonic seizures, followed by intellectual disability. Febrile seizures are rare in distinction from Dravet. Hypsarrhythmia is also rare. Some patients have movement disorder and SUDEP was also reported. Seizures are typically refractory. Carbamazepine and Oxcarbazepine
were useful in the largest number of patients also in distinction from Dravet. • Conclusions: Patient exomes revealed the role of SCN8A in EIEE. Differences among treatment options of EIEE emphasize the importance of early genetic diagnosis for the new era precision medicine: targeted treatment based on genetic profile.

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**Epilepsy**

**ICNC-0217: Cognitive decline in a rodent model for temporal lobe epilepsy**

Introduction Cognitive impairment is frequently observed as comorbidity in patients with temporal lobe epilepsy. Though several causes have been suggested, due to the confounders in clinical studies and shortage of longitudinal data it is difficult to assess the individual contribution of factors. Here, we longitudinally investigated the effects of seizure frequency on cognition, anxiety and anhedonic-like behaviour in a rodent model for temporal lobe epilepsy. Material and Methods Epilepsy was induced by submitting rats to self sustained limbic status epilepticus (SSLSE). Behavioural testing included working memory, spatial memory, recognition memory, anxiety, locomotor activity and anhedonic-like behavior, and was conducted before SSLSE (baseline), immediately after SSLSE and in the chronic phase when spontaneous seizures occurred. Seizure frequency was assessed by video-EEG recordings. Additionally, the severity of the status epilepticus was scored by the latency to first and amount of generalized motor seizures during stimulation. Results Spatial memory was reduced after SSLSE induction, yet this decline was not further reduced in the chronic phase. Compared to baseline, SSLSE animals showed a progressive decline in recognition memory. Also cognitive performance was not confounded by factors such as anxiety, alterations in locomotor activity or anhedonia. There was no correlation between the seizure frequency and spatial- or recognition memory. Moreover, was also no correlation between the severity of the status epilepticus and spatial- or recognition memory. Discussion It has long been hypothesized that seizures cause cumulative brain damage and thereby may result in progressive memory impairment. Though in this animal model we established a progressive loss of recognition memory, seizure frequency did not correlate with this impairment. Alternatively, other dynamic parameters such as interictal events may play a role in cognitive performance.

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**Epilepsy**

**ICNC-0218: Population pharmacokinetics of the antiepileptic drug lacosamide in children aged 6 months to 17 years**

Introduction Clinical trials evaluating pediatric lacosamide use are ongoing. Here we describe development of a population pharmacokinetic model and subsequent simulations to guide pediatric dosing. Methods Sparse plasma samples were collected from children with epilepsy participating in two trials (SP0847, SP1047). The model was developed using nonlinear mixed effects modelling, with a single compartment and first-order absorption and elimination. Effects of demographic variables and concomitant antiepileptic drugs were taken into account. Plasma clearance was modelled using allometric scaling on body weight with a freely estimated allometric exponent, and volume of distribution with a fixed theoretical allometric exponent. Residual error was modelled using additive and proportional error terms. Results Lacosamide plasma concentration-time data (n=402) were available from 79 children (body weight 6–76 kg), with a balanced distribution of 14, 22, 25, and 18 patients in age groups 6 months to <2 years, 2 to <6 years, 6 to <12 years, and 12 to <18 years, respectively. Race, sex, age, renal function or co-administration of valproate had no significant impact on lacosamide plasma clearance, but an increase was observed with co-administration of carbamazepine, phenobarbital or phenytoin. Plasma exposures similar to those in adults receiving lacosamide 400 mg/day were reached using pediatric dosing adaptations by weight bands: 12 mg/kg/day in children <30 kg, 8 mg/kg/day in children from 30 to <50 kg, and 400 mg/day in children ≥50 kg. Conclusion The model adequately described lacosamide plasma concentrations in children. Weight-based adaptations can be used to guide dosing in pediatric clinical trials. UCB Pharma-sponsored
**Epilepsy**

**ICNC-0219: Use of an exposure-response model of lacosamide developed in adults with focal epilepsy to analyze preliminary data from a dose-finding pediatric trial**

**Introduction**
Clinical trials evaluating lacosamide use in paediatric populations are currently ongoing. To support the design of Phase III trials, an adult exposure-response model was developed and subsequently used to analyze seizure count and lacosamide plasma concentration data from children.

**Methods**
The lacosamide exposure-response model was built using daily seizure counts (N=210,234) of 1308 adult patients who participated in three double-blind, placebo-controlled clinical trials in adjunctive treatment of focal epilepsy (SP0667, SP0754, SP0755). The best fit was obtained with a negative binomial distribution with zero-inflation and Markovian element associated with a mixture model, stratifying patients according to reduced or increased seizure frequency (SF). Preliminary SF data from an open-label, dose-finding trial (SP0847) investigating the safety, efficacy and pharmacokinetics of adjunctive lacosamide in children with focal epilepsy were analyzed using the adult exposure-response model. Model development and simulations were performed using nonlinear mixed-effects modeling implemented in NONMEM.

**Results**
At the cut-off date, 28 patients aged 3-17 years had completed SP0847. The model satisfactorily described the daily seizure count and lacosamide plasma concentrations of the children. Furthermore, simulation results showed that the model correctly predicted efficacy outcomes – median percentage reduction in SF from baseline and responder rates – in the pediatric trial population.

**Conclusions**
Based on the limited data from the pediatric SP847 trial, there was no signal indicating a possible alteration of the exposure-response relationship established in adults. Therefore, the lacosamide dosing strategy in children aged 3-17 years will probably be driven only by lacosamide pharmacokinetics.

UCB Pharma-sponsored

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**Epilepsy**

**ICNC-0221: Epileptic encephalopathy secondary to SCN8A mutation**

**INTRODUCTION:** The SCN8A gene encodes the alpha subunit of voltage-dependent sodium channel (Nav 1.6) located in the central nervous system. It is essential for the initiation and propagation of the action potential. Such mutations have recently been described in the clinical spectrum of epileptic encephalopathies (EEs). Refractory seizures, mental retardation, developmental delay, abnormal movements and death in early childhood characterize them. **AIM:** To report a case of secondary epileptic encephalopathy SCN8A gene mutation. MATERIÁL AND METHODS: This is the first child of healthy nonconsanguineous parents. He was born at term with congenital microcephaly. It showed appropriate development until 7 months at which time started refractory seizures. It required intensive care for multiple episodes due to vitamin B12 deficiency.

The patient died at 3 years old. The EEG showed right focal fronto tempo parietal discharges. While neuroimaging were normal at the beginning, over time they showed brain atrophy. All neurometabolic investigations were negative. The karyotype was normal. Finally the genetic panel to study early onset EEs found a novel variant gene sequence in the SCN8A confirmed: C3272A>G. CONCLUSION: Although the clinical manifestations, neuroimaging and electroencephalographic findings described are nonspecific, they are described in the literature in patients with positive mutations due this gene. Early suspicion of this entity would anticipate the diagnosis avoiding many studies. Diagnostic confirmation allows providing accuracy and early genetic counselling.

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**Epilepsy**

**ICNC-0222: West syndrome due to vitamin B12 deficiency**

Vitamin B12 is one of the essential vitamins affecting various systems of the body. Vitamin B12 deficiency in infants often produces haematological and neurological deficits including macrocytic anaemia, neurodevelopmental delay or regression, irritability, weakness, hypotonia, ataxia, apathy, tremor and seizures. In this article, we report the case of a 6-month-old male patient diagnosed with West syndrome associated with vitamin B12 deficiency. Although the patient had no evidence of macrocytci anaemia in complete blood count, we measured the level of vitamin B12 because the patient had hypotonicity and found it to be low. No other problem was found in the other investigations directed to the etiology of West Syndrome. He was being exclusively breast-fed and vitamin B12 deficiency was related with nutritional inadequacy of his mother. Vitamin B12 deficiency should be considered in the differential diagnosis of patients presenting with different neurological findings. In addition, vitamin B12 deficiency should be considered as a rare cause in West
Epilepsy

ICNC-0223: Progressive myoclonic epilepsy syndrome-diagnostic experience with 7 cases-before and after exom sequencing

Summary: Progressive myoclonic epilepsy syndromes (PMEI) are neurodegenerative diseases of childhood or early adolescence. The availability of exom sequencing helps to diagnose the disease at the earliest. Key words: epilepsy, myoclonus.

Objective: To diagnose the clinical course of various PMEIs to identify the clinical and diagnostic methods for early diagnosis.

Methods: Total seven patients were diagnosed in the span of two years (2013-2015). Predominant symptoms were seizures followed by neuroregression either gradually or very rapidly. Family history helped in early diagnosis. Diagnosis was confirmed by skin biopsy or enzyme assay. After the availability of exom sequencing, diagnosis was confirmed and carrier state in parents was identified by Sanger’s sequencing.

Results: PMEI are a group of epilepsy syndromes characterised by predominant epilepsy, myoclonus and ataxia. The disease has a poor response to antiepileptic medications and have overall poor prognosis. In the present series of seven patients, Half of them were consanguineous. Their onset of disease was at early adolescence phase. Lafora body disease was present in two. Three of them had an involvement of elder siblings. Two of them had neuronal ceroid lipofuscinosis confirmed by enzyme assay. Youngest child of two years was detected by Exom sequencing. Carrier states in the parents were identified by Sanger’s sequencing. Conclusion: PMEI are morbid. It has familial involvement. Early detection with exom sequencing and identification of carrier state in parents may help in preventing the disease in future siblings.

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Epilepsy

ICNC-0224: Comparative description of psychic and emotional state of parents bringing up children with chronic neurologic pathology

Introduction. Psychoemotional state of parents with children who have chronic neurological disorders has a direct impact on the effectiveness of their treatment and rehabilitation.

Methods. 23 parents of children with epilepsy psychoemotional state (mean age 30.34 years) (study group - SG) was studied. The control group (CG) consisted of 19 parents of children with cerebral palsy (CP) without symptomatic seizures (mean age 34.35 years). Families were comparable in composition, age of parents and children, social and economic state. Psychoemotional terms of parents were determined by SF-36 questionnaire.

Results. MCS (mental components scale) middle score was 34 (Me 31.3, σ 9.11, m1.9) for the IG and 47.6 (Me 46.1, σ 9.52, m1.77) for CG. Thus, the difference in points of MCS was 13.6 points (p <0.05). The following average scores in the IG and CG for MCS and its components - VT, SF, RE, MH - were revealed: 34 (Me 31.3, σ 9.11, m1.9) and 47.6 (Me 50.3, σ 8.96, m2.1), 49.3 (Me 51.4, σ 8.43, 1.76m) and 55.7 (66.2 Me, σ 7.98, 1.83 m), 59.1 (me 62.5, σ 22.42, m4.68) and 87.5(Me 87.5, σ 15.6, m2.03), 39.4 (Me 40.9, σ 9.73, 2.03 m) and 51.7 (51.7 Me, σ 6.75, 1.55 m), 30.3 (Me 0, σ 40.7, 8.49 m) and 70.2 (Me 100, σ 36.68, 8 m, 42), respectively.

Conclusions. Psychoemotional state of parents in SG is exposed to certain violations to a greater extent than that of parents in CG.

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Epilepsy

ICNC-0226: Novel mutation in CACNA1A gene expressed as myoclonic epilepsy with drop attacks associated with mild cerebellar signs

Introduction: A toddler with global developmental delay and ataxia presented at two months of age with myoclonic jerks which later on evolved into drug-resistant myoclonic epilepsy with drop attack. Methods: Whole exome sequencing was employed and revealed one heterozygous mutation. This alternation was not present in the DNA samples of her parents.

Results: We detected a novel mutation (C.678G>T) in the CACNA1A gene. No single nucleotide polymorphisms were found in this region and its probability score was nearly 1.0. The CACNA1A gene encodes the alpha1-subunit A, a transmembrane pore-forming subunit of the P/Q or CaV2.1 voltage gated calcium channel which mediated entry of Ca(2+) ions into excitable cells and also involved in a Ca(2+) dependent processes, including muscle contraction, hormone or neurotransmitter release and gene expression.

Conclusion: CACNA1A mutations were previously reported in Episodic ataxia type 2, Familial hemiplegic migraine type 1 and in Spino-cerebellar ataxia 6. It was also recently associated with epileptic encephalopathy. The present report expands the clinical spectrum of CACNA1A-associated
neurologic and particular epileptic disorders, and suggests that early disturbance of the voltage-gated calcium channel activity may underlies neuronal insult which lead to ataxia to myoclonic epilepsy.

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Epilepsy
ICNC-0227: Antiepileptic drugs on Bone Metabolism in pediatric patients
Objective: To establish the reference intervals of bone metabolism markers in Chinese children; To explore effects of epilepsy itself on bone metabolism in children; and to study the effects of long-term antiepileptic drugs (AEDs) monotherapy on bone metabolism of pediatric epilepsy-BECT patients, and to provide the consultations for pediatric patients with epilepsy. Methods: A large sample multi-center cross-sectional study was performed. Detailed clinical documents were collected, and fasting blood samples were drawn from pediatric patients diagnosed with epilepsy-BECT. Automatic electrochemiluminescence immunoassay analyzer was applied for the tests of associated bone metabolism markers. Results: According to the inclusion and exclusion criteria, a total of 980 children from 20 centers aged 5 to 14 years old were enrolled, of which 284 cases were health control and 696 cases with BECT. One hundred and nineteen cases were diagnosed with BECT but without treatment, 577 cases BECT patients with long-term AEDs monotherapy, which including 212 cases with oxcarbazepine (OXC), 139 cases with Valproate (VPA), 142 cases with levetiracetam (LEV), and 84 cases with Lamotrigine (LTG). 1. Bone formation markers of P1NP and OC, as well as bone resorption markers of β-CTx have age and sex specific significant differences. The curve was drawed with age and sex. The references of bone metabolism markers were divided into three age groups, respectively in male and female. 2. Compared with health control group, the patients in epilepsy-BECT group without treatment got significantly decreased (P < 0.05) both bone formation and resorption markers as well as serum magnesium and PTH levels. However, Serum calcium, phosphorus, and 25-(OH)VD levels have no significant differences between the two groups. 3. Compared with health control group, bone formation markers were decreased in monotherapy group with OXC, VPA, LEV, and LTG respectively (P < 0.05), but had no significant differences compared with no-treatment BECT group (P > 0.05), except that LTG group got increased OC and β-CTx compared with no-treatment BECT group (P < 0.05). Patients in AEDs monotherapy group had significantly decreased serum calcium concentrations compared with health control group. Serum phosphorus in VPA and LTG treatment group were lower than that in control group (P < 0.05). Patients in AEDs monotherapy group had significantly decreased serum magnesium concentrations, worse in VPA group. 25-(OH)VD levels in groups had no significant differences (P > 0.05), PTH levels were significantly decreased in OXC, VPA, and LEV groups compared with health control group, but had an increased tendency in LTG group. Conclusion: 1. We obtained the distribution curve of bone metabolism markers for children from 5-14 years old, and established the age and sex specific reference intervals for bone metabolism markers. 2. After excluding the confounders of sun exposure, exercise, and AEDs on bone health, this study first proved that epilepsy itself could decrease the levels of serum bone metabolism markers, and damage the bone health. 3. Compared with the no-treatment BECT patients, LTG could compensate for the side effects of epilepsy on bone metabolism; VPA could aggravate the bone effects; OXC and LEV had no obvious side effects on bone metabolism. Compared with the health control, the four AEDs in this study could not compensate for the side effects of epilepsy itself on bone health. Key words: Bone metabolism; epilepsy; antiepileptic drugs; children

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Epilepsy
ICNC-0228: Comparative study on infantile spasms in upper and lower Egypt
Introduction: Awareness of infantile spasms is increasing among Egyptian pediatricians. Consanguinity, Pertussis vaccine, and hypoxic ischemic encephalopathy are known etiologies. Methods: Hundred and seventeen cases of infantile spasms were reviewed. They were divided into two groups according to their residence whether Upper Egypt (UE) or Lower Egypt (LE). Age of first spasms, consanguinity, head circumference and presence of clusters were analyzed. Etiologies were divided into symptomatic or cryptogenic. EEG and brain MRI were done for all patients and genetic studies in some. Results: UE group included 24 cases and LE 93. Male to female ratio was 1.6:1 in UE and 1:1 in LE. Positive consanguinity was 75% in UE and 45% in LE. OS was done on 75% in UE and 61% in LE. Microcephaly was 50% in UE and 25% in LE. Structural brain malformations were 12.5% in UE and 22.5% in LE. Evidence of hypoxic ischemic encephalopathy was 75% in UE and 25% in LE. EEG showed hypsarrhythmia in all cases with infantile clusters (75% in UE and 45% in LE). Focal discharges were recorded in 12.5% in UE and in 22.6% in LE. Two mutations were
Epilepsy

ICNC-0229: CHD2 mutation related epileptic encephalopathy: presentation of 3 novel cases

Introduction: chromodomain helicase DNA-binding protein2 (CHD2) gene mutations have been reported in over 20 patients with epileptic encephalopathy, including Lennox Gastaut syndrome, Dravet syndrome and myoclonic-astatic epilepsy. Common features include myoclonic seizures, photosensitivity and behavioural problems with features of autism spectrum disorder. There is considerable phenotypic heterogeneity in terms of age of onset, seizure burden, development delay, and the presence of associated features. Case description and results: we present 3 novel cases of CHD2-related epilepsy. Seizure onset occurred at age 6 months, 1 year and 3 years, respectively. Myoclonic seizures were present in all three cases. In addition, the first patient developed atypical absences and atonic seizures, the second presented atonic seizures, and the third developed atypical absence seizures. On EEG, patient 1 initially showed a modified hyphsarrhythmia which later evolved to frequent bilateral synchronous or asynchronous sharp waves and spike-waves; patient 2 had a high voltage, disorganized background pattern with focal epileptiform discharges and patient 3 showed generalized spikes, polyspikes and spike-waves. All seizures were refractory to multiple anti-epileptic drugs, including vagus nerve stimulation. Electrical photosensitivity was present only in patient 3. Development was mildly to severely delayed. All patients showed autistic behaviour. Conclusion: our case presentations confirm known features of CHD2 mutation related epilepsies but also highlight the phenotypic heterogeneity which may complicate clear delineation of the syndrome and choice of therapy. Diagnosis should be considered in early onset epileptic encephalopathy with myoclonic seizures.

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Epilepsy

ICNC-0230: Perampanel add on treatment in adolescent epilepsy: PERAD study of efficacy and tolerability

Introduction: Perampanel is a new broad spectrum antiepileptic drug marketed in Spain in January 2014. Resistant drug epilepsies in adolescents have challenging concerns due to unique age peculiarities including bad adherence to treatment, need of autonomy. Moreover highly refractory epilepsies of long evolution decreased quality of life in patients and their parents so that any change in frequency, severity and other features involved in epilepsy make a significant impact in quality of life.Methods: We analyse retrospectively the electronic charts of 63 adolescents (12-21years) from various Spanish Hospitals suffering epilepsies that included focal seizures or focal etiologies. We collected data of epilepsy history, pharmacological previous treatment, neuroimaging studies, comorbid conditions and any previous reaction to antiepileptic drugs.Objective: Evaluate efficacy and tolerability of perampanel in adolescentsResults: 35 were males and 28 females. The etiology of epilepsy was unknown in 16% and symptomatic in 84%. The follow-up period was from 12-6 months. 80% of patients were still on treatment. Responders rate was around 50% with at least 75% showing some improvement in severity of their epilepsies. Main adverse events were irritability or mood changes. Agression was rare but was the major reason for withdrawal. Somnolence and dizziness were also observed. Encephalopathic patients showed an improvement in alertness. No severe or life threatening adverse events were observed.Conclusion: Perampanel was effective to improve epilepsy control during the follow-up period in a highly refractory population of epileptic adolescents Tolerability was very good even addictive to 3 o more antiepileptic drugs.

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Identified in LE group in CDKL5 and KCNO2 genes. Discussion and Conclusion: Higher reports of infantile spasm in LE is related to easier access to Cairo from the Delta. Positive consanguinity among UE was more marked than in LE because of rural closed communities. Hypoxic ischemic encephalopathy was more in UE where secondary and tertiary care are less developed. Structural brain malformations were more in LE whereas microcephaly was more in UE. Hypsarrhythmia with clusters was more in UE whereas focal spikes were more in LE.

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Epilepsy

ICNC-0955: To study the profile and outcome of first acute symptomatic seizure in children and to determine the clinical and laboratory predictors of outcome

OBJECTIVE: To study the profile and outcome of first acute symptomatic seizure (ASS) in children and to determine the clinical and laboratory predictors of outcome. STUDY DESIGN: Prospective observational study METHODS: Consecutive children with acute symptomatic seizures from June to September 2011 were included. Demographic data was recorded with the structured proforma. Follow up was done after 3 and 6 months. Outcome was defined as good or bad depending to the severity of disability. Outcome was analyzed using univariate and multivariate analysis to find independent predictors. The study was approved by the institutional ethical committee. RESULTS: A total of 105 children with median age of 48 months were enrolled. Viral meningoencephalitis was the most common etiology beyond infancy. Poor outcome was observed in 27.6% patients, and was significantly associated with low socioeconomic status (p=0.001), admission glassgow coma score (GCS)<8 (p<0.001), requirement of >1 antiepileptic drug to control seizures (P=0.001), abnormal neuroimaging (p<0.001), abnormal EEG (p<0.001), requirement of intubation (p<0.001), etiology of CNS infections (p=0.02) and status epilepticus at admission (P=0.04). On multiple regression analysis abnormal neuroimaging, abnormal EEG during admission and GCS score <8 were found to be independent predictors of poor outcome CONCLUSION: Outcome of first ASS was primarily determined by aetiology of seizure. CNS infections constitute the predominant cause of ASS. Abnormal neuroimaging, abnormal EEG during admission and GCS score <8 may help in identification of children most likely to need long term follow up and rehabilitation.

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Epilepsy

ICNC-0231: A retrospective study of effectiveness and compliance of ketogenic diet in a single unit

Introduction: Ketogenic diet (KD) has been proven to be beneficial in drug-resistant epilepsy and the treatment of choice in certain in Europe. There are various types of KD ranging from the classic (4:1) form to modified ketogenic diet (50–60% fat, 20–30% carbohydrates, and 10–20% protein) and extreme dietary treatment (60–70% fat, 10–20% carbohydrates, and 10–20% protein). Effectiveness, defined as seizure reduction >50%, and compliance, as blood ketones >2 mmol/L, were studied 3 and 6 months after KD start. RESULTS: Twenty children (45 days-14 years old) were placed on KD. SF and AED number prior to KD initiation was 1.2±0.8. For children on groups B and C, chances were 56% and 100%, respectively, and at 6 months for the same groups were 100%, 75% and 100% respectively. Children with total AED >10, before KD, had 62.5% chance of seizure reduction >50% or KD cessation. Six children (27%) discontinued the diet while on KD.

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Epilepsy

ICNC-0232: Severe EPILEPTICENCEPHALOPATHY SECONDARY TO NEUROCUTANEOUS MELANOSIS- a case study

Aim: To describe the clinical characteristics of severe epileptic encephalopathy associated with Neurocutaneous Melanosis. Introduction: Neurocutaneous Melanosis (NM) is a rare congenital disorder characterised by multiple congenital cutaneous nevi and melanocytic deposits in the central nervous system (CNS). Epilepsy and developmental delay can be associated, with epilepsy progression unpredictable, and often unrelated to neuroimaging. 1. Transformation to leptomeningeal melanoma is found in 2.3% of patients. Severe epileptic encephalopathy associated with NM is rare. Methods: Case report. Results: We present a 9 year old male with NM, severe global developmental delay and
re refractory epilepsy. Seizure onset commenced at 9 months with tonic clonic, atonic seizures and spasms. From 18 months the epilepsy and developmental regression progressed, with frequent tonic seizures that evolved to tonic status epilepticus requiring emergency seizure medication, along with background anticonvulsants. Early interictal EEGs showed generalised and multi focal discharges, which evolved to an abnormal slow background and multifocal spikes with a right frontal predominance. Surveillance cerebral MRI's show no acute changes with seizure evolution, though demonstrate bilateral anteromedial temporal lobe T1 hyperintense lesions and subtle pontine lesion, (a characteristic feature of the CNS involvement of NM). The patient has daily seizures and skin surveillance shows a gradual increase in lesion size and number.Conclusion: NM with severe epileptic encephalopathy in this age group has not previously been described. The right frontal focus could be explored further to include less invasive stereo EEG. However epilepsy surgery has not been considered due to the risk of potential seeding and malignant transformation. References:1. Ramaswamy Y et al. Dev Med Child Neurol 2012;54:563-568.

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Epilepsy
ICNC-0233: Immature myelination in infancy-a window of opportunity to detect focal cortical dysplasia
Aim: To compare the MRI features of malformations of cortical development in the maturing brain, and to describe the utility of T2 weighted imaging in early infancy to detect malformations. Introduction: Myelination is a process in the developing brain that begins as early as the 16th week of gestation and reaches maturity around 24 months.1 Patterns of myelination affect the ability to identify common structural causes of epilepsy. Lesions may “appear” or “vanish” as myelination progresses, as they may be identified as “enhanced myelination” suggesting areas of cortical malformation, which may not be apparent on subsequent imaging years later.2 Methods: 3 children with surgically treated refractory epilepsy and brain scans in early infancy were studied. Comparison was made with T2 weighted sequences of the earliest (4 months, 5.5 months and 2.5 months respectively) and most recent MRI’s. One case had sequential scans. Results: In 2 cases the dysplasia was detected retrospectively on studying the earliest MRI. In all 3 patients the malformations became more difficult to detect with age on conventional MRI sequences, at 2 years 2 months, 2 years 11 months and 6 years 8 months respectively. High resolution MRI subsequently delineated the malformations that were first detected, in retrospect, on the earliest studies. Conclusion: This series highlights an apparent window in early development, not yet defined in the literature, where the unmyelinated white matter provides a contrast to the abnormal cortex of cortical dysplasia to allow detection and delineation of lesions that are subsequently difficult to detect with conventional MRI, as the brain matures. A review of the MRI performed in early infancy is essential in the evaluation of candidates for epilepsy surgery.3 References: 1. Welker KM et al. Seminars in Neurology, 2012;32(1):15-28 2. Sankar R et al. AJNR 1995;16:1265-1272 3. Gaillard W.D et al. Epilepsia, 2009;50(9):2147-215

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Epilepsy
ICNC-0236: Effective antiepileptic drugs for non-idiopathic focal epilepsies are different by precise seizure symptoms
INTRODUCTION: Many guidelines for treatment of focal seizures (Sz) describe simply packed as focal Sz, however, this often fails to obtain good Sz control. We studied effective antiepileptic drugs (AEDs) for precise seizure symptoms (PSSs) in non-idiopathic and non-lesional focal epilepsies (NINLFE). METHODS: Medical records were retrospectively reviewed for 319 patients with NINLFE (aged 2-40 years, mostly < 20 years) treated by the author (KS) for > one year at a tertiary epilepsy center. The subjects included 264 patients with frontal lobe epilepsy, 34 patients with temporal lobe epilepsy, and 21 patients with parietal/occipital lobe epilepsy, with one to three seizure types. The efficacy of the AED was evaluated when the AED was added on or switched from other AEDs at the maximal tolerated dose if needed, and >50% responder rate (RR) was obtained for the AED given to > 10 cases. RESULTS: AEDs with RR > 75% were KBr, LTG, ZNS for tonic Sz (TS), ZNS, LTG for secondarily generalized Sz (SGS), CBZ for clonic Sz (CS), PHT, CBZ, LTG for hypermotor Sz (HMS), ZNS, LTG for atonic falling Sz (AFS), CLB for complex partial Sz (CPS), and none for sensory or autonomic Sz (SAS). AEDs with RR > 50% were PB, CLZ, PHT for TS, PHT, CLB, CZP, PB, CLZ, TPM, CBZ for SGS, CP for CS, LTG for HMS, none for AFS, CLZ, CBZ, TPM for CPS, and CLB for SAS. CONCLUSION: The efficacy of AEDs for PSS is different, and AED should be chosen by PSSs.

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Epilepsy

ICNC-0237: New family with MCT8 transporter deficiency

The male proband was born at term after 5th normal pregnancy and delivery. He was referred to us because of multiple cafe-au-lait spots and severe developmental delay. On examination he was found to have progressive microcephaly, truncal hypotonia, infantile spasms and generalized seizures, as well as an exaggerated Moro reflex. In addition, he had bilateral cryptorchidism and kidney and liver cysts (multiple cysts were also found in father). Interictal EEGs and brain MRI were normal. The boy had first degree relatives with NF1 (sister and father), thus together with multiple CAL he fulfilled criteria for definite NF1. Nevertheless, we believed his condition could not be explained by NF1 only. The brother of our patient suffered the same symptoms and deceased at the age of 5y. Careful history taking discovered maternal uncles and cousins who died because of the same symptoms. X-linked disorder was suspected. At first, ARX mutation was excluded. WES revealed 2 genes running in the family - NF1 gene and SLC16A2 gene. Thus, diagnosis of MCT8 transporter deficiency was made. The mutation was inherited from mother. Fortunately, sisters of patient don't carry the mutation. Our patient has never achieved independent sitting, did not develop speech and died at the age of 3y.

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Epilepsy

ICNC-0238: Cost effective treatment of infantile spasms

Objective: To compare the outcome of ACTH with oral prednisolone for treatment of infantile spasms. Methodology: This is a randomized controlled trial conducted at department of Pediatric Neurology, The Children Hospital, Lahore, Pakistan after ethical approval from January 1st 2013 to November 1st 2015. Seventy patients with infantile spasms were randomized in two equal groups of 35 patients in each group. Patients in group A received prednisolone (2mg/kg/day for 4 weeks followed by tapering over next 4 weeks) and in group B received ACTH (150 IU/m/day) for two weeks followed by tapering over next 4-6 weeks. The two groups were compared for the spasms free period. Statistical significant determined by chi-square test (p< 0.05 was taken as significant). Non-probability purposive sampling was used and an inclusion criterion was children up to age of 5 years with infantile spasms. Exclusion criteria include children who had been previously treated with steroids or ACTH. Seventy patients fulfilling inclusion criteria were enrolled through neurology department of Children Hospital, Lahore. History, informed consent was taken by parents and was divided in two groups by lottery method. All the information was collected on a specially designed proforma. Results: In group A, 28 (80%) patients were spasms free, while in group B, 18 (51.4%) patients were spasms free. (p < 0.05). Conclusion: More patients with IS were spasms free with prednisolone as compared to ACTH. Key words: Epilepsy, ACTH, Prednisolone, Infantile spasms, Hysparthymia.

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Epilepsy

ICNC-0239: Does EEG help in early diagnosis of SSPE?

Background: Subacute sclerosing panencephalitis (SSPE) is a chronic degenerative disorder of invariably fatal outcome. Objective: To find out the role of electroencephlography in the early diagnosis of subacute sclerosing panencephalitis. It was a cross sectional observational study. Material & Methods: After IRB approval, it was started at Department of Neurology Children's Hospital, Lahore from April 15, 2006 to September 15, 2015. Children between the ages of 2 to 18 years (n=129) with myoclonic jerks were admitted in Neurology department. History and clinical examination was carried out and EEG and CSF antimeasles antibodies were performed. Children may have EEG findings consistent with SSPE (EEG abnormalities having burst suppression in high amplitude slow and sharp waves recur at 3-5 second interval on slow background) or other EEG findings like myoclonic epilepsy with normal back ground, normal EEG etc. CSF of all children was sent for antimeasles antibodies for further confirmation which was considered diagnostic. Brain imaging was done in all children to exclude other possible diagnosis. Results: Total of 89 patients with EEG findings of subacute sclerosing panencephalitis were further confirmed with CSF anti measles antibodies. It was positive in 77 children, while 12 children had negative EEG findings and all of them had negative results for CSF antimeasles antibodies. Male to female ratio was 1.4:1. Conclusion: Subacute sclerosing panencephalitis is not an uncommon entity in our population with quite variable clinical presentation and electroencephlography has significant value in early, cost effective and reliable diagnosis.
Epilepsy

ICNC-0240: Adulthood onset epilepsy in 13 patients with Down Syndrome

Epilepsy onset associated with Down syndrome (DS) shows bimodal distribution during infancy and adulthood. Adult-onset epilepsy (AOE) in patients with DS is often referred to as senile or late-onset myoclonic epilepsy. Because of the prolonged life expectancy with advances in medical care, the prevalence of AOE in DS is believed to increase. We reported on cases of AOE in DS that were managed in our hospital in the past 10 years. Of the 267 DS patients who visited our hospital, 77 were aged above 20 years, and 13 (16.9%) of them had AOE. In our patients, AOE onset was mostly in their twenties and thirties. Our patients demonstrated generalized tonic–clonic seizures (GTC) (6/13 = 46.2%), followed by complex partial seizures (CPS) (2/13 = 15.4%).

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Epilepsy

ICNC-0241: Management of infantile spasms in developing countries

Objective: To compare the outcome of ACTH with oral prednisolone for treatment of infantile spasms. Methodology: This is a randomized controlled trial conducted at department of paediatric neurology, The Children Hospital, Lahore, Pakistan after ethical approval from January 1st 2010 to December 31st 2014. Seventy patients with infantile spasms were randomized in two equal groups of 35 patients in each group. Patients in group A received prednisolone (2mg/kg/day for 4 weeks followed by tapering over next 4 weeks) and in group B received ACTH (150IU/m/day) for two weeks followed by tapering over next 4-6 weeks. The two groups were compared for the spasms free period. Statistical significant determined by chi-square test (p<0.05 was taken as significant). Non-probability purposive sampling was used and an inclusion criterion was children up to age of 5 years with infantile spasms. Exclusion criteria include children who had been previously treated with steroids or ACTH. Seventy patients fulfilling inclusion criteria were enrolled through neurology department of Children Hospital, Lahore. History, informed consent was taken by parents and was divided in two groups by lottery method. All the information was collected on a specially designed proforma. Results: In group A, 28 (80%) patients were spasms free, while in group B, 18 (51.4%) patients were spasms free. (p < 0.05). Conclusion: Significant number of patients with IS were spasms free with prednisolone which is more cost effective and as compared to ACTH. Key words: Epilepsy, ACTH, Prednisolone, Infantile spasms, Hypsarhythmia.

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ICNC-0243: The survey of the effectiveness and tolerability of Perampanel in children and adolescents with refractory epilepsy

BACKGROUND: Perampanel is one of the latest antiepileptic drugs (AEDs) approved for treatment of focal and generalised epilepsy in individuals with epilepsy aged 12 years and older. There is sparse data on the use of Perampanel in children under 12. We conducted a survey amongst paediatric neurologists in the United Kingdom (UK) to investigate its effectiveness and tolerability as an adjunctive therapy in children with epilepsy.

METHODS: Data was collected via a proforma sent out to Consultant Paediatric Neurologists in the UK, between December 2013 and May 2015. We gathered both retrospective and prospective data including changes in seizure frequency and unwanted effects at 3, 6 and 12 months' follow-up.

RESULTS: Ninety eight patients (50 females) from 11 of 29 centres were treated with Perampanel with a median (range) age of 14 years 4 months (0.1-17.1). Seventy three (74.5%) had focal epilepsy, eighteen (18.4%) generalised and seven (7.1%) patients had mixed generalised and focal epilepsy. The median (range) duration of treatment was 29(1-70) weeks. At 3 months follow-up, 79(80.6%) patients remained on Perampanel. Thirty six (36.7%) of the 98 patients demonstrated a ≥50% reduction in seizure frequency. This effectiveness was sustained in 14/56 (25%), and in 10/40 (25%) children, from whom follow-up data was provided at 6 and 12 months respectively. Treatment was discontinued due to seizures worsening in 13(13.3%) and unwanted effects in 31(31.6%) of the 98 patients.

CONCLUSIONS: Perampanel was reasonably effective and generally tolerated in a heterogeneous group of 98 children with refractory focal and generalised epilepsy.

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ICNC-0244: Health related quality of life of children 2-18 years old, diagnosed with seizure disorder maintained on Phenobarbital in a tertiary hospital: A cross sectional study

Introduction: Epilepsy or seizure disorder affects greatly the quality of life of children. The traditional medical goal in the management has focused almost exclusively on seizure control with minimal or no adverse medication effect, whereas the importance of assessing quality of life has been ignored. Studies now have been focusing on the quality of life of pediatric patients with different disease entities. Interventions are needed focusing on the behavioral and emotional changes of the child with seizure disorders. Methods: Pediatric patients, 2-18 years old, diagnosed to have seizure disorder maintained on Phenobarbital for ≥6 months. Validated PedsQL questionnaire was used. Analysis of the different variables (age of diagnosis, duration of Phenobarbital intake) was done using the following test statistics: ANOVA, Kruskal Wallis Test, Chi-square Test, Pearson Correlation. Result: There was a significant difference in the school scores as shown by the p value of <0.0001 as the child becomes older. Significant correlation noted on the age of diagnosis and duration of Phenobarbital intake on emotional, social and school with the following results 0.05, 0.04, and 0.02 respectively. Conclusion: The longer the patient taking Phenobarbital and the older the child, the poorer the prognosis in emotional, social and school performance. Interventions designed to address behavioral and emotional problems in children with epilepsy and should be an important management goal and included in long term treatment.

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ICNC-0245: Intranasal midazolam versus intravenous lorazepam in the control of acute seizures in children

Objective Primary Objective To determine the efficacy of intranasal midazolam against intravenous lorazepam in control of acute onset seizures in children aged 6 months to 15 years. Secondary Objective To study any adverse effects of the drugs. Methods, type of study and design: . Setting: Emergency department of KIMS Hospital, which is a multi-specialty hospital.

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Epilepsy

ICNC-0246: Comprehensive genetic analysis in West syndrome and Ohhtahara syndrome: a single center study

Introduction: West syndrome and Ohhtahara syndrome are a continuum of early onset epileptic encephalopathies (EEOEs). Recent genetic studies have elucidated causative roles for genetic abnormalities in EEOEs. In this study, we investigated the underlying genetic causes in patients with West syndrome and Ohhtahara syndrome. Methods: Patients were recruited from Nishi-Niigata Chuo National hospital between 2004 and 2015. 30 patients (26 of West syndrome and four of Ohhtahara syndrome), who had severe developmental delay, unknown etiology, no chromosomal abnormality in G-band, and no cortical malformation on MRI, were included in this study. We performed candidate gene analysis in eight patients for ARX, STXBP1, SPTAN1, or SCNA2 by high-resolution melting analysis or PCR direct sequence. In four patients, target capture and sequencing against 38 genes were performed. Whole exome sequence was performed in 18 patients including three patients with negative results of target sequencing. Chromosomal microarray analysis was performed in six patients. Results: We identified pathogenic mutation in 11 genes (ARX, CDLK5, STXBP1, SPTAN1, GNAO1, SCNA2, CASK, ALG13, EEF1A2, TBL1XR1 and SETD5) in 16 of 28 patients (57%). In two patients, we identified submicroscopic chromosomal deletion in 9q33.3q34.1 and 14q13.1q13.3. No mutations in known causative genes were found in the remaining 12 patients. Conclusion: We found pathogenic genetic alterations in 18 of 30 patients (60%). Genetic backgrounds of EEOEs are heterogeneous. Our results in a single center may reflect the current state of genetic background of EEOEs. Further accumulation of patients with precise clinical evaluation will facilitate genotype-phenotype correlation in EEOEs.

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Epilepsy

ICNC-0247: Morphometric MRI analysis of focal cortical dysplasia in Pediatric Epilepsy

Introduction: MRI features of focal cortical dysplasia (FCD) include cortical thickening and poor gray-white differentiation. These findings are often subtle by visual assessment. Voxel-based morphometric MRI analysis quantitatively compares the individual patient with a control group. This study evaluated morphometric analysis in medically refractory pediatric epilepsy with pathology-confirmed FCD. Methods: We analyzed 21 children with FCD age 5-18 years without prior resection: male 76%; median age at surgery 13 years, IQR 10-15. Using statistical parametric mapping, an automated morphometric analysis program (MAP) generated z-score maps compared to healthy controls grouped ages 5-9 years, 10-13 years, and 14-17 years. A dominant MAP+ focus was determined visually in concert with coregistered T1 MRI.
MAP+ was defined as abnormal extension of grey matter into white matter (extension image) or blurring of the grey–white matter junction (junction image). Results: In this cohort, MAP+ was positive in 20. MRI showed FCD detected by radiologist in 13, abnormalities not specific for FCD in 5, and was normal in 3. MAP+ focus was concordant with resection and MRI abnormality in all 13 cases with radiologist-identified FCD. All 3 normal MRI showed MAP+ focus concordant with resection. In abnormal MRI not specific for FCD, 2 of 5 showed MAP+ focus concordant with MRI abnormality and resection. MAP+ focus was discordant in a case of ventricular dilation and another focal lesion with associated mass effect. Conclusion: Morphometric MRI analysis can be used to visualize FCD in pediatric epilepsy. Caution should be used in applying this method in cases with significant anatomic distortion.

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Epilepsy
ICNC-0249: Sleep architecture and epileptic activity in childhood absence epilepsy spectrum before treatment
Introduction: Childhood absence epilepsy (CAE) is a common pediatric epileptic disorder presenting between 2nd and 10th year. The spells are elicited with hyperventilation (HV) while photosensitivity (PS) is less frequent. Few studies examine the relationship of sleep architecture and epileptic activity, but none comprises overnight-recordings before treatment. Our aim is to describe sleep architecture and its relationship with epileptic discharges (EDs) by using an EEG-polygraphy study in a cohort of CAE patients before treatment. Methods: 28 drug-naive, healthy children were recruited (21 girls, 7 boys) with mean age of 90.1±32.6. Patients were separated in 3 age-groups (A:<60mo, B:60mo & <120mo and C:>120mo). Routine EEG and overnight EEG-polygraphy were conducted upon diagnosis. Sleep parameters, EDs, arousals and complexes’ duration during absence were measured. Results: Seven patients developed photosensitivity. Electroclinical absences were activated in all patients with HV, with a mean HV duration up to first absence of 106.25sec. Nine patients mainly of group C (p=0.042) had polyspikes and 15 demonstrated focal discharges. TST, SE are greater in group B and C demonstrate less stage-I and SWS increased stage-II and shorter REM. EDs are more numerous in group B. There’s positive correlation between discharges and arousals and significant negative correlation between number of discharges and SE (p=0.042).Conclusion: HV of at least 2min remains a very efficient way to diagnose CAE electroclinically. Sleep architecture in drug naive patients with CAE show difference between age groups and especially arousals and SE are correlated with epileptic discharges.

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Epilepsy
ICNC-0250: Resistant form of epilepsy in a child with Lissencephaly. Clinical report
Background: The congenital abnormalities of the CNS in newborns are from 6.5 to 30%. Lissencephaly prevalence is 1 per 100,000 live births, some sources say 1 in 13,000 - 20,000 live births. Was evaluated clinical variants of resistant epilepsy, electrophysiological, neuroradiological characteristics on the example of one patient. Methods: A little girl, 5 months, admitted to the hospital 08.09.2015y with complaints of infantile spasms, 13-15 episodes per day. The case history was analyzed, held: EEG, brain MRI, ophthalmoscopy. Results: child of the 1-st pregnancy, 1-st childbirth; pregnancy with threatened abortion, against the backdrop of a viral infection without fever. Noteworthy is decreased muscle tone, tendon reflexes were normal. Delays in motor development (do not holding head, resting on the foot - weak). Visual reaction reduced. The nature of epileptic seizures as mixed infantile spasms, asymmetric, serial. The EEG: the pattern “flash - depression,”slowing the main activity. Neuroradiological characteristics: the presence of congenital malformations of the central nervous system, namely, smoothness convolutions frontotemporal areas of gray matter
Epilepsy

ICNC-0251: Altered synaptic properties in mature rats with a history of cryptogenic infantile spasms

To understand the etiological basis for learning and memory impairments in the adult patients who experienced infantile spasms, we analyzed synaptic properties in the adult hippocampus, a structure playing essential roles in learning and memory in an animal model of cryptogenic infantile spasms. A rat model of N-methyl-D-aspartate (NMDA)-induced spasms combined with prenatal betamethasone administration was produced and the expression of infantile spasms was confirmed. At 6–12 weeks postnatal, we evaluated morphofunctional properties of pyramidal neurons and the long-term potentiation (LTP) in the hippocampus CA1. We found that the number of dendritic spines of CA1 pyramidal neurons and the frequency of spontaneous excitatory, but not inhibitory, transmissions were significantly smaller while the LTP magnitude was significantly larger in adult rats with a history of infantile NMDA injections. These results indicate that postnatal NMDA treatment with prenatal stress in the early stage of life in rats produces a latent influence on various forms of synaptic alterations in the hippocampus. This study is the first to demonstrate synaptic alteration in a model of cryptogenic infantile spasms, providing a basis for understanding the mechanism underlying latent cognitive impairment in infantile spasms.

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Epilepsy

ICNC-0253: Optimization of therapeutic tactic in treatment of epileptic encephalopathy

Objective: The aim of the investigation was optimization of methods of treatment of pharmacological resistant forms of epilepsy that can be illustrated by the case of the two-year boy with Lennox-Gastaut syndrome. Materials and methods. The child was ill since birth and treated with different combinations of antiepileptic drugs. The treatment was unsuccessful, what forced us to find another approach. Tablets of hydrocortisone were prescribed in the start dose of 1.0 mg per 1 kg of body weight (according to professor Olivier Dulac’s scheme), followed by decreasing of dose up to 2 mg. The treatment carried out during five months. EEG with video monitoring was carried out during 8 hours in active and passive wake, night sleeping and after awakening. Results: In the middle of therapeutic course the child became seizure-free and considerable more active and some life skills developed. During the one-year, follow-up period was not revealed any seizures, though the child did not take AED or hormones. As result of a treatment, there was also observed obvious development of child’s brain, which was manifested in physical and mental activity. Conclusion: Thus, we can conclude that early beginning of individually selected therapy in infants with EE and LGS gives the possibility for the normal development of their brain that may be seen in the normalization of physical and mental development.

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Epilepsy

ICNC-0254: Hemispheric Lateralization in Benign Focal Epilepsy in childhood with Centrottemporal Spikes (BECTS) in Uzbekistan

Introduction. Benign focal epilepsy in childhood with centrotemporal spikes (BECTS) is one of the most common forms of epilepsy. In children, the pattern of lateralized epileptic discharges does not seem to have the same distribution. Purpose: To evaluate the lateralization of interictal spikes in children with BECTS in relation to the sex of the child and the age of onset of epilepsy. Methods. We studied the electroencephalograms (EEGs) of 114 children with a clinical diagnosis of BECTS according to ILAE. The results obtained from two EEGs, performed at intervals of 6 and 12 months, were correlated with the age of onset of the epileptic seizures and the sex of the child. Results. There was no association between the onset of epileptic seizures and the age of the child (p = 0.461). When we analyzed the relationship between laterality and sex we did not observe any difference in the first EEG (p = 0.767) results; however, in the results of the second EEG there was a difference (p = 0.002). In males, left and bilateral interictal spikes were predominant, and in females, the right hemisphere showed predominant spikes and there were continuous spike-and-wave discharges during slow sleep (CSWSS). The analysis between laterality and a child's age did not show predominant interictal spikes in the hemispheres (p = 0.011). Conclusion. In BECTS, the lateralization of interictal spikes was not consistent as described in

hemispheres (p = 0.011). Conclusion. In BECTS, the lateralization of interictal spikes was not consistent as described in slow sleep (CSWSS).
adult patients, but there was a slight left hemispheric predominance in boys and right hemispheric predominance in girls.

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Epilepsy
ICNC-0256: Temporal lobe epilepsy in children: the relevance of interictal epileptiform discharges on executive dysfunction
RATIONALE: Memory deficits are common in TLE and are well documented on neuropsychological evaluation. This relationship is not surprising given the importance of the hippocampus and related temporolimbic structures for memory consolidation. However, the frequent co-occurrence of executive dysfunction is unexpected and implicates more widespread cortical involvement, structural and/or functional. Hermann & Seidenberg advocate that this impairment is related to the "epileptogenic noise" caused by frequent epileptiform discharges in a developing brain. In this study, we analyzed the correlation between frequency, lateralization and location of interictal epileptiforme discharges (IED) and executive performance in one gold-standard test for executive functioning – the Wisconsin Card Sort Test (WCST).

METHODS: In this retrospective study, we reviewed the EEG data of 35 patients with TLE (mean age 11.76 years; SD + 2.21) with well-documented lesions—14 mesial and 21 lateral. Non-lesional patients were excluded. Epileptiform discharges were evaluated according to frequency (rare/infrequent versus frequent IED); lateralization (ipsi versus contralateral predominance) and location (temporal and extratemporal/diffuse). Linear regression was used to test whether localization and frequency had an impact on WCST. Localization was compared using ANOVA and frequency using Student-t test. RESULTS: The most representative sub scores in WCST were perseverative response and number of categories achieved. Patients with very frequent discharges had worse performance in perseverative errors (0.043) and categories (0.019). Extratemporal IED and contralateral IED predominance were not correlated with worse performance in these tests. CONCLUSIONS: Patients with frequent IED showed worse performance in perseverative errors and number of categories achieved of WCST. Location and lateralization of IED discharges were not correlated with this performance. This preliminary data suggests that ED may result from frequent ongoing epileptogenic activity affecting relevant process such as synaptogenesis and apoptosis and generating unexpected cognitive impairment.

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Epilepsy
ICNC-0257: Juvenile Myoclonic Epilepsy: clinical predictors of worse social functioning
Rationale: Most patients with Juvenile Myoclonic Epilepsy (JME) have easy-to-control epilepsy. However, social outcome is controversial and its predictors remain undetermined. In the current study, we aimed to evaluate the role of impulsiveness, depressive symptoms and anxiety traits as well as patient and epilepsy-related factors on social functioning. Methods: We prospectively evaluated 50 patients with JME and 44 controls. Social Adjustment was assessed using The Self-Report Social Adjustment Scale (SAS) that comprises performance on: work; social and leisure activities; relationship with extended family; marital role; parental role; membership in the family unit; and economic adequacy. Depressive symptoms were assessed using Beck Depression Inventory (BDI). Current level of anxiety was assessed using State–Trait Anxiety Inventory (STAI). Personality traits were assessed with the Temperament and Character Inventory (TCI). The impact of epilepsy-related variables (age of onset, duration, seizure frequency and type) and patients-related factors (gender and age) on SAS was also analyzed. Results: Patients with JME had worse score on Global SAS than controls (p = 0.001), especially on Work (p = 0.032) and Extended Family (p = 0.005). Considering patient’s factors, age had an impact the subdomain work. Patients with JME scored significantly higher on depression (P=0.001), state anxiety (P=0.007), and trait anxiety (P=0.001) scales. Higher scores on depression inventory were correlated with worse scores on Work (p= 0.01). Higher scores on state and trait anxiety scale were not correlated with any aspects of Social Adjustment Scale. Higher scores of impulsivity were correlated with worse scores on Global (p = 0.01); Work (p = 0.001) and Leisure (p = 0.002). Higher seizure frequency – myoclonic (p=0.005) and GTC (p=0.035) – were correlated with higher scores on factor Work of SAS. Conclusion: Patients with JME have worse social adjustment, especially those with inadequate seizure control. Higher expression of impulsive traits and depression predicted worse social functioning. Poor impulse control leads to maladaptive behaviors and predicts greater difficulty in distinct areas of social functioning. Therefore, comorbidities and seizure frequency equally impact social functioning; although, this impact occurs in distinct domains.

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**Epilepsy**

**ICNC-0258: Valproate and Lamotrigine: is Clobazam more effective than other drugs as adjunctive therapy?**

**Rationale:** The combination of lamotrigine and valproate-divalproex sodium (VPA-LTG) is effective in the treatment of refractory epilepsy in children and adults, as previously demonstrated (Thome-Souza & Valente 2013). Machado et al. (2011) suggested that the association of VPA-LTG with Clobazam (CLB) seems to be more effective than with other benzodiazepines. In this study, we compared the efficacy of VPA-LTG, in a large sample of patients with refractory epilepsy, with different benzodiazepines. Methods: Seventy-one patients (mean of 13.9 years; 40.8 % female) with refractory epilepsy and no indication for surgical intervention were evaluated. Sixty-four patients were eligible for the study. They were classified in three subgroups: 27 (42.2%) using VPA-LTG alone; 21 (32.8%) using VPA-LTG and CLB; and 16 (25%) using VPA-LTG and other BZD. In order to compare demographic data among groups, we used Chi-square and ANOVA. Efficacy in distinct groups was evaluated using chi-square and Fisher’s exact test. Results: Twenty-six patients (40.6%) had lesional epilepsy; 35 (54.7%) had undetermined; and 3 (4.7%) had genetically determined epilepsy. There were no differences considering seizure type; frequency and etiology among groups. At the end of the first year of follow-up, the efficacy of the VPA-LTG combination to control seizures was > 75% in 22 (30.4%) patients and was > 90% in 29 (40.8%). No differences were observed comparing the three groups – VPA-LTG; VPA-LTG-CLB and VPA-LTG-other BZD (p=0.221 >75% and p=0.591 >90%). The efficacy in patients with VPA-LTG- CLB compared to other two groups showed similar results (p=0.365 >75% and p=0.783 >90%). Conclusion: FDA has recently approved Clobazam and there is renewed interest for this old drug. It is well known that Clobazam is a good option as adjunctive therapy in refractory epilepsy. However, in this study, we observed that the combination of VPA and LTG is effective, regardless of the benzodiazepine used. Larger series are necessary in order to confirm these results.

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**Epilepsy**

**ICNC-0259: Major stressful life events in pediatric and adult patients with psychogenic nonepileptic seizures**

**RATIONALE:** Major traumatic events are known to be highly prevalent among patients with Psychogenic Nonepileptic Seizures (PNES), playing a role in its psychopathology. Most of the literature has focused on physical and sexual abuse, with less being known about other risk factors. In this study, we aimed to verify if these events differ according to the patients’ age – children and adults. METHODS: We reviewed medical records of 146 patients (102 adults – 78 female [76.5%] and 44 children – 21 female [47.7%]) diagnosed with PNES by VEEG from 2006 to 2012. Medical and psychiatric evaluation was analyzed regarding major stressful life events time-related with the onset or worsening of PNES. RESULTS: In 46 adult patients (45.1%; 10 male and 36 female) it was possible to determine a time related major stress factor, without any gender difference. Thirty patients (29.41%) had suggestive history of previous PTSD. Family conflicts were reported by 16 (15.68%) patients, and relevant work related issues by 10 (9.80%). Two women had onset of PNES during pregnancy, and two after miscarriage. Sexual abuse was reported by six female patients (5.88%) and physical abuse by 18 patients (17.64%). Psychological abuse was reported by 12 patients (26.08%). Regarding the pediatric population, in 32 patients (72.72%) it was possible to find a traumatic time-related event, without gender differences. An inadequate family setting was observed in 13 cases (29.5%) and a family conflict was observed in other eight patients (18.18%), mainly parents’ divorce [6 (13.43%)] and family illness (22.72%). School related issues occurred in 17 children (38.63%), mainly bullying in 10 (22.72%) and, learning difficulties or academic failure in six (13.63%). Sexual or physical abuse was reported by eight children (18.18%) and psychological abuse by 4 (9.09%). Only girls reported sexual abuse. Two patients (one adult, and one teenager) initiated PNES during incarceration. CONCLUSIONS: Our results support the high prevalence of major stressful events in patients with PNES. In this study, the type of event was age-related.

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**Epilepsy**

**ICNC-0260: Risk factors for diagnostic delay in Psychogenic Non-Epileptic seizures in children and adolescents**

**Rationale:** In children, psychogenic nonepileptic seizures (PNES) are associated with school-related difficulties and significant psychopathology. Recognition, referral and treatment can save on health resources and alleviate significant distress in affected children and their families. To the best of our knowledge, there is scarce data about the time for the diagnosis of PNES in children and no previous studies documented factors that can be related with a later diagnosis in youth. This study aimed to analyze a pediatric series with PNES in order to establish the diagnostic gap and possible risk factors for this delay in this age group. Methods: All children with PNES documented by video-EEG were consecutively included. None had a previous diagnosis of PNES. This yielded the study of 53 children (mean age of 12.85 years [SD 3.15]; 60.4% girls) who underwent a protocol with neurological and psychiatric interview. Results: The average time...
between seizure onset and referral was 17.75 months (SD 12.62). Age of onset of PNES was negatively correlated with diagnosis (p < 0.001). The late referral group also had more children under AEDs (p 0.019) and who reported psychological abuse (p 0.018). Conclusion: Youth with PNES represent a challenge for the diagnosis. A subgroup of patients emerged as those with longer referral delay; characterized by younger children and children with psychological abuse these factors may preclude earlier identification of PNES, postponing its diagnosis.

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Epilepsy
ICNC-0166: Early resective epilepsy surgery in children with tuberous sclerosis complex: report of two new cases
Tuberous Sclerosis Complex (TSC) is associated with epilepsy in about 70% of patients. Epilepsy is frequently characterized by infantile spasms with focal seizures, early onset (under 1 year) and drug-resistant epilepsy in about 40% of patients (Vignoli A et al. Epilepsia 2013; 54: 2134-42). Case reports. We describe the electro-clinical and neuropsychological outcome (5,5 years and 2 years) of two girls with TSC and drug-resistant focal epilepsy treated with early resective surgery; the time of surgery was at 16 months and 10 months respectively. They were studied with long term monitoring V-EEG and magnetic resonance imaging alone. The resective epilepsy surgery was planned with the concordance of ictal electroclinical/anatomic features. Discussion. The development of new technical analysis of the EEG, functional neuroimaging (SPECT, PET, MEG, fMRI) and invasive cortical mapping have increased the ability to identify acortical epileptic focus. The literature shows that epilepsy surgery can remove or reduce the recurrence of the seizures by limiting the neurocognitive impairment and allowing to achieve a good outcome (seizure free in 57% of cases; seizures reduction of more than 90% in 18% of cases) (Jansen FE et al Epilepsia 2007; 48: 1477–84). We consider early-surgical approach to epilepsy (under 18 months) in the young children with TSC in order to obtain a very good control of epilepsy and allow a better neurodevelopmental outcome. The resective epilepsy surgery could be performed, in selected cases, without invasivefunctional study (intracerebral electrodes) using limited resources and low-cost approach.

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Epilepsy
ICNC-0263: 7 tesla MRI in the pre-surgical evaluation of 19 children with focal epilepsy
INTRODUCTION The promise of 7 tesla MRI is that structural abnormalities can be found in patients without MRI lesions at lower field strengths. The aim of this study was to determine what the diagnostic value of 7T MRI is in children with epilepsy evaluated for the possibility of surgical treatment, who already underwent 1.5 or 3T MRI. METHODS For this series we assessed 19 children who underwent 7T MRI for pre-surgical evaluation in our center, and whose scans (both 7T and lower field) were discussed during epilepsy surgery meetings (ESM). We compared conclusions of visual assessments of 1.5T or 3T, with 7T MRI as agreed upon by the ESM team. RESULTS In 4 of 19 (21.1%) children, assessment of 7T MRI revealed a lesion that was considered relevant for surgical decision making (three were “MRI-negative” at lower field, in one 7T showed additional lesions). These children have been operated on (n=2, with confirmation of focal cortical dysplasia ILAE type IIa or cortical tubers in TSC), or were now planned for surgical treatment under suspicion of FCD (n=2). In 14 out of 17 (82.4%) children with non-lesional lower-field MRI, 7T MRI did not show epilepsy-related lesions either. Two children had confirmed FCD in the absence of any reported MR abnormalities at 7T. CONCLUSION 7T MRI holds a promise to improve identification of epileptogenic structural abnormalities in patients with intractable epilepsy. In our series of 19 children with refractory focal epilepsy, multidisciplinary evaluation of 7T MRI identified additional lesions not seen on lower-field MRI in four (21.1%). Acknowledgements: Tim Veersema is supported by a grant from the Dutch Epilepsy Foundation (12.12).

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ICNC-0264: Seizure duration with and without rescue medication in a European study of children who experience prolonged acute convulsive seizures

Introduction Rescue medication for prolonged acute convulsive seizures (PACS) is widely prescribed for community administration to children with epilepsy, despite limited evidence that it reduces seizure duration and prevents status epilepticus. Methods A cross-sectional study in four European countries enrolled non-institutionalized children with epilepsy (aged 3–16 years) who had experienced ≥1 PACS within the past 12 months and had currently prescribed PACS rescue medication(s). Web-based questionnaires asked parents/guardians how long on average each child’s PACS lasted without rescue medication and when rescue medication was given. Statistical tests were post hoc; p values are descriptive. Results At study entry, most of the 286 enrolled patients had prescriptions for diazepam (69.2%) and/or midazolam (55.9%), and some had two (26.6%) or three (2.4%) prescribed rescue medications. According to parents (n=258), average seizures lasted 0 to <5 minutes in 35.7% of patients, 5 to <20 minutes in 42.6% and ≥20 minutes in 21.7% when untreated; and 0 to <5 minutes in 69.4%, 5 to <20 minutes in 25.6% and ≥20 minutes in 5.0% of patients when given rescue medication. Of 166 children whose untreated seizures lasted ≥5 minutes, parents classified treated seizures as shorter than untreated seizures in 84.9% and as lasting <5 minutes in 54.8%. Rescue medication was significantly associated with shorter seizures lasting <5 minutes, compared with ≥5 minutes (X²=58.8; p<0.0001).

Conclusion Rescue medication is effective in preventing long and potentially neurologically harmful seizures in non-institutionalized children with epilepsy. Study funded by oPharma (part of the Shire Group of Companies).

ICNC-0266: Effects of Epidiolex® after 6 months in pediatric drug resistant Epilepsy

Objective: Epidiolex is an investigational drug containing purified Cannabidiol (CBD), a substance shown to have anticonvulsant properties in pre-clinical models. We describe the effect on seizures, adverse effects (AEs), and other beneficial effects (BEs) of Epidiolex in an FDA/DEA approved open-label trial for children/young adults with drug resistant epilepsy. Methods: 25 subjects received Epidiolex, doses ranging from 2.25 mg/kg/day. Eligibility criteria included drug resistant epilepsy, stable medication doses, and not taking another cannabis product. Patient demographics, CBC, CMP, and AEs or BEs reported. Seizure burden (type/frequency/severity) recorded daily by caregivers. Data at 6 months of Epidiolex use were compared with baseline. Results: Outcome data reported in tables. Total seizure number reduced by median of 31% in the 22 subjects still on Epidiolex after six months. Seventeen (77%) experienced fewer seizures, with 38% mean reduction. Seven subjects (31%) had >50% seizure reduction. AEs were common, but majority were mild and transient. Seven serious AEs reported, none considered related to Epidiolex. Seven subjects reduced dose due to AEs; one discontinued for diarrhea and lack of efficacy, another for persistent nausea/vomiting, a third for lack of efficacy. Additional BEs (>12%; more alert/social, less irritable) were more sustained throughout treatment. Conclusions: Caretakers reported decreased seizures in majority of patients treated with Epidiolex. Common AEs included fatigue and diarrhea, but drug was generally well tolerated. Other reported benefits complemented or sometimes even outweighed seizure control. Caregiver surveys and 12 month data currently being analyzed, but current results support future controlled trials of Epidiolex (CBD) in various pediatric epilepsies. Acknowledgments: We thank our participating families and patients. Study medication and administrative/regulatory advice graciously provided by GW pharmaceuticals.

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Epilepsy

ICNC-0269: Nedd4-2 and CIC-2 channel regulate Neuronal Excitability, in the Pathogenesis of Mesial Temporal Lobe Epilepsy

Abstract: To date, more and more studies pay attention to the role of Nedd4-2 regulating neuronal excitability, and then in the mechanism of epilepsy. But, how does it do effect exactly? We don’t know. Here, we explore the role of Nedd4-2 and CIC-2 channel regulating neuronal excitability, then in the pathogenesis of mesial temporal lobe epilepsy (MTLE). Firstly, we used pilocarpine to induce MTLE rat models. In the status epilepticus group, EEG-recording demonstrated continuous epileptic discharges; Morphological stains of hippocampus showed neurons swelling and lysis; aberrant mossy fibers; Meanwhile, western blot results revealed that the expression of Nedd4-2 down-regulated, P-Nedd4-2 up-regulated and CIC-2 down-regulated. Then, the cell epilepsy models were induced by Mg2+-free culture, whole-cell current clamp recording demonstrated spontaneous action potentials markedly frequent and regular in many cells. Also, western blot results showed that the expression of Nedd4-2 down-regulated, P-Nedd4-2 up-regulated and CIC-2 down-regulated. We inhibited the function of Nedd4-2 by using Nedd4-2-shRNA and observed that CIC-2 down-regulated and spontaneous action potentials increased. On the other hand, we inhibited the function of CIC-2 by using CIC-2-shRNA and observed that Nedd4-2 up-regulated, P-Nedd4-2 down-regulated and spontaneous action potentials increased. To conclusion, our studies explored that phosphorylation of Nedd4-2 regulated the expression of CIC-2, which involving in neuronal excitability, participated in the pathogenesis of MTLE.

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Epilepsy

ICNC-0270: Off-label AEDs (antiepileptic drugs) Use in in-patients of a tertiary pediatric epileptic center in China: A cross sectional study

- Objective: To determine the extent of off-label AEDs use in wards of a tertiary pediatric epileptic center in China. To analyze risk factors, so as to understand the current situation of AEDs use and label AEDs use in different AEDs.
- Method: We analyzed and collected basic information and prescriptions related to AEDs use for 292 patients of a tertiary pediatric epileptic center in China from 2014.9.30 to 2014.10.31. We calculated the incidences of different drugs and categories of off-label use. We analyzed risk factors through the methods of single factor and multiple factor logistic regression analysis.

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Epilepsy

ICNC-0271: Thalamic Lesions Associated with Epilepsy and ESES

Introduction: Early thalamic injury has been shown to predispose to electrical status epilepticus in slow wave sleep (ESES); however underlying mechanisms are still unclear. The possible mechanism can be an imbalance between GABAA and GABAB mediated receptor due to thalamic injury, especially of the GABAergic reticular thalamic nucleus. Method: We report six patients with thalamic lesions associated with epilepsy and ESES followed at our department. We retrospectively reviewed clinical findings, EEG, MRI and seizure outcome. Results: Three patients were male and three were female. The mean age at the time of evaluation was 6.3 years (9 months-11 years). The mean age at seizure onset was 3.8 years (6 months-9 years). Neurological examination showed abnormal findings and/or developmental/intellectual problems in all patients. Seizure types were focal seizure with or without progression to bilateral convulsive seizure, generalized tonic-clonic, atypical absence and atonic. Three cases had unilateral and three cases had bilateral thalamic lesions on MRI. EEG showed ESES pattern in 4 patients who had unilateral or predominantly unilateral thalamic lesion. The underlying etiologies were head trauma in three patients, encephalitis in two patients and tumor in one patient. All patients were maintained on polytherapy. Five patients had refractory epilepsy, one was seizure free on a combination of two antiseizure medications. Conclusion: Patients with thalamic lesions may suffer from refractory epilepsy. The presence of ESES should be evaluated with sleep recordings in these children for appropriate management of epilepsy.

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Epilepsy

ICNC-0275: The clinical spectrum of PCDH19 mutations in a Chinese study

Introduction Mutations in PCDH19, encodes protocadherin 19, have been identified in epilepsy patients mainly affected females. We aimed to summarize the clinical spectrum of PCDH19 mutations in a Chinese study. Methods 75 girls diagnosed as DS without SCN1A mutations and 21 girls with fever sensitive and cluster of seizures were searched for PCDH19 mutations by Sanger sequencing. Results 20 heterozygous PCDH19 mutations were detected in six out of 75 (8%) DS girls and 14 out of 21 (66.7%) girls with fever sensitive and cluster of seizures. Except one’s inheritance was unavailable, nine patients’ mutations were inherited, the remaining 10 were de novo mutations. 17 types of mutations were identified, all were located in exon 1. 11 were novel mutations (c.488T>G, c.1347_1348insAAC, c.1017delC, c.1184G>C, c.1408_1417delGCCTATCTGC, c.1825G>T, c.1240G>A, c.370G>A, c.1375C>T, c.339C>A and c.471C>A). Mutations c.1019A>G and c.1091dupC were recurrent identified in three and two unrelated probands respectively. Seven out of nine probands with inherited mutations were familiar cases, one was inherited from her asymptomatic father and one was inherited from her asymptomatic mother. Mental retardation was present in 18 probands with PCDH19 mutations. Two DS patients with PCDH19 mutations had autistic features. All patients with PCDH19 mutations shared the similar clinical features, including early onset seizures (5-18 months), seizures sensitive to fever, focal seizures or generalized tonic-clonic seizures in clusters. Conclusion The clinical spectrum of PCDH19 mutations include female DS, epilepsy and mental retardation limited to females (EFMR), epilepsy with normal development and asymptomatic female carrier. 【Keywords】Dravet syndrome; fever sensitive epilepsy in girls; PCDH19 gene

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Epilepsy

ICNC-0276: GRIN2A mutations in epilepsy-aphasia spectrum disorders

Introduction Epilepsy-aphasia spectrum disorder (EAS) are a group of epilepsy syndromes denoting an association between epilepsy, speech and language disorders and the EEG signature of centro-temporal spikes. Mutations in GRIN2A, encoding the α2 subunit of the N-methyl-d-aspartate (NMDA) receptor, have been identified as a monogenic cause for EAS. Here, we report GRIN2A mutations in a cohort of Chinese patients with EAS. Methods Patients with Landau-Kleffner syndrome (LKS), epileptic encephalopathy with continuous spike-and-wave during sleep (ECWS), atypical benign partial epilepsy (ABPE), and benign childhood epilepsy with centrotemporal spikes (BECTS) were recruited. Mutation screening of GRIN2A was performed using PCR and Sanger sequencing. Results 122 probands, including 9 LKS, 26 ECWS, 42 ABPE and 45 BECTS were enrolled. The mean age of seizure or aphasia onset was 5 years (range 10 months-11 years). GRIN2A mutation screening detected 4 pathogenic missense mutations including c.2278G>A (p.G760D), c.4153G>T (p.D1385Y), c.1364G>A (p.C455Y) and c.691T>C (p.C231R) in four probands respectively. Four probands with GRIN2A mutation comprised one case with LKS and three cases with ABPE. To LKS, the mutation rate was 11.1% (1/9). To ABPE, the mutation rate was 7.2% (3/42). No GRIN2A mutation was found in the 26 probands with ECWS and 45 probands with BECTS. In 25 (20.5%) of 122 probands had a positive family history of febrile seizures or epilepsy. Conclusion GRIN2A gene is a rare causative gene in Chinese patients with EAS, suggesting the possibility of other gene involved in the pathogenesis of EAS. 【Key words】epilepsy; aphasia; GRIN2A gene; mutation

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Epilepsy

ICNC-0277: The efficacy of a 6-month classical ketogenic diet and influencing factors - A retrospective analysis of 87 children with drug-resistant epilepsy

Objective: To evaluate the efficacy of a 6-month ketogenic diet (KD) in children with drug-resistant epilepsy at different therapeutic stages and to analyze the associated factors that affect the efficacy of a KD. Methods: Eighty-seven pediatric patients with drug-resistant epilepsy who followed a KD for at least 6months were included in this study. The efficacy of a KD was assessed based upon the seizure frequency, as recorded by parents and caregivers. The number of cases and the efficacy of each grade in different age ranges were also considered. The effects of gender, age, seizure type, etiology, blood glucose and ketone levels, seizure frequency before the diet and cognition on the length of time on a KD were analyzed. Results: (1) There was no significant correlation between the length of time on a KD and efficacy (χ² =2.31. P=0.51). The efficacy of a 3-month KD was 51%, which did not further increase when the course was extended to 6 months. (2) There was a positive correlation between increased cognition and the efficacy of a KD after 3 months

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(γ=0.31, P=0.003). (3) Efficacy analysis of treatment with a 3-month KD revealed, with respect to seizure types, that there were 37 patients with multiple seizure phenotypes and 50 patients with a single seizure phenotype. The overall efficacy of a KD in the multiple seizure phenotypes group was 61%. The efficacy of a KD was not statistically associated with a co-existing syndrome or a type of syndrome; however, the efficacy of a KD had a tendency to be increased in certain types of syndrome. Meanwhile, the overall efficacy in the single seizure phenotype group was 87%, and the efficacy was not associated with seizure type. (4) The efficacy of a 3-month KD was not correlated with age, gender, etiology, blood glucose or ketone levels, or the seizure frequency before treatment. Conclusion: An observation time of 3 months is appropriate for assessing the efficacy of a KD in treating children with drug-resistant epilepsy. The factors that likely influence the efficacy of a KD are unclear, but our study suggests that incorporating more patient samples will help determine whether patients with certain syndromes can benefit from a KD.

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Epilepsy

ICNC-0278: Clinical characteristics of simple and complex febrile seizures

Objective There is a growing awareness of the developmental importance of distinguishing complex from simplex febrile seizures [FS] in early childhood. The aim of this study was to investigate the association between risk factors and clinical characteristics of simple and complex febrile seizures. Methods We assessed risk factors and clinical features of febrile seizures in all children who were admitted to the Pediatric Clinic with the diagnosis of FS from January 2010 to January 2012. Two hundred and ten children having a history of FS were evaluated for age at onset of FS, age of repeated FS, total number of FS in the past, family history of FS and epilepsy. The febrile seizures were classified as simple and complex. Results Compared with children with simple FS, complex FS were associated with more seizures in the past [OR=2.20, 95%CI: 1.31, 1.70, p=0.003]. Furthermore, family history of FS increased the odds of repeated seizures within 24h [adjusted OR =2.98, 95%CI: 1.14, 7.79, p=0.026]. Similarly, family history of epilepsy increased the odds of repeated FS within 24h [adjusted OR=6.20, 95%CI: 1.01, 39.4, p=0.049]. Conclusion Our study showed that higher number of FS in the past might be associated with complex FS. Our findings also show that early detection of repeated seizures within 24h in children with family history of FS and epilepsy might be a gateway to improve early diagnosis of epilepsy. However, larger prospective study with parent’s involvement in FS detection is needed.

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Immune-mediated disorders

ICNC-0371: A paediatric case of an Unexplained Steroid-Responsive Neuroinflammatory Disorder (CLIPPERS)

Introduction: Chronic Lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is a specific clinic-radiological syndrome with an unknown aetiology. It is frequently considered in the differential diagnoses of adults with CNS inflammation. Biopsy proven cases have not been reported in children.

Case: A previously healthy 3-year-old boy presented with sub-acute onset truncal ataxia with slurred speech and drooling. He had an unsteady gate, bilateral VI nerve palsies, reduced tone with hard to illicit reflexes and a resting tremor with past pointing. Brain MRI demonstrated bilateral disease of the dorsal pons, thalamus, cerebellar white matter, with swelling and faint enhancement. CSF was acellular with no oligoclonal bands and normal lactate. EEG was bilaterally slow. Infective, inflammatory and metabolic screen were negative. He was treated with intravenous methylprednisolone (IVMP) with dramatic improvement of symptoms but then required repeated boluses of IVMP and oral tapers due to multiple relapses.

Azathioprine was used and he briefly came off steroids prior to another relapse. At age 12 years he developed osteoporosis and a vertebral fracture leading to cessation of steroid therapy. Currently, aged 15 years he still has some gait abnormalities, bilateral VI nerve palsies and has significant learning difficulties. Lesional brain biopsy revealed prominent lymphocytes infiltrates suggestive of CLIPPERS. Conclusion: The imaging features with the speckled appearance of the pontine lesions alongside the striking steroid responsiveness, is suggestive of CLIPPERS. As this condition is thought to be inflammatory in nature, earlier recognition with more aggressive immunotherapy could have resulted in a better outcome.

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Immune-mediated disorders

ICNC-0372: Our experience with Opsoclonus-Myoclonus Syndrome

Introduction: Opsoclonus myoclonus syndrome (OMS) is a rare movement disorder of autoimmune ethiology, the majority associated with neuroblastoma. A child develops a combination of neurological features (opsoclonus, irritability, myoclonus, ataxia) during a few days or weeks. If the full clinical picture is not present at onset, the diagnosis can be challenging, but its recognition is useful in guiding investigations and treatment.

Methods: Patients diagnosed with OMS in our clinic in the last 5 years were selected, and the hospital records, medical letters, notes from checkups were analysed. Information gathered included age of onset, symptomatology at onset, investigations done in search for diagnosis, delay to diagnosis, association with neuroblastoma, treatment given, response to treatment and results of follow-ups, where this information was available.

Results: We identified a total of 11 children, of which 7 had associated neuroblastoma. Although the analyzed group was not large, we noticed a trend to quantify the clinical symptomatology using standardized scores; initial treatment were corticosteroids and where necessary, surgical resection of tumor formation; overall outcome was favorable. Data is in accord with the literature.

Conclusion: OMS is a severe affliction of early childhood, that can have a noisy onset. Early diagnosis is possible if evaluated by a pediatric neurologist and the syndrome is recognized; this is helpful with limiting unnecessary interventions (investigations and treatment). There is need for a standardised clinical reporting form, to help evaluate response to treatment and diminish inter-rater variability. Rapid appropriate treatment improves prognosis. Long term follow-up is usually difficult, but necessary.

Key words: opsoclonus, myoclonus, OMS, neuroblastoma, corticosteroids

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Immune-mediated disorders

ICNC-0374: Neurological manifestations heralding systemic lupus erythematosus

Objectives: To identify neurological manifestations (MN) as initial symptoms of systemic lupus erythematosus (SLE). Methods: Review of charts of 200 SLE patients who met the CAR1997/SLICC2012 criteria seen over the last 15 years. Results: Thirty presented MN, 11 (36.6%) as initial symptoms. Mean age at diagnosis was 12.5 years, 10 were girls. MN were as follows: 3 neuropsychiatric disorders, 3 abnormal movements, 2 headaches, and seizures, NMO, meningeal syndrome in 1 each. Three patients had pure MN: abnormal movements, epilepsy, NMO and subsequently developed systemic manifestations: prolonged febrile syndrome, arthritis, and anemia. Eight patients simultaneously presented with NM and systemic symptoms (5 arthritis, 5 hematologic manifestations, 4 renal manifestations, 3 prolonged fever, 2 weight loss, 8 mucocutaneous manifestations). All had anti-DNA (+), ANA (+), and low complement.
Immune-mediated disorders

In all 3 patients with pure MN, SLE was confirmed between two months and eight years after symptom onset. In all three abnormalities were found on brain MRI: contrast-enhanced ring buckle of the corpus callosum and periventricular hyperintensity on Flair (1); hyperintensity on T2 in frontal areas (1); hyperintensity in T2 and Flair in bulb and spinal cord (1). Conclusions: Patients with SLE may present with a spectrum of neurological manifestations at onset, that may be isolated or associated with other symptoms. When MN present without other symptoms, the entity represents a challenge for the neurologist, while the association with systemic involvement facilitates the diagnosis. In the former setting, antibody testing should be included in the diagnostic work-up.

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Immune-mediated disorders

ICNC-0375: Cognitive impairment in children with multiple sclerosis

Multiple sclerosis (MS) is a demyelinating autoimmune disease that leads to axonal degeneration and brain atrophy. Although typically a disease of young or middle aged adults, MS manifests under 18 years in 2-5% of cases. Presentation and course of the disease are said to be different in these age groups. In particular, impairment of brain development and cognition are reported to be severe in children. In order to investigate this aspect of the disease, we tested 50 pediatric MS patients with the Wechsler Intelligence Scale for Children-R (WISC-R), line orientation test, verbal fluency test and stroop word color test. All tests were performed at least one month after an attack. Patients’ ages were between 8-17 years, mean 14.4 years. Male/female ratio was 9/41. The results showed IQ levels were lower than 80 in 33% of the patients, between 90-109 in 38% and above 110 in 29%. Control tests, performed at least 12 months after the first evaluation, showed no significant difference except shorter response latency in the stroop test. Our results disagree with the findings of other groups reporting early cognitive impairment and arrest of the age-expected development in pediatric MS patients. This discrepancy might be explained by the effects of medications and emotional factors such as anxiety, depression, or concentration difficulties on the test results. The limitations of the present study is the short follow-up period for a chronic disease: longer follow-up of this cohort is being conducted. However these results are encouraging in terms of cognitive outcome of pediatric MS patients.

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Immune-mediated disorders

ICNC-0376: Pediatric neuromyelitis optica spectrum disorders (NMOSD) in a Brazilian center

Introduction: NMOSD consist in an inflammatory central nervous system condition associated with serum aquaporin-4 immunoglobulin G antibody (AQP4-IgG). Diagnostic criteria were recently reviewed for NMOSD with or without AQP4-IgG and takes into account clinical characteristics and neuroimaging findings. The incidence in children is unknown and its presentation is similar to adults although there are some caveats. Method: data review of records of children enrolled in our neuromununology service who met the diagnostic criteria from January 2005 to September 2015. Results: analysis revealed seven patients (five girls), average age 10 years at onset. Two patients were caucasian and five of mixed ethnic background. Clinical manifestations at onset were myelitis (2), optic neuritis (4), area postrema syndrome (1), and acute brainstem syndrome (2). Cerebrospinal fluid cell count ranged from 3-320 cells, and protein from 24-143 mg/dl. Four (57.1%) tested positive for AQP4-IgG. First neuroimaging findings revealed nonspecific alterations in three patients; none diencephalic lesions were found. Mean relapse number were 2.8 during a mean three-year follow-up. All patients were acutely treated with methylprednisone, two with plasmapheresis and two received cyclophosphamide. Maintenance treatment consisted of azathioprine and mycophenolate. Four patients presented important visual impairment, two school difficulties, and one physical disability. Conclusion: The most common clinical manifestations were myelitis and neuritis, although atypical forms have occurred. The antibody positivity was lower, possibly because of various laboratory methods. Although rare in childhood, NMOSD is associated with significant neurologic sequelae, especially visual deficit.

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Immune-mediated disorders

ICNC-0377: Relapsing Neuromyelitis Optica in a young child

Relapsing Neuromyelitis Optica in a young child

Introduction: Neuromyelitis Optica (NMO) is a rare autoimmune inflammatory disorder of the central nervous system characterized by optic neuritis and transverse myelitis. It predominantly affects middle-aged adults; however, pediatric cases are increasing recently. Here we present a young child with a relapsing course of NMO. Case report: A previously healthy 3-year-old girl presented with fever and vomiting for three weeks associated with inability to walk and swallowing difficulties. Physical examination showed conscious, irritable child with right side torticollis. She has normal cranial nerves with left-sided weakness. CSF analysis was negative for viral and bacterial infections. MRI brain showed focal lesion at the posterior aspect of medulla oblongata of uncertain nature. One month later, she presented with lethargy and vomiting. MRI brain and spine revealed multiple lesions involving medulla oblongata, right facial colliculus and left anterior thalamus with diffuse intramedullary lesion involving the whole cervical spine consistent with neuromyelitis optica. CSF protein was high. The diagnosis was confirmed by high CSF Aquaporin 4 antibody (116.9 u/ml), (normal 0.0-3.0). She was treated with Intravenous immunoglobulin, pulse steroid therapy and Rituximab. She showed a dramatic improvement with completely resolved weakness. One year later, she presented with severe headache, sluggished pupillary reaction and hyperemic disc in the left eye consistent with optic neuritis. She was treated similarly. Her recent follow up in neurologic clinic at age of five years was essentially normal. Conclusion: NMO is a rare autoimmune disorder in children. Early diagnosis and effective treatment with immunosuppressive therapy prevent permanent neurological damage, this patient represents one of the youngest ever reported patients with NMO.

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Immune-mediated disorders

ICNC-0378: Neuromyelitis optica in children

Introduction: Neuromyelitis optica (NMO) is inflammatory - demyelinating disease of the CNS in which the axial symptoms concerning the optic nerves and the spinal cord. Many patients may also include relapsing neurological symptoms suggesting multiple sclerosis. Less frequently, especially in younger children, NMO relapses are accompanied by symptoms of encephalopathy, which should be differentiated from acute disseminated encephalomyelitis (ADEM). NMO characteristic feature is the presence of antibodies against aquaporin 4 (AQP4). According to the current knowledge, patients with confirmed presence of specific antibodies are at risk of severe relapses and require chronic, preventive immunosuppressive therapy. Case description: The authors present diagnostic and therapeutic problems on the example of two patients. The diagnosis of NMO was established on NMO spectrum diagnostic criteria and the applicable for children the International Pediatric MS Study Group criteria. In both patients the presence of AQP4 antibodies was confirmed. In the treatment of acute exacerbation methylprednisolone pulses and immunoglobulin was applied with good effect. Then remission of symptoms was supported by oral prednisone therapy in combination with azathioprine. Due to the recurrence of symptoms in our patient, Rituximab was introduced to the treatment. Conclusion: Careful differential diagnosis of MS, ADEM and NMO based on neuroimaging, CSF testing and antibody test for AQP4 is very important to select an appropriate treatment option.

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Immune-mediated disorders

ICNC-0379: Autosomal dominant acute necrotizing encephalopathy due to RANBP2 mutation (ANE1 or Infection-induced acute encephalopathy 3, IIAE3): preventive therapy and counseling

Introduction: Acute necrotizing encephalopathy (ANE) is characterized by rapidly progressive encephalopathy, seizures and polyfocal neurological signs associated with a febrile illness. MRI and CSF show more or less characteristic findings. Early treatment including steroids provides the best outcome. One third of the affected individuals die during the acute phase. Of the survivors, one half have serious neurological deficit. In case of recurrent or familial episodes, a RANBP2 or CPT2 mutation can be found. However, penetrance is incomplete: 40% of heterozygotes for a RANBP2 pathogenic variant will manifest an episode of ANE. Episodes occur primarily before age four, but events up to 40 years of age are reported. Case description: In recent years, three children of whom two brothers presented to our department with ANE. Despite intensive treatment, both brothers died and the other boy had serious residual deficit. Pathogenic mutations in the RANBP2 gene were found in all three. The asymptomatic father of the two brothers carried the mutation as well. The family history of the other boy reported a paternal half brother who had died with encephalopathy. The father of this
patient was said to have had meningitis as a child. Currently, he is being tested for the RANBP2 mutation. Discussion: For all carriers of pathogenic RANBP2 mutations, routine vaccinations and yearly influenza vaccinations are recommended. Molecular genetic testing of at-risk first degree relatives, especially children, is warranted since they may benefit from early treatment including steroids of episodes of encephalopathy. Prenatal testing is possible, but warrants thorough counseling.

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Immune-mediated disorders

ICNC-0380: Cyclophosphamide-responsive anti-NMDAr Encephalitis in a Filipino Adolescent Girl: Her journey towards recovery
AbstractAnti-N-methyl-D-aspartate (Anti-NMDAr) encephalitis is a potentially fatal disease that presents with a typical neuropsychiatric syndrome, which is a result of an autoimmune reaction against the NR1 subunit of the NMDA receptors. We present the case of our 17-year old Filipino female patient who was confirmed to have anti-NMDAr antibodies on both CSF and serum who manifested with initial non-specific flu-like symptoms developing to prominent psychosis, paranoia, bizarre orofacial and limb dyskinesias and encephalopathy. She was initially treated for viral encephalitis but a high index of suspicion for autoimmune limbic encephalitis was considered from the outset. First line immunomodulating therapy (IVIG) was provided as early as possible but she reacted with anaphylaxis, thus upon resolution of hospital acquired infections, methylprednisolone was administered followed by another course of IVIG which was tolerated but did not resolve the dyskinesias and encephalopathy. Second line cyclophosphamide was then administered with subsequent patient improvement. Anti-NMDAr encephalitis should always be a consideration in those with prominent neuropsychiatric history and in encephalopathic patients who screen negative for infectious etiologies. Second line immunomodulatory therapy with cyclophosphamide was proven to be successful as seen in our patient. HighlightsWe describe the clinical course of a Filipino adolescent female diagnosed with anti-NMDAr encephalitis responding to second line cyclophosphamide after treatment failure with first line immunotherapy.KeywordsAnti-NMDAr encephalitis, adolescent, cyclophosphamide

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Immune-mediated disorders

ICNC-0381: Cognitive outcome of Anti-N-Methyl-D-aspartate-receptor encephalitis in children

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis has been described with a well defined set of clinical features: seizures, decreased level of consciousness, dyskinesias and autonomic instability. Although there is an increasing amount of information about the diagnosis and acute treatment strategies, little is known about the cognitive outcomes. Aims: To describe the subacute/chronic cognitive and neuropsychological profile in four children with anti-NMDAR encephalitis. All patients had normal premorbid development; severe neurological involvement in the acute phase of the illness; and received a first-line treatment (corticosteroids, plasma exchange or intravenous immunoglobulins), in one followed by a second-line. Methods: Four patients, age: 8-18 years. Time from disease onset to neuropsychological evaluation: 2-62 months (one patient was re-assessed). Neuropsychological assessment included: orientation, memory, intelligence, visuoperception, and executive function testing. Results: IQ levels ranged from average to mild intellectual disability (108-62). Deficits in attention, memory and executive functions were observed in three patients, but these were according to their level of intellectual functioning. In most patients inhibitory response and verbal memory (word list) were found to be strengths in their profile. Significant improvements in intellectual functioning and general cognitive profile was found in the patient that was re-assessed 7 months after the initial evaluation. Conclusion: Cognitive abilities were significantly improved providing immunomodulatory treatment and specific rehabilitation therapy, but in most patients some deficits remained. No clear neuropsychological profile was found in our patients. More studies with a larger cohort are needed.

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Immune-mediated disorders

**ICNC-0825: A case of Autoimmune encephalitis simulating PANDAS (Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus)**

A 10 years old male patient, two months prior to admission he had behavioral changes with emotional lability, poor control of impulses, apathy, motor clumsiness and sleepiness, which were exacerbating progressively. Then he presented left focal motor seizure, followed by visual hallucinations, involuntary movements like chorea, balism and oro-facial dyskinesias. He developed a clear and predominant obsessive compulsive disorder, he had the antecedent of pharyngitis prior of the beginning of the symptoms and the levels of Antistreptolysin O (ASO) was slightly higher. He was treated with Ceftriaxone and the course of the ill was the same. Then he started pulses of methylprednisolone and immunoglobulin when the result of the study of anti NMDAR in LCR was positive. On the third day of starting therapy he had an important clinical improvement. The brain MRI and CT scan, searching tumoral process were normal. EEG was abnormal because of slow activity. Discussion This was a peculiar case of autoimmune encephalitis because the obsessive compulsive disorder was the main in the presentation, and the high levels of ASO confused us about the diagnosis. However the study of anti NMDAR in LCR was conclusive. The autoimmune encephalitis can begin with the most various kind of neuropsychiatric disorder, progressing to encephalopathy, associated to involuntary movements, seizures and autonomic instability. It requires aggressive Immunomodulatory treatment, the delaying onset is associated with devastating consequences.

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Immune-mediated disorders

**ICNC-0382: Successful treatment of Acute Cerebellitis with IV immunoglobulin in pediatric case**

Introduction Acute cerebellitis is uncommon inflammatory diseases of cerebellum. Its exact cause is not fully understood but viral infection is considered to be associated; direct infectious damage or via immunological mechanism. Clinical manifestations are abnormal functions of cerebellum characterized by ataxia. The abnormal findings in brain MRI scan representing as T2 hyperintensity is important for diagnosis. There has been no established standard treatment. In this report, the authors report a case of acute cerebellitis who showed quick improvement in symptoms and MRI results after intravenous immunoglobulin treatment. Case A six-year old boy was hospitalized complaining ataxia. Eighteen days before the admission, he experienced fever, headache and vomiting for 7 days and he was hospitalized for 6 days under the diagnosis of meningitis and was treated with antibiotics with symptoms improvement. Right after discharge, he complained dizziness and ataxia for 4 days and he was re-admitted to the hospital. On the second admission, Romberg sign was positive and tandem gait abnormality, and truncal ataxia were observed. Brain MRI scan showed hyperintensive shadows in the bilateral cerebellar cortex in the T2-weighted image. The patient was diagnosed as acute cerebellitis and high dose of steroid was administered for next 3 days and then changed into oral steroid without improvement. At 6th hospital day, we used immunoglobulin (1g/kg) intravenously and he showed improved gait and orthostatic balance from the seventh hospital day. On the 8th hospital day, the follow-up MRI scan showed some improvement of cerebellar lesions and he was discharged. On outpatient follow-up, he showed full recovery of ataxia. Conclusion The authors experienced a case of acute cerebellitis whose symptoms and MRI lesions were improved after immunoglobulin treatment. Intravenous immunoglobulin treatment is expected to help quick improvement in acute cerebellitis.

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Immune-mediated disorders

**ICNC-0384: An adolescent with demyelinating plaques and cerebral venous thrombosis; is it childhood multiple sclerosis or Behcet disease?**

Introduction We present an interesting adolescent case with demyelinating plaques and cerebral venous thrombosis.

Case Description The patient was a 13-year old boy. He was admitted to our unit for further investigation of demyelinating disorder which was diagnosed 25 days ago in another hospital. Magnetic resonance imaging (MRI) of the brain showed right transverse and sigmoid sinus and the superior sagittal sinus thrombosis and infra and supratentorial contrast enhancing T2 hyperintense lesions. Whole spine MRI revealed lesion with and withouth contrast enhancement. When we checked the previous brain MRI, there was not any sinus thrombosis. His previous complete blood work-up for exclusion of infectious and autoimmune diseases resulted negative. Cerebrospinal fluid examination showed positive oligoclonal bands. We learned that he received methylprednisolone pulse therapy for 3 days. Therefore he was administered an intravenous methylprednisolone pulse therapy for 3 days together with low molecular weight heparin followed by oral prednisolone. Extensive work up for thrombophilia was normal. The ophthalmologic examination revealed dimmed signs of uveitis AND HLA B51 allele was positive. During a 3-month follow-up examination, an MRI was...
performed, which revealed a significant regression of the lesions and complete resolution of sinusal thrombosis. Conclusion Although CVT is very important non-parenchymal central nervous system involvement in Behcet Disease, there is no report which MS-like plaques and CVT simultaneous occurred in same patient in literature. The association between CVT and MS has also been reported very rarely.

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Immune-mediated disorders

ICNC-0308: A case of Guillain-Barré syndrome associated with influenza B viral infection

Introduction Guillain-Barré syndrome (GBS) is an autoimmune disorder often considered a postinfectious polyneuropathy involving mainly motor but also sensory and sometimes autonomic nerves. The motor paralysis usually follows a nonspecific gastrointestinal or respiratory infection by approximately 10 days. An antecedent, presumably viral infecton, triggers inflammation and demyelination. Influenza virus is a rare recognized cause of antecedent infection; type A is mainly associated, but type B is rarely reported in GBS. Case report A 4 year 5 month-old girl was admitted to our hospital due to pain and weakness of both legs occurred 1 day ago. She suffered from upper respiratory symptoms with high fever 1 week ago, but recovered 4 days later. Weakness proceeded rapidly to both arms and respiratory muscles within 24 hours of onset, so mechanical ventilation was applied to her. Tendon reflexes were also diminished. Initial CSF examination and MRI of brain and spine showed normal results. Influenza B was positive by rapid antigen test. Through clinical findings, she was diagnosed as Guillain-Barré syndrome associated with influenza B, and IVIG (400 mg/kg/D) and oseltamivir were administered for 5 days. Follow up CSF examination after 1 week showed albumino-cytologic dissociation (WBC 2 /mm3, protein 272 mg/dL). She was alert during mechanical ventilation, but presented incomplete opening, closure, and movement of both eyes (cranial nerve involvement), hypertension and tachycardia (autonomic involvement). On 10th hospital day, she began to recover respiration and arm power, and recovered completely 2 months later. Conclusion We experienced a case of Guillain-Barré syndrome that occurred after influenza B viral infection. The patient recovered completely after IVIG administration and supportive care, although progressed rapidly to respiratory muscle paralysis.

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Immune-mediated disorders

ICNC-0305: Acute Necrotizing Encephalopathy of childhood: Imaging findings and clinical outcomes

Introduction: Acute necrotizing encephalopathy of childhood is a devastating form of acute febrile encephalopathy triggered by central nervous system infections. Magnetic resonance imaging is characteristic and helps in early identification. We describe the clinic-radiological characteristics and response to treatment in 4 children with acute necrotizing encephalopathy from North India.Methods: Retrospective data collection from patients’ case sheets and prospective follow-up in neurodevelopmental clinic Results: All patients presented with encephalopathy and low Glasgow Coma Scale. Magnetic-resonance-imaging of the brain showed T1 hypointense and T2/FLAIR hyperintense asymmetrical lesions in bilateral thalami with variable involvement of the brain stem, presence of intense diffusion restriction, hemorrhagic foci and absence of post-contrast enhancement in all 4 patients. Cerebrospinal fluid examination showed absence of pleocytosis and presence of elevated proteins. Serum aminotransferase levels were variably elevated. Genetic testing is not available at our centre. Pulse methylprednisolone was administered to all these children. On the follow-up images, the brain lesions were reduced in extent for all patients, and gliosis was seen in thalamic lesions. All four children survived; mild to severe neurological deficits persisted in all of them. Conclusion: Acute necrotizing encephalopathy in Asian children is a distinct form of acute encephalopathy triggered by acute febrile illnesses. MRI is essential for early identification and initiation of timely treatment.

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Immune-mediated disorders

**ICNC-0386: Bilateral Internuclear Ophthalmoplegia and D vitamine deficiency in pediatric age multiple sclerosis: a case report**

Introduction: Experimental and epidemiological studies have already provided a sufficient immunomodulator role of vitamin D in MS patients. Case report: A 15 year old girl was admitted to pediatric neurology department with the complaint of blurring of vision, visual confusion and unsteadiness. In her neurological examination, she had an adduction deficit in the right eye and nystagmus in the left eye on leftward gaze. She also had an adduction deficit in the left eye and nystagmus in the right eye on rightward gaze. Our patient was a pediatric age presentation of BINO. Her MRI revealed acute demyelinating disorder. Oligoclonal band was positive. Ig G index was 1.64 (>0.6). She was given pulse steroid treatment for 5 days and at the end of the treatment her eye movements were normal and she had no complaint. Serum 25(OH)D level was 13ng/ml (< 20ng/ml). As our patient had D vitamin levels in the deficiency range, she was replaced with the dosage of 800IU/day D3 for a month. After this treatment, 25(OH)D level was 12.8ng/ml. The daily routine usage was strictly advised, and then the checked level after a month was yet 20ng/ml. We discussed to use high dose for immunomodulation and agreed with the dosage of 2000IU/day, a high dose advised in a pediatric age MS patient. At the third month of administration, there wasn’t any new attack. Conclusions: We offer to use high dose of vitamin D in pediatric age MS patients as we know the protective immomodulator effects on the pathophysiological mechanisms of the disease.

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**Immune-mediated disorders**

**ICNC-0389: Pediatric Autoimmune Encephalitis; a retrospective cohort study**

Introduction: Autoimmune encephalitis (AIE) is being increasingly recognized as the cause of acute encephalitis syndrome. They are caused due to antibodies that bind to neuronal proteins (surface or intracellular) and produce typical clinical syndromes. Currently it is an evolving entity.

Methods: The current study has been conducted in a tertiary care teaching hospital in north India. The clinical profile of AIE patients over a 3 year period were retrospectively reviewed. AIE was suspected in children in relevant clincioepidemiological scenario after excluding common infectious, metabolic and other systemic etiologies. AIE were sub-classified into definite (antibody positive in serum and/or cerebrospinal fluid), possible (seronegative but responsive to immunotherapy) and unlikely (seronegative and no response to immunotherapy).

Results: Overall 32 patients were diagnosed as definite AIE (19 Anti NMDA receptor encephalitis, 3 Anti GAD encephalitis, 6 antibasal ganglia encephalitis and 1 each of Anti MA, Anti YO, Anti Hu and Anti-thyroperoxidase antibody encephalitis). The spectrum of clinical manifestations included behavioral abnormalities, encephalopathy, seizures, movement disorder and autonomic disturbances. None of the patients were positive on tumor screen and they are on annual tumor surveillance. All except one (Anti GAD encephalitis patient who died) showed variable favourable response to immunotherapy which included pulse methylprednisolone, intravenous immunoglobulin, oral steroids, plasma exchange and cyclophosphamide rituximab therapy in various combinations. All seven seronegative patients demonstrated favourable response to immunotherapy. Conclusion: In view of favourable treatment and outcome related implications, AIE should always be considered in acute encephalitis syndrome scenario.

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**Immune-mediated disorders**

**ICNC-0390: A mutation positive case of recurrent acute necrotising encephalopathy of childhood**

Introduction: Acute necrotizing encephalopathy (ANE) is a rare disorder characterized by encephalopathy following a febrile illness, mostly viral. Most cases are sporadic; however, recurrent and familial cases have been linked to RANBP2 mutation. Description of the case: This is a description of a three and half years old girl with recurrent ANE with RANBP2 mutation (c.1735 C>T (p.T158S)). She had two episodes of encephalopathy, each following a short non-specific febrile illness. Neuroradiologically, she had typical findings involving bilateral thalami during the first episode and involving bilateral temporal and occipital lobes, bilateral cerebellar hemispheres and brainstem during the second episode. She was managed with intravenous gamma globulin and dexamethasone during both the episodes. She recovered significantly with minimal residual deficits in her cognitive and language domains. Conclusion: In relevant clinical-radiological scenarios both isolated and recurrent ANE should be considered because of treatment and long-term outcome related implications.

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**Immune-mediated disorders (Continued)**

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Immune-mediated disorders

ICNC-0391: Tumefactive Demyelinating Lesions in children
Tumefactive demyelinating lesions (TDL) are large areas of demyelination described as larger than 2 cm which often produce a mass effect. They are relatively rare and need to be distinguished from tumors. We present three pediatric cases with TDL, two boys and one girl, aged 7, 10, and 14 years. One had optic neuritis 1 year ago with full recovery, the others had no health problems before the current presentation. Ataxia and weakness were the first symptoms. Magnetic resonance imaging (MRI) studies showed space-occupying lesions. Brain tumor (n=2) and acute disseminated encephalomyelitis (ADEM) were the primary diagnoses on referral. Neurological examination revealed hemiparesis in two patients and quadripareis in one patient, hypoesthesia and dysmetria in all. The patients were unable to maintain a standing position even with support. MRI demonstrated solitary giant (4.5 cm) TDL in one patient, multiple TDLs in two patients. Wide work up for differential diagnosis were made including cerebrospinal fluid examinations and spinal MRI. The patients were started on pulse intravenous methylprednisolone at 30 mg/kg/day for 5 days. One patient subsequently received intravenous immunoglobulin at 400 mg/kg/day for 5 additional days and later, plasma exchange. They were ambulatory on discharge. They did not have any further neurological problems in minimum 1 years of follow-up and their final diagnosis was made as multiple sclerosis in two and ADEM in one. Tumefactive demyelinating lesions can be a manifestation of acute demyelinating diseases or multiple sclerosis in children, and must be considered in the differential diagnosis of space-occupying lesions

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Immune-mediated disorders

ICNC-0423: Presentation Relapsing central nervous system demyelination in children with Myelin oligodendrocyte glycoprotein antibodies (MOG) antibodies
Background: Myelin oligodendrocyte glycoprotein antibodies (MOG-Ab) have been identified in 30-50% of children with acquired demyelinating syndrome. However, less is known about the wider spectrum and the clinical course of patients who relapse. Objective: To evaluate the clinical features of patients with MOG-Ab associated relapsing demyelination. Methods: Twenty-six children with relapsing CNS demyelination and MOG-Ab were recruited from three paediatric neurology referral centers (London and Birmingham), between September 2014-September 2015. Patients were tested for MOG-Ab as part of their clinical evaluation. Clinical, investigative and neuroimaging features were reviewed and treatment and outcomes were evaluated. Results: Of the 26 children (16 females, median age 6yr, range 2-15); 9 patients presented with relapsing acute disseminated encephalomyelitis (ADEM, more than 3 month apart with dissemination in space); two patients presented with monophasic/recurrent episodes of ADEM followed by monophasic-relapsing optic neuritis (ADEM-ON); 14 fulfilled criteria for AQP4-Ab negative neuromyelitis optica spectrum disorder (NMOSD) and one presented with recurrent ON. Patients presented initially wit ADEM (n=10), ON (n=9), TM (n=4), brainstem CIS (n=2) and one child presented with simultaneous ON and TM. Abnormal brain MRI at onset was seen in 17/26 (65%). Oligoclonal bands were positive in the CSF in 3/22 tested (14%). Median time to first relapse (TTFR) was 1 year (range 0.08-8) Conclusion It is becoming evident that relapsing patients with MOG-Ab may fulfill new criteria for NMOSD and may benefit from B-cell targeting therapies to prevent further relapses. Importantly, TTFR may be up to 8yr, which need to be considered when evaluating treatments.

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Immune-mediated disorders

ICNC-0393: An unusual paediatric presentation of N-methyl-D-aspartate receptor (NMDA-R) encephalitis: clinical course and treatment strategies
Introduction: We present a case of NMDA-R encephalitis with unusual clinical and MRI findings. We discuss treatment strategies. Methods: Primary literature search and review of patient notes. Case Description: A previously well 4-year-old girl presented with focal seizures and mild right-sided weakness. Five days later she developed dysarthria, dysnomia, dense right hemiparesis, and further focal seizures. MRI suggested left parietal infarction, triggering treatment for stroke. Repeat MRI revealed extensive left cerebral hemisphere signal abnormality. A thalamic lesion suggestive of inflammation led to intravenous methylprednisolone therapy. On day twelve, transient behavioural disturbance prompted exploration
for autoimmune aetiologies. High blood/CSF NMDA-R antibody titres were found, and treatment for NMDA-R encephalitis with IVIG, followed by mycophenolate mofetil, commenced. No tumour was identified. At 2 years a right hemisindrome and high antibody titres persisted. MRI showed maturing cortical damage and volume loss. Results: NMDA-R encephalitis, a leading cause of paediatric autoimmune encephalitis, typically presents with behavioural change, language deterioration, autonomic disturbance, seizures and movement disorders. Though previous cases have shown hemi/tetraparesis as a milder, or later feature (Dalmau J et al. Lancet Neurol 2008;7(12):1091-1098), unusually we found dense hemiplegia as a predominant presenting symptom, with associated 'stroke-like' MRI changes. Conversely, behavioural disturbance occurred later and was short-lived. Repeat MRI findings (of both extensive cortical damage and atrophy) are unique. Disease remission was not achieved, necessitating consideration of second/third-line immunosuppressants. Conclusion: The characteristics of this case illustrate the need to consider NMDA-R encephalitis in children with unexplained focal deficits or atypical symptom evolution.

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Immune-mediated disorders

ICNC-0394: B cell, Th17 and neutrophil related cerebrospinal fluid cytokine/chemokines are elevated in MOG antibody associated demyelination

Background: Myelin oligodendrocyte glycoprotein antibody (MOG Ab) associated demyelination represents a subgroup of autoimmune demyelination that is separate from multiple sclerosis and aquaporin-4 IgG-positive NMO, and can have a relapsing course. Unlike NMO and MS, there is a paucity of literature on immunopathology and CSF cytokine/chemokines in MOG Ab-associated demyelination. Aim: To study the differences in immunopathogenesis based on cytokine/chemokine profile in MOG Ab-positive (POS) and negative (NEG) groups. Methods: We measured 34 cytokines/chemokines using multiplex immunoassay in CSF collected from patients with serum MOG Ab POS [acute disseminated encephalomyelitis (ADEM=8), transverse myelitis(TM=2), n=10] and serum MOG Ab NEG [(ADEM=5), (TM=4), n=9] demyelination. We generated normative data using CSF from 20 non-inflammatory neurological controls. Results: The CSF in MOG Ab POS patients showed predominant elevation of B cell related cytokines/chemokines (CXCL13, APRIL, BAFF and CCL19) as well as some of Th17 related cytokines (IL-6 AND G-CSF) in the MOG Ab POS group compared to MOG Ab NEG group (all p<0.01). In addition, patients with elevated CSF MOG antibodies had higher CSF CXCL12, CCL19, IL-17A and G-CSF than patients without CSF MOG antibodies. Conclusion: Our findings suggest that MOG Ab POS patients have a more pronounced CNS inflammatory response, particularly cytokines/chemokines involved in predominantly B cell recruitment, Th17, and neutrophil activation suggesting a differential inflammatory pathogenesis associated with MOG antibody seropositivity. Cytokine/chemokine profiling provides new insight into disease pathogenesis, and improves our ability to monitor inflammation and response to treatment. In addition, some of these molecules may represent potential immunomodulatory targets. Key words: Myelin oligodendrocyte glycoprotein antibody, acute disseminated encephalomyelitis, cytokines, chemokines, autoimmune, demyelination Abbreviations: MOG-Myelin oligodendrocyte antibody, ADEM-Acute Disseminated Encephalomyelitis, TM-Transverse Myelitis, CSF-Cerebrospinal Fluid, Ab- Antibody, POS-Positive, NEG-Negative. References: Dale RC, Neurology(R) neuroimmunology & neuroinflammation. 2014;1(1):e12. Brandes M, International immunology. 2000;12(9):1285-92. Neurath MF, Cytokine & growth factor reviews. 2011;22(2):83-9

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Immune-mediated disorders

ICNC-0395: Acute disseminated encephalomyelitis followed by optic neuritis in a pediatric patient

Introduction: Myelin oligodendrocyte glycoprotein (MOG) is localized at the outermost surface of the myelin sheath and oligodendrocytes in the central nervous system. Autoantibodies against MOG are reportedly found in patients with spectrum of inflammatory demyelinating diseases of the CNS, including acute disseminated encephalomyelitis (ADEM), multiple sclerosis, and neuromyelitis optica. In addition, recent studies have emphasized an association between anti-MOG antibodies and optic neuritis. Case Report: We present the first case report of a 11-year-old Turkish boy who is positive for anti-MOG antibodies. He was diagnosed with ADEM by fulfilling the diagnostic criteria. Magnetic resonance imaging (MRI) revealed T2-hyperintense lesions in the subcortical white matter, midbrain and basal ganglia and there was also enhanced involvement of a cervical lesion extending from C2 to C7. Six months after his diagnosis with ADEM, he developed unilateral optic neuritis (ON). Gadolinium-enhanced MRI of the brain showed thickening and enhancement...
at the right optic nerve from the orbit to the chiasma. Steroid pulse therapy (30 mg/kg/d, in 7 days) followed by one month treatment with oral steroid have given to manage the ON. His visual acuity and his peripheral vision are gradually improved with the treatment. Established cell-based immunoassays revealed that he is positive for anti-MOG antibodies and negative for anti-aquaporin 4 antibodies. Conclusion: This case suggests that the anti-MOG antibody can be associated with the pathogenesis of ADEM followed by ON. Thus, patients with ADEM who are positive for the anti-MOG antibody may be at risk of developing subsequent ON.

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Immune-mediated disorders

ICNC-0397: Guillain-Barré syndrome: Clinical and electrophysiological profile and comparision with Diphtheritic Polyneuropathy in children

Background: Guillain-Barré syndrome (GBS) is most common cause of acute flaccid paralysis worldwide which closely resembles with Diphtheritic Polyneuropathy (DP). The literature concerning GBS and comparision with DP is very scant. Methods: Children aged 2-18 yrs presenting within 4 weeks of onset of illness were included. Detailed clinical assessment were done. Diagnosis of GBS was based on modified Asbury and Cornblath criteria. -1990 and DP was made in patients of polyneuropathy with probable diphtheria within 3 months. Unilateral nerve conduction studies (NCS) done at admission. Functional ability were tested by using GBS Disability score and MRC Sum score at admission and at followup. Results: Out of 50 patients enrolled, 36 were GBS and 14 were DP. Onset of weakness was from lower limb in 30(83%) of GBS while from cranial nerves (bulbar weakness) in 12(85.7%) of DP. At admission loss of ambulation was present in 33/36(91%) GBS patients while 5/14 (35%) of DP patients (p=0.00). Cranial nerve (CN) involvement was present in 24(66%) of GBS [bulbar-24 (66%), facial-9 (25%)] while all DP patients had CN involvement [bulbar(100%), facial-2 (14.3%)] (p= 0.02). Respiratory weakness was present in 12/36(33%) GBS and 3/14(21%) DP, among them 6(16.6%) GBS and 2(14%) DP required mechanical ventilation. On NCS among GBS, AMAN 21(58%), AIDP 13(38%) while in DP 8(57%) were demyelinating, 5(35%) had normal study and one patient had motor axonal neuropathy. MRC Sum Scores at admission, discharge and 3 months follow up were (24, 31.4, 46.8) and (38.4, 42.2, 51.9) in GBS and DP respectively. Conclusion: AMAN (58%) form of GBS is more common in North India.

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Immune-mediated disorders

ICNC-0629: Multiple nerve palsy with coxsackievirus A 16

Introduction: Coxsackievirus A16 is closely related with Enterovirus 71 and they both cause Hand-Foot-Mouth disease. Sometimes, Enterovirus 71 can cause severe neurologic infection, on the other hand, infection with Coxsackievirus A16 is associated with few neurologic complications. Case: We report a case of multiple nerve palsy that was developed in a 14-year-old girl with Coxsackievirus A16. The girl was admitted due to dysphagia, dysarthria, diplopia for 3 days. She had had febrile sense and fatigue, general weakness from 10 days ago. She had taken herbal medicine for 6 days from 9 days ago and stopped it after the neurologic symptoms began. She had no family history with neurologic disease and cardiovascular disease. At admission, she had diplopia with dizziness, difficulty with swallowing water, dysarthria, numbness with the fifth finger and lateral side of left hand. She didn’t have fever. In the neurological exam, CNII, CN VI, CN IX, CN X, CN XII and left ulnar nerve showed abnormal finding. Ophthalmic examination revealed that ice bag test was normal and diplopia was shown when lateral gazed, but there was no pain. The result of laboratory test showed GAD-Ab positive (1.75U/ml) and Anti GM Ig M negative, acetylcholine receptor Antibody negative in blood. CSF exam showed WBC 0 /µl, RBC 0 /µl, Glucose 66 mg/dl, Protein 47.0 mg/dl. She underwent Brain MRI, EMG, NCV, Jolly test, blink test, neostigmine test which were all normal. In VFSS, velopharyngeal function was decreased and incomplete glottis closure was shown in laryngoscopy. Coxsackievirus A16 was detected in stool. She was diagnosed as polyneuritis cranialis due to preceding CA 16 infection. After 5day IVIG injection (0.4g/kg/day for 5day), on 15 day after starting symptoms, dysphagia, dysarthria were improved and discharged. Binocular diplopia had persisted for 21 days and disappeared spontaneously. Conclusion: We report a case of polyneuritis cranialis of multiple nerve palsy with coxsackievirus A 16.

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Immune-mediated disorders

ICNC-0399: Brain lesion load and anatomic distribution in patients with juvenile clinically isolated syndrome predicts rapid conversion to multiple sclerosis

Background: Juvenile clinically isolated syndrome (JCIS) is defined by the onset of neurologically symptomatic suggestive of multiple sclerosis (MS) between 12 to 18 years of age. Objectives: To assess brain lesion load and anatomic distribution in MS patients and define MRI variables associated with rapid conversion to MS. Methods: MRI data were analyzed from JCIS patients at onset. Patients were followed for a year and patients that experienced a second relapse were defined as rapid converters. Parameters were compared between sustained JCIS and rapid converters to MS. Results: 47 JCIS patients, mean age 16±2.7 years, 17 males, 29 females. A year from onset 28 JCIS converted to MS, and 18 remained JCIS. Overall rapidly converted JCIS to MS demonstrated higher number of Fast Falir (FF) lesions (14.59±3.85 vs 5.22±1.34, p=0.0302) and GAD lesion volume (0.52±0.17 cm³ vs 0.05±0.03 cm³; p=0.0056). Looking at lesions distribution in specific brain regions, the number of T2 lesions was higher in the parietal lobe (3.83 ± 1.02 vs 1.5±0.62; p=0.031) and the corpus callosum (0.62±0.13 vs 0.1±0.08; p=0.0072), in rapid converters as compared to JCIS patients. The number of FF lesions in the parietal lobe and the corpus callosum was higher in the rapid converters group. In accordance, the number of GAD positive lesions was higher in rapid converters in the frontal region, temporal region and parietal region. Conclusions: Rapid JCIS converters demonstrated higher lesion load and higher volume of active GAD lesions mainly in the frontal and parietal lobes and in the corpus callosum at disease onset.

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Immune-mediated disorders

ICNC-0400: Panuveitis in Association with Pseudotumor Cerebri

Panuveitis is the inflammation of all layers of the uvea. In this case we report an 5 year old girl who was treated with therapy for pseudotumor cerebri, also had panuveitis. The differential diagnosis for panuveitis is extensive and includes; infectious disease (eg, Lyme disease, syphilis, tuberculosis, toxoplasmosis) autoimmune disease (eg, sarcoidosis, SLE, Behçet disease) and malignant etiologies (eg, leukemia, lymphoma) In the absence of any infectious, autoimmune and malignant etiology, we started steroid treatment. After 5 day treatment her complaints resolved. In this case we suggest that panuveitis may be an associated finding in pseudotumor cerebri. Our purpose for sharing this case with you; panuveitis may be clinical finding of pseudotumor cerebri after eliminating other disease. Keywords: panuveitis, pseudotumor cerebri, steroid

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Immune-mediated disorders


INTRODUCTION: Optic neuritis is defined as a functional disorder of the optic nerve where the main clinical feature is the deficit in visual acuity, pupillary abnormalities and color differentiation. Objective: To describe the clinical features, diagnosis and visual prognosis of patients with optic neuritis treated at Instituto Nacional de Salud del Niño during the period 2003 - 2014. METHODS: Observational, retrospective, longitudinal descriptive study, whose population consisted of 21 Patients diagnosed with optic neuritis in the neurology department of Instituto Nacional de Salud Del Niño during 2003 to 2014. RESULTS: 57% of the cases were males predominante school group 76.19%; the average age of 7.76 years +/- 2.80 years.76.19 % reported a concomitant infectious prior event; The most frequent symptoms were ocular pain (47.52%), discromatopsia (38.10%) with visual acuity counting fingers (42.87%). The compromise was bilateral (85.72 %). 76% had bulbur neuritis with papilledema. Visual evoked potentials showed a demyelinating disorder by 66%, the MRI showed abnormalities in 38% of patients: The visual prognosis was good (normal visual acuity) at 80.95%. 19% of patients presented recurrence, and 42% present in the evolution subsequent acute disseminated encephalomyelitis, none had progression to multiple sclerosis or neuromyelitis optical CONCLUSIONS: The characteristics of optic neuritis in INSN, are similar to those reported in other pediatric studies.Key words: Optic neuritis, acute disseminated encephalomyelitis , multiple sclerosis1. Medico Asistente del servicio de Neurología Instituto Nacional de Salud Del Niño,a. Médico Pediatra.b. Medico Neurológico Pediatra.Neuritis Óptica en Pediatría. Experiencia en el Instituto Nacional de Salud del Niño 2003- 2014.P. Muñoz Huerta1,b, V. Granados Alzamora1,b, J. Montiel Blanco 1,b , I. Caro Khan1,b, D. Koc Gonzales1,b, J. Flores Bravo 1,c, E. Lázaro Ignacio1,a, N. Ramos Timaná 1,a;RESUMENINTRODUCCIÓN: Se define neuritis óptica como una alteración funcional del Nervio óptico donde la característica clínica principal es el déficit en la agudeza visual, alteraciones pupilares y de diferenciación del color, OBJETIVO: Describir las características clínicas, diagnóstico y el pronóstico visual de los pacientes con Neuritis Óptica atendidos en el Instituto Nacional de Salud del Niño durante el periodo 2003 - 2014. METODOLOGÍA: Estudio observacional, retrospectivo, longitudinal descriptivo, cuya población es estuvo constituida por 21 pacientes diagnosticados de neuritis óptica en el servicio de neurología del Instituto Nacional de Salud del Niño durante los años 2003 al 2014. RESULTADOS: El 57% de los casos fueron varones, grupo predominante escolar 76.19%; la edad media de 7.76 años +/- 2.80 años.76.19% del total refirieron
un evento infeccioso previo concomitante; los síntomas más frecuentes fueron dolor ocular (47.52%), discromatopsia (38.10%) con Agudeza visual cuenta dedos (42.87%). El compromiso fue bilateral (85.72%). 76% tenían Neuritis bulbar con papiledema. Los Potenciales Evocados visuales mostraron una alteración desmielinizante en un 66%, la Resonancia Magnética mostro alteraciones en un 38% de pacientes: El prónóstico visual fue bueno (agudeza visual normal) en el 80.95%. 19% de pacientes cursaron con recurrencia, y el 42% presento en la evolución una encefalomieliitis disminuida aguda posterior, ninguno presentó evolución hacia esclerosis múltiple o Neuromielitis óptica.

CONCLUSIONES: Las características de la neuritis óptica en el INSN, son similares a las publicadas en otros estudios de población pediátrica. 

Palabras Clave: Neuritis óptica, encefalomieliitis disminuida aguda, esclerosis múltiple.

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Immune-mediated disorders

ICNC-0402: New outcome measures in pediatric acquired demyelinating syndromes

Introduction: Pediatric acquired demyelinating syndromes (ADS) including multiple sclerosis (MS) are associated with a wide range of symptoms. Clinical trials in pediatric-ADS use traditional measures including the Expanded Disability Status Scale (EDSS), rarely useful early in the disease. Adult clinical trials have started using disease specific quality of life (QOL) measures such as the MS Impact Scale (MSIS-29). No disease-specific QOL pediatric outcome measures have been evaluated. Similarly, there is limited data on adaptive behavior functioning determining how children with ADS respond to daily demands. We aimed to test the utility of new parent-report MSIS-29 outcome measures. Methods: The new parent-report MSIS-29, generic Pediatric QOL Inventory (PedsQL), and Adaptive Behavior Assessment System (ABAS) were completed, 6 months after ADS onset as part of a multicentrenational prospective study. Cases were followed up for 2 years to establish diagnosis. Item analysis was carried out by fit to the Rasch model. Results: Data for 37 cases (median age=11 years [5-18]) were available. Mean ABAS conceptuale and social scores were low (76.2 [SD 21.5]; 77.6 [SD 20.3]). The MSIS-29 correlated well with the PedsQL. Rasch analysis showed support for the psychometric properties of the MSIS-29 physical (item mean squarefit=0.97; item reliability=0.63); and the PedsQL-psychosocial domains (item mean squarefit=1.04; Item reliability=0.82). 15/15 PedsQL-psychosocial and 18/20 MSIS-29-physical items had good item fit stats. Analysis did not support the MSIS-29-psycho social and PedsQL-physical domains. Conclusion: We propose use of a composite measure of MSIS-physical, PedsQL-psycho social, and adaptive functioning domains as primary outcomes in future studies.

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Immune-mediated disorders

ICNC-0404: Pediatric multiple sclerosis (MS) is well-studied clinically and radiologically, but age-related characteristics are not well described in early-onset groups

Background Pediatric multiple sclerosis (MS) is well-studied clinically and radiologically, but age-related characteristics are not well described in early-onset groups. Objectives To assess the characteristics of MS starting before 12 years old in Turkey. Methods Demographic, clinical and neuroimaging data of patients with MS starting <12 years of age were retrospectively reviewed in a multicenter (25 centers) cohort. Results Among total 188 patients in the pediatric MS database, 54 (28%) (23 boys, 31 girls) had onset <12 years of age. Mean age of onset was 9.6 (4 to 11); mean follow-up, 2.9 years. Time to second attack ranged from 0.3 to 5 years. Three patients (5%) had a family history, and 17 (31%), an antecedent infection before the first attack. Initial clinical signs were monofocal in 21 and polyfocal in 33 patients. Brainstem involvement, motor weakness, and cerebellar findings were at similar frequency (38, 35 and 33% respectively). Lesion distribution on MRI was supratentorial in 98%, periventricular in 83%, and spinal in 59% patients. An elevated IgG index and/or presence of CSF oligoclonal bands were found in 34/46 patients (73%). EDSS score was recorded in 30 patients at latest follow-up; all were <3, except three patients whose scores were >4 at 1, 3, and 5 years follow-up. Discussion Although some patients developed disability at 1-5 years of the disease, most cases of childhood-onset MS in Turkey have a relatively mild course in the first decade.
Immune-mediated disorders

ICNC-0405: Posterior Reversible Encephalopathy Syndrome as clinical manifestation of CNS involvement in Henoch-Schonlein Purpura in children

CNS involvement in Henoch-Schonlein Purpura (HSP) is rare but poses diagnostic difficulties. CNS involvement could be as vasculitis or Posterior Reversible Encephalopathy Syndrome (PRES) as a result of systemic disease, especially with arterial hypertension. PRES is a clinicoangiographical syndrome (a unique presentation of vasogenic cerebroedema) which presents with headache, visual disturbances, seizures, altered consciousness, focal neurological deficit. We present a case with HSP manifested as PRES. It comprised 0.9% of all HSP cases, treated in our Department of Pediatrics for 5-year period. The case was an 8-year-old girl with atypical HSP which started with abdominal pain requiring surgery. On the third day after the operation a transient macular rash appeared, followed by visual disturbances, right-sided hemiconvulsive epileptic seizures with post-ictal hemiparesis and confusion. There was transient arterial hypertension. Head CT showed occipital hypodense lesions, and MRT - a T2 hyperintense lesion in the left occipital lobe. EEG showed slow-wave activity in the left parieto-occipital region. There was a second episode of similar neurological symptoms in 2 weeks and then palpable purpura appeared. On follow-up at 1 month – no abnormal signs and symptoms, on EEG the slow-wave activity had disappeared. CNS involvement may be a result of CNS vasculitis or arterial hypertension. In conclusion, although neurological complications are rare in HSP clinicians must be aware of them and avoid diagnostic and therapeutic delays. HSP can be the etiological factor for PRES in childhood, and MR DWI should be preferred method for diagnosing PRES.

ICNC-0406: Clinical profile and outcome of Anti-NMDAR Encephalitis -Series of 25 children, A multi-center study from India

Introduction: Anti NMDAR encephalitis is a treatable cause of encephalopathy, with increasing incidence. We report 25 children with Anti-NMDAR encephalitis. Methods: Twenty five children were diagnosed anti-NMDAR encephalitis between January 2012 and September 2015. Other workup including EEG, neuroimaging, CSF viral studies and autoantibodies antibodies was done. Clinical severity was assessed using the Glasgow outcome scale. Results: Sixty percent of the children were <5yrs (median age of 60 months), with girls being 60%. The presenting complaints included seizures (23/25) and behavioral abnormalities (17/25). Clinical course evolved in to stages of encephalopathy, mutism and movement disorder. Speech disturbance was present in all, while involuntary movements in 23. Perioral dyskinesia and choreathetoid movements in 17 as combination. In 3 cases, HSV infection preceded Anti-NMDAR encephalitis. MRI brain showed cortical atrophy in three, subcortical T2 hyper intensities in two and right occipital gliosis in one. EEG showed diffuse cerebral dysfunction in cases. Immunotherapy with steroids or IVIG was given to all except one who improved spontaneously, while 19/25 received Rituximab and 3 children received Cyclophosphamide. 24/25 children received antiepileptics. 24/25 children survived and on follow-up, 18 children had good recovery, based on the Glasgow outcome scale. 2 children died cause of death being autonomic instability. Conclusion: High index of suspicion and early diagnosis of anti-NMDAR encephalitis is critical for better outcomes. Majority of children did not respond to Corticosteroids and/or IVIG. There is a need for better immunomodulatory drugs with quicker onset of action. Refractory seizures and severe autonomic disturbances may carry poor prognosis.

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Immune-mediated disorders

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Immune-mediated disorders

ICNC-0408: Anti-Mog detected in a paediatric case of raised ICP and optic neuritis
Background: MOG (myelin oligodendrocyte glycoprotein) is a transmembrane protein expressed on the surface of oligodendrocyte cells and myelin sheaths. Antibodies to MOG have been implicated in MS, ADEM (1), NMO spectrum disorders, transverse myelitis and optic neuritis. There have been reported cases in Japan of MOG-positive optic neuritis responding to immunotherapy, but with evidence of CNS inflammation on neuroimaging (2). Case report: AT is a 10 year old girl. She presented with headache, vomiting and blurred vision. Lumbar puncture demonstrated raised intracraniel pressure with an opening pressure of 51cm3 H2O. She was positive for anti-MOG. There was a progressive reduction in visual acuity. At the time of presentation her visual acuity was 6/6 but subsequently reduced to 6/60 with an enlarged blind spot. There was slowing of her VEP suggesting retrobulbar nerve pathology. MRI brain, spinal cord, and MRV were all normal. Treatment with 2 courses of steroids and Acetazolamide had minimal effect on her symptoms. She was commenced on Topiramate to manage her headaches. Following a single course of IVIG her symptoms resolved. There was resolution of her visual disturbance, improvement of visual acuity, and normalisation of colour vision. Acetazolamide and Topiramate have been successfully weaned. Discussion This case describes the presence of anti-MOG antibodies with clinically significant raised intracraniel pressure in the absence of any neuroimaging evidence of demyelination. Knowledge of the antibodies guided us towards immune treatment. Testing for anti-MOG should be considered in cases of optic neuritis even in the presence of a normal neuroimaging. (1) Hupkpe P, Rostasy K, Karenfort M, Hupkpe B, Seidl R, Leiz S, Reindl M, Gartner J. Acute disseminated encephalomyelitis followed by recurrent of monophasic optic neuritis in pediatric patients. Multiple Sclerosis. Jun 2013; 19(7):941-6. (2) Tsuburya RS, Miki N, Tanaka K, Kageyma T, Irahara K, Mukaida S, Shiraishi K, Tanaka M. Anti-myelin oligodendrocyte glycoprotein (MOG) antibodies in a Japanese boy with recurrent optic neuritis. Brain & Development. Jan 2015; 37(1):145-8.

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Immune-mediated disorders

ICNC-0409: Double trouble: A stiff baby with Guillain-Barré Syndrome associated with GAD autoantibodies
Introduction:Guillain-Barré Syndrome (GBS) is typified by weakness, areflexia and elevated CSF protein. We present a unique case with severe pain, opisthotonos and positive anti-glutamic acid decarboxylase (GAD) antibodies, leading to a concurrent diagnosis of stiff person syndrome (SPS).Case:A previously healthy 17 month old developed lethargy and reluctance to sit. MRI brain and spine, serum inflammatory markers and CSF results were unremarkable. His symptoms evolved to pain on truncal flexion and areflexia without significant weakness. Whole body MRI, septic, neurometabolic and vasculitis screening were negative. Week three CSF showed raised protein and positive oligoclonal bands. Intravenous immunoglobulin (IVIG) was given but he worsened with severe opisthotonos. Repeat MRI brain and spine remained normal. Nerve conduction studies confirmed sensory motor demyelinating polyneuropathy consistent with GBS. GAD autoantibody levels were significantly elevated. He improved after a second dose of IVIG alongside multimodal analgesia and rehabilitation. Discussion:Opisthotonos is poorly described in GBS. Although other features point towards a demyelinating polyneuropathy, an additional diagnosis should be considered when opisthotonos is present. SPS is an autoimmune condition characterised by muscle stiffness, painful spasms and GAD autoantibody positivity. Axial forms can present as opisthotonos and positive oligoclonal bands have been reported. SPS is associated with other autoimmune disorders such as diabetes mellitus and thyrotoxicosis, although its association with GBS has not previously been described.Conclusion:SPS should be considered when a child is found to have a diagnosis which does not clearly explain opisthotonos. Anti-GAD antibody levels should be measured in this instance.

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Immune-mediated disorders

ICNC-0412: Pediatric relapsing CNS Demyelinating disease associated to MOG ABS
INTRODUCTIONMyelin oligodendrocyte glycoprotein antibodies (MOG-Abs) are associated to a wide spectrum of central nervous system demyelinating diseases, and have been reported at presentation in up to 35% of patients with childhood acquired demyelinating syndrome. MOG antibody has functional effects on oligodendrocyte cytoskeleton.AIM: to report a pediatric patient with relapsing CNS demyelinating disease associated to MOGAbs.CASE DESCRIPTION Six year-old boy, that following a prolonged febrile syndrome, developed multifocal neurological symptoms. Initial Brain MRI: Normal. Laboratory findings with progressive increase of acute phase reactants and CSF hypercellularity. Evolutive course,
appearance of CNS inflammatory images in MRI with abnormal VEP. Excellent steroid response. Asymptomatic during a year, presents with clinical and imaging relapse after infectious disease. Complete recovery after high dose steroid treatment. Negative Aq4 Abs and oligoclonal bands, positive MOG-Abs. Currently in remission with low titers of serum MOG-Abs and acute phase reactants. CONCLUSION As it has been previously reported in literature, the relapsing, steroid responsive and relapsing status epilepticus disease seen in our patient, didn’t have specific clinical or radiological features to distinguish from seronegative cases. Even though MOG-Abs. are still discussed as aseful biomarker in clinical practice, high MOG-IgG levels are promising candidates for the prediction of treatment responsiveness and a decrease in antibody titers might indicate an association with a favorable clinical outcome and remission.

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Immune-mediated disorders
ICNC-0413: Retrospective analysis of Pediatric Guillain-Barré Syndrome patients
Guillain-Barré syndrome (GBS) is characterized by symmetric weakness and areflexia. Severity is assessed by the Hughes scoring system. We present a retrospective analysis of our GBS patients (n=42, M/F:20/22, age median 8.2, range 0.16-16 years). Symptom duration was 4 (1-30) days. June was the most common month of presentation (n=6). Preceding infections were upper respiratory (n=22), gastrointestinal (n=12), urinary (n=3), and unreported (n=4). One had antecedent vaccination. Initial symptoms were paraparesis (n=12), tetraparesis (n=16) and tetraparesis+bulbar symptoms (n=14). Sensory symptoms were present in 11, cranial nerve dysfunction in 10, sphincter failure in two, need for mechanical ventilation in 7 patients. Electroneuromyography was performed in 35 patients: 18 had demyelinating, 14 axonal and 3 unclassified pattern. Axonal injury was defined as motor in 10, motor and sensory in three and unclassified in another patient. Cerebrospinal fluid (CSF) of 35 patients showed normal or increased protein (range 18-460, median 75 mg/dL). Of the CSF analyses done after day three, 85% showed elevated protein. All patients except one with spontaneous recovery received IVlg. Five patients also had plasma exchange, and one, pulse steroid. Hospitalisation lasted median 7.5 (3-100) days. One patient was deceased. Median Hughes score was 4 (2-5) at presentation, 2 (1-6) at discharge and 2 (0-4) at 1st month. Of those who had 6-month follow-up, 78% had completely normal neurological examination. Although GBS is the most common cause of acute flaccid paralysis in childhood, the outcome, as shown in our series, is good with low mortality and no or mild sequelae.

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Immune-mediated disorders
ICNC-0855: Responsiveness of high dose of phenobarbitone in refractory status epilepticus associated with autoimmune encephalitis –associated with antiNMDAR encephalitis-A study of 7 cases
Summary: Autoimmune encephalitis associated with antibodies against the N-methyl-D-aspartate (NMDA) receptor is usually associated with refractory recurrent status epilepticus and neuropsychiatric manifestations. Key words: Autoimmune encephalitis, Phenobarbitone
Objectives: To study the variable presentations of autoimmune encephalitis
To study the responsiveness of various antiepileptic drugs
To study the responsiveness of phenobarbitone in refractory status epilepticus
METHOD: Total 7 patients were enrolled in a span of 1 year. (2013-2014). They were diagnosed on the basis of clinical presentations of autoimmune encephalitis- seizures, orofacial dyskinesias, choreoathetosis and neuropsychiatric manifestations in a previously symptom free child. All patients had previous short febrile illness. They were initially diagnosed based on characteristic clinical features which were further confirmed by measuring the level of CSF IGA- NMDA antibodies. The patient who had refractory status epilepticus was given a high dose of phenobarbitone 60 mg/kg followed by 20 mg/kg 12 hourly (blood level 40 microgram/dl) with immunosuppressive therapy. This led to seizure free outcome. All subsequent patients were given 20 mg/kg of phenobarbitone at the onset of disease within a week. Results: The onset and clinical presentations of NMDA encephalitis were typical. All patient responded to phenobarbitone and were maintained on that for 1 year. They were seizure free with some irritability but without untoward reaction. Conclusion: Autoimmune encephalitis is a well known entity with recent recognition of various antibodies. Early diagnosis and immunosuppressive therapies may lead to good outcome. Use of age old drug like phenobarbitone in a very high dose would lead to early seizure free outcome if used at the onset or in refractory status epilepticus.

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Immune-mediated disorders

**ICNC-0952: Opsoclonus myoclonus Syndrome in children with neuroblastoma**

Introduction: Opsoclonus myoclonus syndrome (OMS) is a rare paraneoplastic syndrome associated with neuroblastoma (NB) in 50-80% of cases. The aim is to provide an overview of the experience of the two federal medical centers in Russia in treating patients with NB and OMS. Methods: 19 patients with NB associated with OMS were included for the period 01.2012-05.2015 (41 months). Neurological status has been evaluated by two neurologists in both centers. The diagnosis has been established on the basis of international criteria of OMS. The diagnosis of NB has been confirmed by histological examination in all cases. Results: Male: female ratio was - 1:2.8. The median age at the diagnosis of OMS and NB was 16.6 months (range 14.9-54.0). The median time from the appearance of the first neurological symptoms till the diagnosis of NB was 2.9 months (range 0.7-28.0). The tumor sites were distributed as follows: retroperitoneum - 11 (57.8%), posterior mediastinum - 6 (31.6%), adrenal gland - 1 (5.3%), pelvis - 1 (5.3%). Paravertebral location was noted in 15/19 (78.9%) cases. Most tumors were small (median volume - 6.5 ml (range 0.4-80.9 ml). In 11/19 (58.0%) patients the tumor was visualized only by CT/MRI. Increased neuron specific enolase was observed in 1/19 (5.3%) case. Scintigraphy with metaiodobenzylguanidine (MIBG) was positive in only 9/17 (53.0%) cases. Conclusion: CT and/or MRI are the most informative diagnostic methods to detect tumors in patients with OMS given the small size, location and low metabolic activity of NB.

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**Immune-mediated disorders**

**ICNC-0416: Childhood Anti-NMDA receptor encephalitis: A report of six cases**

Background: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an important and potentially treatable cause of autoimmune encephalitis in pediatric age group. There are only a few reports describing clinical features, management and outcome of children with anti-NMDAR encephalitis from India. Objectives: To study the clinical profile, therapeutic approach and outcome of children with anti-NMDAR encephalitis. Methods: Retrospective case series of children <12 years of age diagnosed with anti-NMDAR encephalitis from a tertiary care institute during the period May 2013 to June 2015. Results: We tested 20 patients for suspected anti-NMDAR encephalitis over this 2 year period. Of these, six children were positive for anti-NMDAR antibodies. Four of these six children had completed treatment and two are currently receiving immunotherapy. Behavioral changes, psychosis, seizures and oro-lingual-facial dyskinesia were the presenting features. Extreme irritability, insomnia and mutism were noted in all children. The symptoms were persistent, and the course was progressive over 4-8 weeks duration. Neuroimaging and electroencephalography were non-specific. Intravenous pulse methylprednisolone and immunoglobulins were used as first-line therapeutic agents. Only one patient responded to first line immunotherapy; five out of six children required second-line immunotherapy. One patient recovered following rituximab, and two patients showed a good response to cyclophosphamide pulse therapy, two patients are currently under treatment with second line immunotherapeutic agents. Tumour screen was negative in all children. Conclusion: Anti-NMDAR encephalitis is rare but a potentially treatable condition. Timely recognition is essential because treatment is entirely different from other viral encephalitis. Aggressive immunotherapy is the key to favourable outcome. Acknowledgement: The authors wish to thank Dr. Josep Dalmau, (ICREA Senior Investigator, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clinic, University of Barcelona, Spain) for his support in testing the samples.

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A rare presentation of isolated oculomotor nerve palsy due to multiple sclerosis in a child

Introduction Demyelinating disorders of the CNS cause acute or relapsing-remitting encephalopathy and other multifocal signs of brain, brainstem, and spinal cord dysfunction. Multiple Sclerosis (MS) is being frequently diagnosed and it forms the differential diagnosis of many myelopathies. Here we report the rare clinical manifestations of multiple sclerosis such as isolated oculomotor nerve palsy in a child. Case Report A 10 year old boy presented with complained of sudden onset drooping of eyelid. Three weeks before admission, ptosis of the left eyelid developed and during the next few days right eyelid ptosis developed as well. Examination of eye revealed ptosis, associated with medial gaze restriction. The result of extraocular muscle examination demonstrated bilateral adduction palsy, impaired upward and downward deviation, and bilateral ptosis (Figure 1). Abduction was bilaterally intact. Bilateral papillary sizes were equal, as were bilateral responses to light. There was no nystagmus and other extraocular movements were normal. Other system examination revealed no abnormality. On investigations, complete blood cell was normal. Chest X-ray revealed normal lung fields. Cerebrospinal fluid examination revealed normal protein (28 mg/dL) and sugar (67mg/dL), with 3 lymphocytes and no polymorphonuclear cells on cytology. Nerve conduction study was normal. MRI brain revealed area of altered signal intensity involving mid brain and pons appearing iso intense on T1W1 and hyperintense on T2W1 suggestive of demyelination. Oral steroid was given for 5days. His cranial nerve palsy right sided slightly improved before discharge.

Immune-mediated disorders

ICNC-0804: A rare presentation of isolated oculomotor nerve palsy due to multiple sclerosis in a child

ICNC-0417: Outcome in infectious and immune childhood encephalitis is better defined by clinical course rather than aetiology

Immune-mediated disorders

ICNC-0418: Anti-GAD antibody associated encephalopathy in a major University hospital in Taiwan: what is the role of anti-GAD antibody?
Immune-mediated disorders

ICNC-0420: A case of Fisher-Bickerstaff Syndrome overlapped by Guillain-barré Syndrome

Bickerstaff brainstem encephalitis (BBE) including ophthalmoplegia, ataxia, consciousness disturbance or hyperreflexia has been considered a monophasic which can affect santral nervous system with peripheral nervous system. Whereas Fisher syndrome has been regarded as a inflammatory neuropathy with ophthalmoplegia, ataxia and areflexia. Both disorders share common features including preceding infection, albumin-cytological dissociation, good spontaneous recovery and association with Guillain-Barré syndrome. Although the exact etiology of BBE is unknown, it is thought to be a process of an autoimmune mechanism. Thelesions in Fisher syndrome and Bickerstaff brainstem encephalitis are presumably determined by the expression of ganglioside GQ1b in the human peripheral and central nervous systems. There are limited number of studies indicating the benefits of plasmapheresis, IV immunoglobulin and corticosteroids treatment. A 6 year old girl was admitted to hospital because of fever and gait difficulties. On neurological examination, she had confusion, internal ophthalmoplegia, areflexia, muscle weakness, and abnormal sensations for pain. On the 3rd day, she was comatose. Albuminocytological dissociation was present in CSF, and the IgG anti GQ1b antibodies was negative serologically. Cranial and spinal magnetic resonance imaging were normal. The case was almost completely cured with intravenous immunoglobulin and high dose methylprednisolone for 5 days followed by a taper of oral prednisolone. She showed dramatic response. The clinical progress, electrophsiological findings and treatment results of a case of BBE with central and peripheral involvement was presented and discussed due to its rare incidence.

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Immune-mediated disorders

ICNC-0421: Acute Necrotising Encephalitis associated with endocardial fibrosis in two siblings

Acute necrotising encephalitis is a rare but deadly condition characterized by rapidly evolving encephalopathic state and accompanying classical neuroimaging findings. This is postulated to be related to a massive release of cytokines which is indicated as a “cytokine storm”. We report on two siblings who suffered from acute necrotizing encephalitis concomitantly and both were found to have endocardial fibrosis. This association has not been described before. Case history A 7 year old girl developed acute encaphopathic state with rapid deterioration and convulsive status following a viral fever. She remained in coma over next three days followed by death. Her CT brain showed hyperdensities involving the white matter of the external capsules bilaterally and bilateral pons in a fairly symmetrical distribution. Her postmortem confirmed evidence of patchy haemorrhagic encephalitis involving most of the cortex and the white matter. Her endocardium and some areas of the myocardium was found to have macroscopic evidence of thickening and fibrosis. This was confirmed histologically. Her 18 month old sibling also presented with mild initial fever followed by rapid deterioration with coma and several focal seizures. Considering the sibling’s clinical and radiological findings, he was immediately treated with high dose methyl prednisolone and intravenous IVIG concomitantly. This was followed by several cycles of plasma pharesis. The CT brain revealed identical imaging findings to that of the sister. He showed very slow improvement over next 8 weeks to eventually achieve his premorbid developmental status. Both siblings did not have any proven viral aetiology to explain the clinical presentation. The brother’s echocardiography also showed evidence of similar endocardial fibrosis which progressively improved with time. This is the first documentation of involvement of endocardium in association with acute necrotizing encephalitis.

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Immune-mediated disorders

ICNC-0415: Cytokine and chemokine expression in CSF differentiate viral and autoimmune NMDAR encephalitis in children

Introduction: Childhood encephalitis is a potentially devastating condition with significant morbidity and mortality. We currently lack biomarkers for differentiating encephalitis of infectious origin from those with autoimmune causes which may delay adequate treatment. Methods: We studied the possibility of using cerebrospinal fluid cytokine and chemokine levels for this purpose. Children admitted to hospital care fulfilling criteria for encephalitis were prospectively included. Children that underwent lumbar puncture but were not classified as CNS infections served as controls. Cytokine- and chemokine-levels in the CSF obtained upon initial presentation were analysed using Luminex technology. Results: In
children with infectious encephalitis (n=13), the CSF displayed markedly elevated levels of IL6, IL7 and IL13 as compared to NMDAR encephalitis (n=4) and controls (n=13). The expression of IL6 appeared to precede that of IL13. A cutoff for IL6 at 100 pg/ml identified all infectious cases and gave no false positives in the NMDA group, whereas a cutoff for IL13 at 100 pg/ml failed to identify 5/13 infectious cases. The combination of IL6 over 100 pg/ml or IL13 over 100 ng/ml identify 100% of the infectious cases, and did not give any false positives in the NMDA group.

Discussion: Analysis of selected CSF cytokines allows differential diagnosis of infectious and NMDAR encephalitis already at the initial lumbar puncture, and hence enables immediate therapy.

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**Immune-mediated disorders**

**ICNC-0422: Antibody-associated encephalitis in children; a series from a single center**

Introduction: Antibodies (Ab) against neuronal surface proteins, N-methyl-D-aspartate receptor (NMDAR) and subunits of the voltage-gated potassium channel complex (VGKC), are being detected in children and adults with encephalitis. Because these cases are potentially treatable and early treatment affects outcome, it is important to consider Ab-associated encephalitis in any case a typical for acute viral encephalitis. We present our cases with Ab-associated encephalitis.

Method: Patients (n=19) with anti-NMDAR or anti-VGKC complex antibodies diagnosed in our department were retrospectively reviewed for clinical findings, seizure type, EEG, MRI, cerebrospinal fluid (CSF) findings, treatment and outcome.

Results: Ten patients were female, nine male, median age 9 years (6 months-18 years). Eleven patients had NMDAR, eight had VGKC-complex antibodies. Fifteen patients presented with seizures which were focal, secondary generalized or generalized tonic-clonic seizures. Other clinical findings were encephalopathy (n=16), neuropsychiatric symptoms (n=13), abnormal movements (n=9), fever (n=7) and autonomic dysfunction (n=4). Five patients had increased protein or cells in the CSF. MRI was abnormal in 7 out of 19 patients: findings increased T2 signal in the mesiotemporal lobe, gliosis, loss of cerebral volume. Immunotherapy was given to seventeen patients: intravenous immunoglobulin, intravenous pulse methylprednisolone, oral steroid, rituximab, azathioprine, ACTH and plasmapheresis.

Conclusion: The diagnosis of anti-NMDAR and VGKC-complex encephalitis requires a high index of suspicion. Patients presenting with subacute onset, seizure, encephalopathy, neuropsychiatric findings and abnormal movements should be evaluated for Ab-associated encephalitis. On the other hand fever is less common presenting symptom in Ab-associated encephalitis than viral encephalitis.

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Infectious diseases

ICNC-0424: Acute viral encephalitis in a tertiary government hospital 2011-2014: clinical profile and outcome using modified rankin scale

Objective: To determine the clinical profile and outcome of patients with acute viral encephalitis syndrome admitted from January 2011 to December 2014. Design: Retrospective descriptive study Methods: All pediatric patients who were admitted with a final diagnosis of acute encephalitis syndrome (AES) were included. Demographic information, presenting signs and symptoms and results of viral studies were collected. The outcome was determined using the Modified Rankin Scale. The clinical outcomes of patients were compared using median test and analyzed. Results: There were 64 medical records retrieved. The highest number of cases was seen in the 1 to 4 years age group with 21 (32.81%) and in males (68.75%). New onset seizure was the most frequent presentation. There were 11 patients (17.19%) that tested positive for Japanese encephalitis virus, 9 (14.06%) for Dengue virus and 6 (9.37%) for Herpes simplex virus. Eighteen patients had negative viral studies. The modified Rankin scale showed 41 (64.08%) had good outcome while 23 (35.23%) had poor outcome. There was no significant difference in the modified Rankin scale between the two groups. Conclusion: Acute viral encephalitis syndrome has a wide-spread distribution mostly on seen on males and 1-4 years age group. Majority had good neurological outcomes. There was no significant difference in the modified Rankin scale of patients with Japanese encephalitis and other etiologic agents. However, the results are based on a small sample size and larger studies involving a greater number of patients are needed before definite conclusions can be made.

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ICNC-0425: Herpes simplex encephalitis presenting with acute retinal necrosis: a rare case report

Introduction: Acute retinal necrosis is rare entity characterized by substantial ocular inflammation with progressive retinal necrosis, occlusive vasculitis and sometimes extraocular features. Concurrence of acute retinal necrosis with herpes simplex encephalitis is associated with an even more lower incidence especially in childhood. Case: The present study describes such a rare case of this concurrence, in which a four years old girl presented with decreased vision in the right eye. Ophthalmological examination revealed a profound visual loss due to extensive retinal necrosis. Two days after the initial symptoms, she developed encephalopathy and her neurological examination revealed nuchal rigidity, dysmetria and decreased strength, sensation, and proprioception of the right upper extremity. Brain magnetic resonance imaging (MRI) demonstrated multiple left temporoparietal enhancing lesions. Immediate acyclovir treatment was initiated and was lasted for for three weeks. Acute retinal necrosis with meningoencephalitis caused by herpes simplex virus type 2 was confirmed by PCR studies performed on cerebrospinal fluid. After the treatment, Although the neurological condition improved, vision in the right eye deteriorated. Discussion: A literature search showed only a few case reports of herpes simplex encephalitis presenting with acute retinal necrosis in children have been reported to date.

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ICNC-0427: Neuroborreliosis: A rare case report

An 8-year-old girl patient applied to our hospital with the complaints of vomiting, high fever and headache, although she had no complaint before. There was no significant feature in her blood tests. Lumbar punction was performed because high temperature source was not known. In cerebrospinal fluid (CSF) examination, 25x10 cells were seen in every area. Ceftriaxone and acyclovir were started by considering meningitis. In the cranial and spinal magnetic resonance imaging (MRI), at the level of bilateral brainstem, cerebellum and spinal cord, acute disseminated encephalomyelitis (ADEM)?, demyelinating pathology? were reported as infectious findings. IVIG treatment was initiated for the patient's ADEM clinic. CSF culture were sterile. CSF herpesvirus PCR was negative. Acyclovir was discontinued. Borrelia burgdorferi serology analyzed with western blot method, and whose IgM antibody turned out positive. Ceftriaxone treatment of the patient was completed in 21 days. As there was an increase in the involvements at the level of brainstem and cerebellum in the MRI taken for the patient’s control whose clinic recovered after the treatment, one more cure of IVIG and simultaneous steroid treatment was supplied to the patient. In the follow-up MRI control taken after one week, a remission was seen in the lesions. After the MRI findings were detected to be polyphasic and the lymph serology turned out to be positive, the patient was diagnosed as neuroborreliosis. In conclusion, the purpose of this case report is to emphasize the need to bear neuroborreliosis in mind in patients presenting with noncharacteristic symptoms and neurological manifestations. Keywords: Child, Borrelia burgdorferi, Neuroborreliosis.

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ICNC-0428: Activation of the TLR2-mediated downstream signaling pathways NF-κB and MAPK is responsible for B7-H3-augmented inflammatory response during S. pneumoniae infection

Introduction Pneumococcal meningitis remains a life-threatening infectious disease, and causes death in approximately 25% of cases, and neurological sequelae in nearly half of survivors. Most of cases are children. B7-H3 has been shown to play a contributory role in the development and progression of experimental pneumococcal meningitis by augmentation of the innate immunity-associated inflammatory response via a TLR2-dependent manner. Methods This study attempted to clarify the component(s) of TLR2-mediated signal transduction pathways responsible for B7-H3-augmented inflammatory response during S. pneumoniae infection. Both murine microglial cell line N9 cells and primary murine microglial cells were stimulated with S. pneumoniae alone or in combination with B7-H3. TLR2 mRNA was measured by Quantitative real-time RT-PCR. TLR2 expression and Phosphorylation of NF-κB p65, MAPK p38, ERK1/2, and c-Jun were determined by FACScan analysis. The concentrations of proinflammatory cytokines TNF-α, IL-6 and chemokine MCP-1 were assessed by ELISA. Conclusion/Discussion Although B7-H3 failed to further enhance S. pneumoniae-upregulated mRNA level and surface expression of TLR2, it strongly augmented S. pneumoniae-induced phosphorylation of NF-κB p65, MAPK p38, and MAPK ERK1/2 in both N9 cells and primary microglial cells. Notably, B7-H3 itself did not activate either NF-κB p65 or MAPK p38 and ERK1/2. Furthermore, Deactivation of NF-κB p65, MAPK p38, and MAPK ERK1/2 with their specific inhibitors substantially attenuated B7-H3-amplified proinflammatory cytokine and chemokine release from S. pneumoniae-stimulated primary microglial cells. These results indicate that activation of both NF-κB and MAPKs is predominantly responsible for B7-H3-augmented inflammatory response during S. pneumoniae infection. Acknowledgements this study was supported by grant from the National Natural Science Foundation of China (No. 81273242)

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Infectious diseases

ICNC-0429: Steroids use in the treatment of children with Herpes Simplex Virus Encephalitis (HSVE): a case series and review of the literature

Objective: HSVE in children is a serious intracranial infectious disease, with poor prognosis for most patients. The role of Steroids in the treatment of herpes simplex virus encephalitis (HSVE) in children is controversial. This study evaluates if steroids are useful in the treatment of children with HSVE. Methods: 15 children aged from 5 months to 11 years old (12 males, 3 females) with HSVE received glucocorticoid treatment. Intravenous methylprednisolone (1-2 mg/kg/d) was given in 9 cases, intravenous dexamethasone (0.3-0.5 mg/kg/d) was given in 3 cases, and oral methylprednisolone (20 mg/kg/d) was given in 3 cases. In each case, the dose of intravenous methylprednisolone was reduced every 2-3 days, switched to oral prednisone, and tapered within a week. Results: The average length of stay was 30.8±14.664 days. Patient’s temperatures normalised within 3-5 days after steroid use. All patients were followed up for more than 6 months. 4 of the 15 children recovered completely without any neurological deficits, while 11 children (73.33%) had different degrees of CNS sequelae: 10 children (66.66%) had motor deficits, 10 children (66.66%) developed epilepsy, and 6 (40.00%) of which developed intellectual impairment. Compared to the mortality rate of 15-20% from HSVE reported in the literature, no deaths were observed in this study. Complications such as infections or disease relapse were not seen during follow ups. Conclusion: Our data shows that use of steroids did not result in disease relapse and there were no apparent complications due to steroid treatment. Steroids are useful in the combined treatment of children with HSVE. Acknowledgements this study was supported by grant from the National Natural Science Foundation of China (No. 81273242)

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Infectious diseases

ICNC-0430: Non-typhoidal salmonella encephalopathy treated successfully with methylprednisolone pulse therapy

Introduction: Non-typhoidal salmonella infection generally causes a self-limiting diarrhoeal illness in healthy children but encephalopathy may occur rarely. Non-typhoidal salmonella encephalopathy can result in severe neurological sequelae and currently treatment is generally empiric. This study was to report an experience of successful non-typhoidal salmonella treatment using methylprednisolone pulse therapy. Method: We reviewed pediatric patients who presented with non-typhoidal salmonella in a tertiary referral hospital during August 2013 to August 2015. We collected clinical, laboratory, electroencephalographic and microbiological features of consecutive patients with non-typhoidal salmonella encephalopathy and compared the treatment and outcomes. Result: Three boys aged 11-month, 15-month and 36-month respectively, presented with complex febrile seizures. Two patients were admitted to intensive care unit due to severe encephalopathy. Extensive infectious pathogen investigation for virus, bacteria and mycoplasma pneumonia were negative in cerebrospinal fluid and blood but non-typhoidal salmonella was isolated from stool samples in the acute phase. The brain magnetic resonance images were unremarkable while their electroencephalogram disclosed bilateral focal slow wave. Methylprednisolone pulse therapy (30mg/kg/day for 3 days) was used due to persisting coma and electroencephalographic evidence of encephalopathy in one patient, which treatment resulted in a full recovery without any neurological sequelae. Another patient developed into postencephalitic epilepsy with antiepileptic drugs. Conclusion: Pulse therapy of methylprednisolone is a choice of therapy if presence of encephalopathy after non-typhoid salmonella infection. The possible mechanisms might be due to hypercytokinemia in central nerve system.

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Infectious diseases

ICNC-0431: A cross-sectional observational study of cognitive, adaptive, and behavior profiles of preschool and school aged HIV infected and HIV affected children

Introduction: This study aimed to compare cognitive, adaptive and behavior profiles of HIV infected and HIV affected children aged 2-9 years and to evaluate the influence of sociodemographic factors on their profile. Method: Fifty HIV infected, 25 HIV affected and 25 presumably uninfected 2-9 year old children were enrolled excluding children with known neurodevelopmental disorders. Parents were administered Developmental Profile (DP3), Vineland Adaptive Behavior Scale (VABS 2) and Child Behavior Checklist (CBCL) for assessing cognitive function, adaptive function and behavioral profile respectively. Primary outcomes included the number of children with significant cognitive or adaptive impairment or maladaptive behavior. Inter-group mean scores were compared with unpaired t test and correlation using regression analyses. Results: Significant cognitive impairment was observed in 76% HIV infected, 64% HIV affected and 24% controls. Mean General Developmental Scores was significantly lower for HIV infected than HIV affected and controls (59.2, 70.1, and 77.36 respectively; p<0.01). Significant adaptive impairment was observed only in 24% HIV infected and 8% HIV affected children. Mean Adaptive Behavior Composite scores were also lower for HIV infected group than HIV affected and controls (75.27, 82.48, and 85.36 respectively; p<0.01). Maladaptive behavior was not found in any group. Strong associations were found between combined clinical and environmental covariates with cognitive and adaptive impairment in HIV infected children. Conclusion: A large proportion of HIV infected and HIV affected Indian preschool- and school aged children have significant cognitive and adaptive impairment. Global impairment among various domains of cognitive and adaptive was observed in HIV infected children.

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Infectious diseases

ICNC-0432: Cerebral Sino-Venous Thrombosis in childhood Tuberculous Meningitis

Background: Reports of CSVT in children with TBM are restricted to case reports. Aims and objectives: To determine incidence, profile, and outcome of CSVT in a prospective cohort of children with TBM. Methods: In this single center prospective cohort of children TBM, neuroimaging was evaluated for presence of CSVT. Children with CSVT were treated with anti-tubercular drugs, steroids and anti-coagulation. Outcome was assessed using Pediatric Cerebral Performance Category scale. Results: Of the 242 children with TBM, 77 children (31%) had arterio-ischemic stroke. Twelve children (4.9%) had CSVT [Median age - 24 mo (range 12-120 mo)]. Eight of the 12 children had both CSVT and arterio-ischemic stroke. Among children with CSVT, the median duration of symptoms was 59.5 days (IQR 30.5-77.5). CSVT was detected at admission in single case while in others it was detected on subsequent neuroimaging. CSVT was symptomatic in only 4 children. Eleven children had involvement of superior sagittal sinus, 6 had involvement of transverse sinus, 4 had sigmoid sinus while 1 child also had affliction of straight sinus. Protein C was deficient in 1 child while protein S was deficient in 3 children. On a median follow up of 8 months, 9 children survived, 2 children had normal
functioning, 5 were in vegetative state, one each had moderate and severe disability. Conclusion: CSVT is an uncommon complication of TBM. A preliminary analysis suggests that those with CSVT appear to have a poorer outcome in children diagnosed with TBM

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Infectious diseases

ICNC-0433: Whole cord myelitis due to rabies
Introduction: Progressive ascending weakness after rabid dog bite needs to be differentiated from acute disseminated encephalomyelitis (ADEM) which demands different treatment. Clinical and radiological differentiation between the two is challenging in the absence of cranial involvement. We describe a case of whole cord myelitis after rabid dog bite which is extremely rare in literature. Case Description: A seven year old child presented with high grade fever, paraparesis, urinary retention and truncal weakness 20 days after a rabid dog bite on the right foot. He was managed at local dispensary with wound care and 4 doses of rabies vaccine but no rabies immunoglobulin. Twenty-four hours after his presentation at our institute, he developed bulbar & neck weakness and aerophobia. On examination, hypotonia, areflexia and mute plantar were demonstrated. Sensory examination and fundus were normal. MRI showed hyperintensities in whole central cord (myelitis), brainstem, left thalamus, putamen and globus pallidus. Clinical diagnosis of rabies encephalomyelitis was made. The child was provided supportive care in strict isolation. Discussion: Cervical and brainstem areas are commonly affected in paralytic rabies. Although ADEM closely matches the presentation, sparing of white matter makes ADEM less likely. Virus isolation was not done in the index case but aerophobia, thalamic, basal ganglia, brainstem and central involvement supports the diagnosis of rabies. MRI findings in rabies are poorly reported since MRI may not be feasible in sick patients. MRI showing whole cord myelitis in rabies is rare in literature. Conclusion: In evolving presentation of clinical symptoms like aerophobia, radiology may help in differentiating ADEM and rabies myelitis.

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Infectious diseases

ICNC-0434: Post traumatic pyogenic meningitis with extensive central nervous system vasculitis and Moyamoya vasculopathy: A case report
Introduction: Meningitis is a rare complication of head trauma seen in 1% cases. Vascular complications in bacterial meningitis are seen in 9-25% of patients. Neurological deficits especially dense deficits like quadriplegia is rare. We discuss a child with post traumatic pyogenic meningitis characterised by basal meningitis, quadriplegia, extensive vasculitis and moyamoya vasculopathy. Case Report: A 7 year old boy presented a history of with fall followed by encephalopathy. CT showed fracture of right frontal bone and extradural haemorrhage in right frontal region. Child developed fever, progressive encephalopathy and neck stiffness on day 3 after initial improvement. CSF was suggestive of meningitis and gram stain showed gram positive cocci. After 72 hours, encephalopathy improved and child was noticed to have quadriplegia. MRI showed multiple infarcts, diffuse leptomeningeal enhancement and diffuse irregular narrowing of suprachoroidal parts of both internal carotid arteries, bilateral proximal middle cerebral artery, anterior and posterior cerebral arteries suggestive of moyamoya vasculopathy Child was treated with vancomycin and meropenem for 42 days with repeated CSF monitoring. After 5 months of follow up, child is ambulatory with residual deficits and has epilepsy Discussion: Vasculitis in bacterial meningitis is due to endothelial cell swelling, subintimal proliferation and transient vascular spasm. Post meningitis moyamoya vasculopathy has been described in cases of streptococcus pneumoniae, mycobacterium tuberculosis, Neisseria meningitides, HIV, Haemophilus influenzae and Mycoplasma pneumoniae in isolated case reports. Moyamoya vasculopathy in the index case may be due to basal meningitis. Conclusion: Pediatricians and pediatric neurologist should be aware of vascular complications like vasculitis and moyamoya vasculopathy which can be seen rarely with pyogenic meningitis.

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Infectious diseases

ICNC-0436: Clinicoradiological profile and outcome of children with tubercular meningitis: still there is missed opportunity

Introduction: This study was aimed to evaluate clinical findings and radiological findings of pediatric patients with tubercular meningitis (TBM) over 3 year period. Methodology: Thirty patients with TBM were studied. The mean age was 5.6 years. Average time elapsed before diagnosis was 37.2 days. The diagnosis was based on abnormal neurologic symptoms and signs, CSF findings and abnormalities on brain-imaging studies. CT and MR examinations were performed in 12 and 22 patients, respectively. Most common clinical features were fever (93%), signs of meningeal irritation (53.33%), unconsciousness (46%) and headache (43%). Neuroimaging findings were hydrocephalus (53%), tuberculoma (36.6%), thalamoganglionic infarct (26.6%) and basilar cistern enhancement (20%). Finding compatible to diagnosis of CNS tuberculosis were observed more clearly on MR than CT. Patients were followed up for 2 week to 3 years. 3(10%) patients died and 16.6% came out normal while rest of the patients had some form of complications. Common complications were epilepsy, hydrocephalus, mental retardation, visual impairment etc. This is one of the very few studies done in developing countries in pediatric TBM. Conclusion: Most important finding of the study seemed prolong duration before diagnosis which is a missed opportunity as TBM should be suspected when the duration is more than 6 days of illness. This study also highlighted the neuroimaging finding of TBM and MRI seemed to be preferable.

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Infectious diseases

ICNC-0437: Valgancyclovir versus Gancyclovir in treatment of symptomatic Cytomegalovirus infected cases: A randomized controlled trial

Introduction: Congenital cytomegalovirus(CMV) infection is the most common viral infection transmitted via placenta causing significant neurodevelopmental impairment in infant and children. Methodology: This randomized controlled trial was done to compare oral valgancyclovir(VL) with injectable gancyclovir (GC) in treatment of 60 cases symptomatic CMV infected infants. Pre drug virus level, side effects, psychological, visual and hearing assessment was done. Post drug virus level was monitored. At 6 month follow up psychological, visual and hearing assessment was done again. Results: Mean age of patients in VL group was 7.10±3.58 and GC group 7.50±3.99 months. Nineteen patients presented with developmental delay, 13 patients with seizure, 4 with movement disorder. Twenty one percent of the patients were preterm and 38% were low birth weight. Eighteen patients had neonatal seizure. Regarding visual assessment patients had chorioretinitis, optic atrophy, squint and cortical blindness. On hearing assessment, none of patients deteriorated after drug administration rather some of the patients showed improved hearing. None of the patients showed deterioration of cognition but some of the patients showed improvement in cognitive assessment but there was no significant difference in two groups. The side effects of GC were significantly greater than VL. Conclusion: In symptomatic CMV infection in infants, Valgancyclovir is as efficacious as Gancyclovir and the former has less side effects.

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Infectious diseases

ICNC-0438: Acute Encephalopathy with biphasic seizures and late reduced diffusion- A developing country experience

Introduction: Acute encephalopathy with biphasic seizures and reduced diffusion (AESD) is a newly described encephalopathy syndrome characterized by biphasic seizures and disturbance of consciousness in acute stage, and restricted white-matter diffusion– “bright-tree” appearance on magnetic-resonance-imaging (MRI) in subacute stage. We describe the clinico-radiological features, response to treatment and short-term follow-up of five children with AESD from India. Methods: Retrospective analysis of case-sheets and prospective follow-up for 6-24 months. Case Description: All five cases presented with acute febrile encephalopathy and seizures; case 2 and 3 were infants with preceding acute gastroenteritis; case 4 developed acute, bilateral, painless loss of vision on day 3 of illness and case 5 had pre-existing static encephalopathy with epilepsy. Results: Age of presentation was 1-9 years. Four patients showed characteristic, bilaterally symmetrical, diffuse diffusion restriction involving periventricular and subcortical white-matter by day 4 of illness; case 4 showed an occipital dominant pattern involving bilateral optic radiations. Cerebrospinal fluid examination was normal; no organism could be identified in any of the cases. Metabolic screen in three patients was normal; testing could not be done in two patients. Pulse methylprednisolone was administered to all children. Duration of hospitalization was 7-14 days. All patients except case 5 have normal psychomotor development and neurological examination in follow-
up; case 5 returned back to his pre-illness status. Conclusion: It is important to recognize AESD by typical diffusion-weighted MRI and characteristic clinical course especially in Asian children. MRI shows no acute abnormality during the acute stage; and hence, the diagnosis may be missed.

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### Infectious diseases

**ICNC-0472: Neuro-developmental consequences of severe neonatal infections in rural Kenya**

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**ICNC-0440: Congenital Rubella Syndrome surveillance in Yogyakarta Indonesia**

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Infectious diseases

**ICNC-0472: Neuro-developmental consequences of severe neonatal infections in rural Kenya**

Introduction: Serious neonatal infections including pneumonia, sepsis and meningitis account for a third of neonatal deaths around the world. However data on neuro–cognitive impairment after neonatal infection, particularly following clinical diagnosis of possible serious bacterial infection (pSBI) used to guide empiric treatment are lacking. Methodology: This prospective study included 102/196 children born in a rural hospital in Kenya who survived neonatal pSBI (excluding those with confirmed meningitis) and 94/196 well neonates born in the same hospital. Children had neurodevelopmental assessments (including vision, hearing & motor impairment and epilepsy) at between 18 to 36 months. Odds of developing impairment were compared between the two groups using penalised multiple logistic regression. These comparisons were adjusted for birth weight, gestational age, clinical diagnosis of hypoxic–ischaemic encephalopathy and bacteraemia. Results: Children who had neonatal pSBI had a higher risk of developing neurodevelopmental impairment (18/102, 17.6%; Odds ratio (OR) 1.78, 95% confidence interval (CI) 1.60–1.99) compared to those without pSBI (5/94, 5.3%). Speech and language (13/102, 12.7% vs 3/94, 3.2%; OR 1.41, 95%CI 1.29–1.58) and neuro–motor domains (11/102, 10.8% vs 4/94, 4.3%; OR 1.38, 95%CI 1.22–1.58) were most commonly affected domains. Those who were exposed had a significantly higher risk of developing epilepsy (3/102, 2.9% vs 0/94; OR 1.83, 95%CI 1.56–2.19). Conclusion: Neonatal pSBI (excluding cases of confirmed meningitis) caused significant neurodevelopmental impairment in children after adjusting for confirmed bacteraemia. This has important implications for improving prevention, supporting effective neonatal care and managing the long–term consequences of neonatal infection in resource–poor settings.

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Infectious diseases

**ICNC-0440: Congenital Rubella Syndrome surveillance in Yogyakarta Indonesia**

ABSTRACT: Introduction: Congenital Rubella Syndrome (CRS) have many severe neurological manifestation and other systemic consequences. Rubella infection is a disease that can be prevented by vaccination; however, the rubella vaccine is not a national program yet in Indonesia. Objective: To investigate the prevalence and clinical manifestation of CRS at Dr Sardjito Hospital Yogyakarta, Indonesia. Methods: A descriptive study involving a review of congenital anomalies associated with CRS in Dr. Sardjito Hospital, Yogyakarta Indonesia from July 2008 to June 2013. CRS cases were categorized according to WHO diagnostic classification. Result: There were 312 infants who met the criteria for CRS during 5-year surveillance. Of these, 75% were classified as suspected cases, 19% were clinically confirmed, and 6% were laboratory confirmed cases. It makes a CRS prevalence being 39.4 per 10,000 outpatient infants. Majority (55%) of CRS cases were diagnosed at the age less than 6 months. All mothers have not been given a MMR vaccine. Among laboratory confirmed CRS cases, 72% of children had cataract, 72% suffered from congenital heart disease, 67% had hearing impairment, and 55% showed microcephaly. Global developmental delay and malnutrition were noted in 56% (10/18) and 17% (3/18) infants, respectively. Conclusion: The prevalence of CRS in infants in Yogyakarta Indonesia is considered high, with the majority of clinical manifestations being congenital heart disease, cataract congenital, and hearing problem. This emphasizes the necessity to strengthen CRS surveillance in other hospital in the future. It might also imply the importance of rubella vaccine becoming a national program in Indonesia. Key word: Congenital Rubella Syndrome; severe anomalies; rubella vaccine; surveillance; Indonesia.
Infectious diseases

ICNC-0442: A pediatric case of a solitary cerebellar hydatid cyst along with findings of hydrocephalus
Background: Hydatid cyst disease is a parasitic infestation caused by the larval form of Echinococcus granulosus that is relatively rare in children. It is a member of the group of diseases naturally transmitted between animals and humans. Intracranial hydatidosis is rarely seen, and is estimated to 1-2% of all cases with hydatid disease. Primary cerebellar involvement is more rarely encountered.Methods and results: We describe the case of a 7-year-old boy who presented with history of progressively worsening headaches, vomiting, and difficulty in walking since 21 days. He developed transient alteration of consciousness in the last 2 days. Magnetic resonance imaging (MRI) of the brain showed a cystic lesion in the right paracentral cerebellar region, measuring 49x45 mm, along with findings of hydrocephalus. Surgery was performed with a suboccipital standard craniotomy approach. Cyst was ruptured during surgical removal, and drainage was carried out before removal of capsule. The patient developed non-bacterial meningitis during follow-up after surgery.Conclusion: Hydatid cyst disease continues to be an important health problems in many countries, especially where livestock farming is prevalent. We would like to emphasize that patients with intraoperative cyst rupture should be careful follow-up after surgery in terms of non-bacterial meningitis. Because there is no definite medical treatment, environmental health and protective care are crucial for control and eradicate to this disease.Keywords: Hydatid cyst, Cerebellar involvement, Hydrocephalus, Child

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Infectious diseases

ICNC-0443: Acute Encephalitis Syndrome in children in Northern India -Role of Herpes Simplex Virus
Introduction: Herpes simplex encephalitis (HSE) is most common encephalitis worldwide. This is a routine practice to start intravenous acyclovir empirically in all suspected viral encephalitis cases; however in Indian scenario this leads to unnecessary treatment as most of cases are not due to Herpes simplex virus (HSV). So, this study was done at a tertiary care teaching hospital of Northern India to find out the proportion of HSE in acute encephalitis syndrome (AES) cases. Secondary objective was to assess the overall clinical aspects in AES along with distribution of HSE throughout the year. Methods: This prospective observational study was conducted over one year from September 2013 to August 2014. Children between 6 months to 14 years of age admitted as AES according to WHO, 2006 definition were enrolled. Patients went under workup for HSE including CSF IgM, DNA PCR and MRI. Any of them tested positive was considered as HSE. Results: Out of total 100 patients enrolled only four were diagnosed as HSE, 3 HSV PCR positive & 1 CSF IgM positive. Mean age was 5.73± 3.1 yrs. Convulsion, headache, vomiting and diarrhea were present in 93%, 21%, 34% and 4% respectively. Mean duration of altered sensorium, fever, seizures and hospitalization were 12.53±17.8, 11.22±11.38, and 4.54±3.36 and 16.59±17.05 days respectively. Conclusion: Encephalitis in our region is mainly due to causes other than HSV during epidemic as well as non epidemic season and if we start acyclovir empirically in all AES cases will be beneficial to a very low proportion of AES.

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Infectious diseases

ICNC-0444: CSF pleocytosis in infants with Enteroviral meningitis
Introduction: The clinical features of Enteroviral (EV) meningitis can mimic meningitis due to bacterial and other viral causes leading to unnecessary antibiotic treatment and period of hospitalisation. CSF pleocytosis has been noted in infants. Methods: Descriptive study by retrospective review of EV meningitis cases presenting to our tertiary hospital during a 5 year period. Inclusion criteria: Children with positive CSF Enterovirus PCR. Results: Data was obtained on 44 infants in the age range 5 days to 11 months (median 6 weeks). The WBC count ranged from 5.7 to 22 X 10^9/litre (mean 10.77 X 10^9/litre). CRP ranged from <5 to 85 mg/l (mean 13.55, median 8). CSF WCC was in the range from 0 to 630 X 10^6 cells / litre (median 4 X 10^6 cells/litre, IQR 0-38 X 10^6 cells/litre).CSF Neutrophil predominance of more than 50% was seen in 62% of patients in 0-28 days, 20% in 29-56 days age group and 15% in 57-365 days age group. Conclusion: Enteroviral meningitis is common in infants. There was no significant rise in peripheral WBC count and CRP in most of the patients. CSF WBC profile can show leucocytosis but neutrophil predominance and absence of CSF pleocytosis is also observed. Rapid results by EV PCR and improving clinician’s knowledge about possibility of pleocytosis can help to reduce the duration of antibiotics.
Infectious diseases

ICNC-0445: Acute encephalopathy with biphasic seizures and late reduced diffusion in a patient with Miller–Dieker syndrome: a case report

Introduction Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is a unique subtype of acute encephalopathy in children. No patient with Miller–Dieker syndrome suffered from AESD has been reported. Method We assessed the clinical symptoms and magnetic resonance imaging (MRI) findings of a patient with Miller–Dieker syndrome diagnosed as AESD. Results A 2-year-old girl with Miller–Dieker syndrome was admitted to our hospital due to status epilepticus and high fever. Her seizure continued for > 1 hour but resolved after intravenous administration of diazepam and phenobarbital. A brain MRI was performed on day 3 of admission because the patient had not recovered consciousness after the seizure stopped. The MRI revealed abnormally high signal intensity, predominantly in the frontal subcortical white matter area. Apneic episodes with oxygen desaturation due to clustered seizures occurred frequently on day 5 after admission, and AESD was diagnosed. Although the clinical seizures stopped with continuous intravenous administration of midazolam, subclinical seizures were detected during monitoring of the amplitude-integrated electroencephalogram (aEEG) and were stopped by increasing the midazolam dose. Conclusion Miller–Dieker syndrome is characterized by a four-layered structure lacking normal gyrri or sulci that replaces the normal six-layered cortex and can occur with AESD. In this case, subclinical seizures were detected after clinical seizures stopped and were controlled using aEEG monitoring. These findings suggest that aEEG monitoring is helpful to monitor and control subclinical seizures in patients in the acute phase of AESD.

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Infectious diseases

ICNC-0447: Role of oral minocycline in acute encephalitis syndrome in India - a randomized controlled trial

Background: Acute encephalitis syndrome (AES) is a public health problem in India. Neuroinfections are believed to be the most important etiology. Minocycline is a semisynthetic tetracycline having excellent penetration into cerebrospinal fluid, established neuroprotective and antiviral properties besides action on nonviral causes of AES. Objective: Randomized, controlled trial of nasogastric/oral minocycline in AES at a single centre in Uttar Pradesh, northern India.. Methods: Patients beyond 3 years of age - but excluding women aged 16-44 years - hospitalized with AES of <=7 days duration were enrolled and block randomized to receive nasogastric/oral minocycline or placebo suspension and followed up. Patients, study personnel and those entering data were blinded as to drug or placebo received. Primary outcome was cumulative mortality at 3 months from hospitalization. Analysis was by intention to treat. Results: 281 patients were enrolled, 140 received drug and 141 placebo. While there was no overall statistically significant difference in 3 month mortality between drug and placebo groups [RR = 0.83 (0.61-1.1)], there were encouraging trends in patients older than 12 years [RR = 0.70 (0.41-1.18)] and in Glasgow Outcome Score (GOS) at 3 months (x2=7.44, p=0.059). These trends were further accentuated if patients dying within one day of reaching hospital were excluded [OR for 3 month mortality =0.70 (0.46-1.07), p=0.090; 3 month GOS p=0.028] Interpretation:. A trend towards better outcomes was observed with minocycline, especially in those patients who survived the initial day in hospital. These findings should form the basis for planning a larger study and possibly including minocycline in the initial management of AES as seen here.

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Infectious diseases

ICNC-0448: Neurologic manifestations of enterovirus 71 infection in Korea

Introduction: Enterovirus 71 frequently involves the central nervous system and may present with a variety of neurologic manifestations. Here, we aimed to describe the clinical features, magnetic resonance imaging (MRI) findings, and cerebrospinal fluid (CSF) profiles of patients presenting with neurologic complications of enterovirus 71 infection. Methods: We retrospectively reviewed the records of 31 pediatric patients hospitalized with acute neurologic manifestations accompanied by confirmed enterovirus 71 infection at Ulsan University Hospital between 2010 and 2014. Results: The patients’ mean age was 2.9 ± 5.5 years (range, 18 days to 12 years), and 80.6% of patients were less than 4 years old. Based on their clinical features, the patients were classified into four clinical groups: brainstem encephalitis (n = 21), meningitis (n = 7), encephalitis (n = 2), and acute flaccid paralysis (n = 1). The common neurologic symptoms
included myoclonus (58.1%), lethargy (54.8%), irritability (54.8%), vomiting (48.4%), ataxia (38.7%), and tremor (35.5%). Twenty-five patients underwent an MRI scan; of these, 14 (56.0%) revealed the characteristic increased T2 signal intensity in the posterior region of the brainstem and bilateral cerebellar dentate nuclei. Twenty-six of 30 patients (86.7%) showed CSF pleocytosis. Thirty patients (96.8%) recovered completely without any neurologic deficits; one patient (3.2%) died due to pulmonary hemorrhage and shock. Conclusion: In the present study, brainstem encephalitis was the most common neurologic manifestation of enterovirus 71 infection. The characteristic clinical symptoms such as myoclonus, ataxia, and tremor in conjunction with CSF pleocytosis and brainstem lesions on MR images were useful for making a diagnosis of neurologic involvement.

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Infectious diseases

ICNC-0449: Clinical features of hydrocephalus in 28 cases with purulent meningitis in children

Background The severe purulent meningitis still has a high mortality rate and often results in severe sequelae among survivors, especially in children. Recently, the study about the neurological complications of meningitis has attracted more and more concern. The purpose of our study is discussed the clinical features of purulent meningitis with hydrocephalus in children. Methods We Select 269 children with purulent meningitis from pediatric neurology department of ¹¹ hospital, January 2010 through January 2015. We conducted a retrospective study of the clinical features in the cases with hydrocephalus, which were diagnosed by the radiologists’ reports on cranial imaging. Results The morbidity of purulent meningitis with hydrocephalus is higher, the diagnostic rate of neuroradiology is 10.41%. Most patients are from rural, the age of onset concentrated under 6 months old, time from onset to diagnosis of hydrocephalus mainly concentrated 2-4 weeks after purulent meningitis, and classified as communicating hydrocephalus. Gram-negative bacteria is mainly pathogenic bacteria. We didn’t find the relationship between CRP, bacterial culture of blood or laboratory indicators of cerebrospinal fluid (CSF) and hydrocephalus through logistic regression analysis. About two-thirds patients received irregular treatment in the local hospital. Conclusions Hydrocephalus is a common complication of purulent meningitis and still has a high incidence. As a pediatrician, correct recognition and treatment of purulent meningitis with hydrocephalus in children are very important.

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Infectious diseases

ICNC-0450: Neurological complications of varicella zoster virus infection

Introduction: Chickenpox is still regarded as a harmless childhood infection, its complications however, may cause significant morbidity. Authors aim was to estimate the incidence and describe the spectrum of neurological complications of varicella zoster virus (VZV) infections. Methods: Epidemiologic, demographic and clinical data of patients with VZV-associated neurological complications were statistically analysed. Results: In a 16-year-period 108 consecutive patients with acute neurological manifestations associated with either chickenpox or shingles were included. All of them were immunocompetent and unvaccinated for varicella. 90 of them originated from one geographical region where the incidence of neurological complications could thus be calculated to be 1 in 1950 varicella cases. Of all 108 patients 78 (72.2%) had acute cerebellar ataxia (ACA) and 20 (18.52%) had encephalitis. 3 patients had facial nerve palsy. 2 patients each had aseptic meningitis, optic nerve neuritis and central nervous system vasculitis, 1 each had abducens nerve palsy, external ophthalmoparesis, internal ophthalmoplegia and central retinal artery occlusion, respectively. 3 patients developed two complications each. Neurological dysfunction most often occurred after the primary infection, only 4 encephalitis cases were related to reactivation of VZV (shingles). Patients with encephalitis tended to be older than those with ACA (mean age 7.11±4.25 vs. 5.26±2.31 years). In 3 of them neurological symptoms preceded the appearance of the rash. Conclusion: Despite the public concept of varicella being a harmless childhood disease, it may cause a wide range of neurological complications. Most of these could be prevented by a more widespread use of varicella vaccination.

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Infectious diseases

ICNC-0452: Clinical outcomes in children with Herpes Simplex Encephalitis receiving steroid therapy

Objective. Herpes simplex virus encephalitis (HSE) is a significant cause of morbidity and mortality. Neurologic sequelae are common even after early initiation of acyclovir treatment. The host immune response during HSE can also lead to brain damage. There are an increasing number of reports favoring steroid use in HSE. We aimed to compare the prognosis of children with HSE with and without steroid therapy. Methods. We retrospectively screened our hospital
Ventriculoperitoneal shunting surgery

Abstract

Object. The object of this study was to evaluate the role of ventriculoperitoneal shunt surgery in children meningitis with severe hydrocephalus. Methods. Cases of meningitis with hydrocephalus were collected from 2010 to 2015 in pediatric department from Xiangya Hospital, a single, large teaching medical center in China. All patients were given VPS placement combine with medicine care after the failure of adequate and effective non-surgical treatment. We collected data on complications after the surgery and outcomes including neuropsychological sequelae, mortality at the end of our follow-up. Results. A total of 22 children who were diagnosed as meningitis with hydrocephalus and had been given VPS surgery were recruited into our study. Among all these cases, there were 15 patients of bacterial meningitis, 4 of tubercular meningitis in poor grade, 2 of HIV-negative cryptococcal meningitis, 1 of viral meningitis, 8(53%) patients suffer from premature delivery. The interval from initial symptoms to VPS surgery was 3.4 months (range 1 to 11 months.). 9(10/22) patients had complications after VPS surgery, and the causes were infection (5,22%), catheter obstruction(2.9%), incision abnormal healing (1.4%), CSF leak(1.4%).At follow-up of averagely 34 months, 19 patients (86%) survived and 3(14%) patients expired. 16 of them got a fair outcome and 6 of them had suffered from the neurologic sequelae. Conclusions. In our study , VPS surgery generally provided sustained relief from intracranial hypertension symptoms caused by hydrocephalus in children meningitis. Keywords Children hydrocephalus. Meningitis. Ventriculoperitoneal shunting surgery

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Infectious diseases

ICNC-0456: Neuropsychological outcomes of intracranial abscesses in the paediatric population

In contrast to other causes of acquired brain injury in childhood, outcomes of intracranial abscesses have not been well-characterised. Previous studies suggest intracranial abscesses in children can have adverse neuropsychological outcomes, including impairment of short-term memory and cognition. In our study, we describe intracranial abscesses in our paediatric population, with a particular focus on outcomes at follow-up. We identified a case series of intracranial abscess patients treated at our institution between 2010 and 2015. Patients aged 0 – 18 years, with a diagnosis of extradural abscess, subdural empyema or cerebral abscess, were searched for in Neurosurgery, ENT, and Paediatric Intensive Care databases. This yielded 28 patients (13 female, 15 male) aged 0 – 15 (median 11) years. There were 45 abscesses in total, with 1 – 4 abscesses per patient. 60% of these were frontal. 61% of patients had abscesses attributed to sinusitis. 93% were treated with a combination of a 3rd-generation cephalosporin and metronidazole. All had surgical intervention. There were 48 operations in total, with 1 – 4 operations per patient. Follow-up time ranged from 1 month to 3 years. 100% survived and 54% had no complications at follow-up. 25% of our patients had evidence of cognitive or behavioural disturbance at follow-up. These were all detected within 5 months of discharge. Our case series highlights the incidence of adverse cognitive, emotional and behavioural outcomes of intracranial abscesses in the paediatric population. It emphasises the need for long term surveillance of these patients even after acute neurological signs and symptoms have resolved.

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Infectious diseases

ICNC-0457: Acyclovir treatment of internal ophthalmoplegia caused By Varicella Zoster Infection

Introduction: Internal ophthalmoplegia is an ophthalmologic complication of varicella zoster virus infection. This complication is uncommon and few cases have been reported before. Case report: A nine-year-old girl was referred to our department for a 3-week history of an enlarged pupil in her right eye and blurry near vision. Past medical history was remarkable for chickenpox 1 month prior. Her parents closely watchedover her eyes afterwards and observed a tonic pupil and conjunctivitis 1 week later. She had been treated with oral acyclovir suspension 400 mg four times a day for 10 days. The mydriasis and vision showed mild improvement, as her parents noticed it. When she admitted, on ocular examination, her visual acuity was normal. The right pupil was mydriatic in room lighting with a 3-mm anisocoria between two eyes. The pupillary light reflex was slightly responsive on the right eye and whatever the eye lightened, the right pupil contracted less. On follow-up, there was an improvement in mydriasis, reaction to both light and accomodation of the right pupil. Internal ophthalmoplegia did recover within 6 months from presentation. Discussion: Varicella is a common self limiting and relatively benign illness. Therefore, antiviral medication is not routinely received. We report a previously healthy girl who presented with varicella zoster virus infection complicated by internal ophthalmoplegia which is an atypical presentation and uncommon complication of the disease. This case questions whether antiviral treatment using or not because of potential response to oral acyclovir.

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Infectious diseases

ICNC-0458: Fulminant Epstein Barr Virus Encephalitis

Epstein Barr virus (EBV) encephalitis is rare in children but can have severe neurological complications and sometimes fatal. It can manifest with varied neurological presentations like meningoencephalitis, brain stem encephalitis, GBS etc. This can appear alone or with clinical picture of infectious mononucleosis. Establishing a diagnosis of EBV encephalitis is difficult and consequently molecular, serological and imaging techniques should be used when investigating a child withencephalitis. To highlight this entity we report two fatal cases of EBV meningoencephalitis presenting with sole neurological manifestations. Key words: Encephalitis, Epstein Barr virus.

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Infectious diseases

ICNC-04560: Neutotuberculosis in an infant: A case report

Introduction Tuberculosis is a serious public health problem, especially in emerging countries. Neurological complications were common and tuberculosis meningoencephalitis is very drastic in children, causing high risk of sequelae and death. Description Case Infant was 1 year and 2 months old, female, normal neuro-psychomotor development and all fully vaccination. She was receiving a systemic corticosteroids by her mother without medical prescription. The mother had a chronic cough. The patient was admitted in the emergency room presenting cough, intermittent fever, vomiting and
drowsiness for 6 days. During hospitalization had a progressive decreased of level consciousness and status epilepticus, needing to be removed to a Pediatric Unit Care. Brain tomography showed dilatation of the ventricular system and multiple nodular lesions underlined by edema (granulomas). Chest radiograph had diffuse nodular infiltrate and CSF analysis showed pleocytosis, elevated level of protein and low glycorrhachia. By the tracheal aspirate technique was isolated the tuberculosis bacillus. The treatment for neurotuberculosis followed the public health government guidelines, but she died in the 18th day of hospitalization. Discussion In Brazil, only at 2013 were diagnosed 71,123 new cases of tuberculosis, about 35.4 / 100,000 inhabitants. Most commonly in immunocompetent and immunocompromised patients that have high risk to develop neurotuberculosis. Conclusion The CNS involvement is the most lethal form of tuberculosis, particularly in children and an impaired immune system. This case also warns about self-medication, a dangerous practice, particularly in children.

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Infectious diseases

ICNC-0631: Demographic profile, Neurological status and Outcome in children with Tubercular Meningitis

Introduction: We studied the clinical profile, radiological characteristics, outcomes and its predictors in children with tubercular meningitis (TBM). Methods: Records of 350 children admitted from Jan 2010 to Dec 2014 in Advanced Pediatric Centre with diagnosis of TBM were screened. Data was recorded on pre-structured questionnaire and prospective follow-up was done. Results: Mean age at presentation was 43.8±40.5 months (range 3-150 months), 71% were males. Mean duration of illness was 40.5±51.5 days (range 1-365 days). At presentation, 91% fever (91%), intracranial hypertension (85%), seizures (63%), vomiting (51%), irritability (48%), cranial nerve involvement (36%), focal deficits (33%) and headache (25%) were noted. Mean GCS was 10±3.1 (range 3-15). Majority of children presented in stage III (44%), followed by stage II (41%) and stage I (15%). Severe (56%) and moderate (14%) malnutrition, history of contact with a case of tuberculosis (47%), positive family screening (40%), BCG scar (36%), positive Mantoux-test (30%) and abnormal chest-radiograph (28%) were noted. CSF showed predominant lymphocytes (64%) followed by neutrophils (26%), elevated proteins (71%) and hypoglycorrachia (70%). Neuroimaging showed hydrocephalus (91%), basal exudates (57%), infarcts (39%) and tuberculomas (15%). Hydrocephalus was categorized as grade 3 (63%), grade 1 (18%) and grade 2 (8%); ventriculo-peritoneal shunts were inserted in 67% patients. Extracranial tuberculosis was noted in 10%. All patients were started on anti-tubercular therapy (ATT); 10% patients were already on ATT; compliance was good in majority (94%); paradoxical reactions were noted in only 2 patients. Mortality was 20%; at discharge 63% had sequelae while 17% were normal. Long-term outcome is being assessed and will be presented. Presence of basal exudates (p=0.01) and hydrocephalus (p=0.03) correlated significantly with outcomes. Conclusion: Our study provides important clinical data from a single centre in a developing country. In this cohort of children in resource constraint setting, in-hospital mortality and morbidity at discharge was high.

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Infectious diseases

ICNC-0461: Integrated management of childhood illness indicators of childhood tuberculous meningitis at a tertiary hospital in the Western Cape Province of South Africa

BACKGROUND: Tuberculous meningitis (TBM) is the most common type of bacterial meningitis in the Western Cape of South Africa. Early clinical diagnosis is notoriously difficult and often delayed, with disastrous consequences for patients. The Integrated Management of Childhood Illness (IMCI) strategy is the primary child-care approach of choice for South Africa which ensures accurate assessment of sickchildren using simple yet reliable clinical signs at the first contact level. METHODS: A retrospective observational study of 30 consecutively diagnosed TBmchildren at Tygerberg Children’s Hospital with the aim of identifying IMCI clinical indicators which would warrant urgent referral and earlier treatment. RESULTS: Of the 30 TBM children, 17 male, median age 35 months, 6 (20%) presented with stage I TBM, 6 (20%) with stage II TBM and 18 (60%) with stage III TBM. The median number of healthcare visits prior to hospital admission was 4.0 (range 1-6). At the 1st healthcare visit, 10 (33%) of TBM children had at least one IMCI general danger sign, 22 (73%) had TB-specific signs/symptoms and 18 (60%) “TB-specific signs/symptoms”. CONCLUSION: If correctly applied, IMCI clinical indicators would ensure earlier diagnosis of TBM.

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Infectious diseases

ICNC-0465: A case of Anti-NMDA-receptor encephalitis presenting with acute psychosis; a case report

INTRODUCTION: Autoimmune encephalitis is a heterogeneous group of disorders, which occur as a result of the immune response to neuronal antigens and manifest with cognitive and behavioral impairment. Anti-NMDA receptor encephalitis is the most common cause of autoimmune encephalitis. In this report, we present a case of anti-NMDA receptor encephalitis to demonstrate the difficulties in diagnosis and treatment. CASE REPORT: A 15-year-old girl had an onset of complaints of whole body numbness and meaningless speaking. She was started on medication at the psychiatry department with the preliminary diagnosis of psychosis. She was referred to our hospital since she had fever on follow-up. The patient was admitted to the pediatric intensive care unit with the diagnosis of encephalitis. Her physical examination revealed a poor overall status, absence of consciousness, no response to painful stimulants. Laboratory and radiological investigations were normal. Patient was started on treatment for encephalitis. Cerebrospinal fluid NMDA receptor antibody test performed upon absence of clinical improvement in the patient with normal serum and CSF viral panel revealed a positive result. The patient was administered pulse steroid, IVIG treatment and plasmapheresis alternately. She started gaining consciousness at 3 months of admission and was discharged at 4 months. The patient has no convulsions and her cognitive status is normal at outpatient follow-up visits.

CONCLUSION: Immunomodulatory and immunosuppressive drugs are used for treatment. As is the case in our patient, autoimmune encephalitis should be considered in patients, who present with manifestations of encephalitis, clinical findings more severe than expected, and inadequate response to treatment.

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Infectious diseases

ICNC-0466: Clinico-radiological response of neurological tuberculous abscesses in children treated with thalidomide

Introduction: Neurological tuberculous (TB) abscesses that clinically progress despite conventional anti-tuberculosis therapy may be responsive to adjuvant thalidomide, a potent tumour necrosis factor-alpha (TNF-α) inhibitor. Aim: To describe the clinico-radiological response of TB abscesses in 20 consecutive children treated with thalidomide. Results: The median age of the 20 children was 36 months (range: 8-168 months), 10 were female and 5 were HIV infected. Presenting neurological features included focal motor deficit (n=7), ataxia (n=6), raised intracranial pressure (n=3), spastic paraplegia (n=2) and epilepsy partialis continua (EPC) (n=2). The mean Thalidomide dose was 3.7 mg/kg/day (range 3.1-5.0 mg/kg/day), the medium duration of administration was 6 months (range 1-12 months) and median cumulative dose was 9g (range 4.5-31.5g). None of the children experienced any Thalidomide adverse effects. Thalidomide resulted in cessation of tuberculoma-associated EPC within 2 weeks of therapy, resolution of ataxia and restoration of walking in previously paraplegic children. Clinical improvement followed a reduction in perilesional edema and preceded regression in lesion size on magnetic resonance imaging (MRI). Loss of MRI T2 relaxation signal in previously liquefied TB granulomas resulted in a satisfactory treatment response. MRI T2 black TB granulomas may persist for years in asymptomatic children. Conclusion: In this study, the addition of thalidomide provided substantial clinical benefit in the majority of patients and magnetic resonance imaging (MRI) evolution of lesions from early stage “T2 bright” with oedema to “T2 black” represented a marker of cure.

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Infectious diseases

ICNC-0467: Five year case series of childhood tuberculous meningitis from Sri Lanka

Sri Lanka is a low middle income country with a lower national estimate of Annual Risk of Tuberculosis Infection (ARTI) of 0.4%. This is much lower than estimates from other developing countries. This study was performed to evaluate the epidemiology and the clinical features of Tuberculous meningitis (TBM) among Sri Lankan children. Method A retrospective chart review of all cases treated as probable TBM over a five year period (2011-2015) at the premier children’s hospital in the country was performed. Results Total number of admissions to the hospital during this 5 year period was 404,498. Out of this, 21 children were diagnosed and treated as for probable TBM. The median age was 4.89 years, Male : female ratio was 2:3. Presence of fever was seen in all but one at admission, and this was for more than 7 days in 76.19%. Other presenting features were headache in 17 (above 4 years), focal neurological signs in 52%. The commonest TBM clinical stage at time of admission was stage 2 in 61.9%. TBM related complications such as hydrocephalus, Cerebellitis, Ventriculitis, 3rd cranial nerve palsy, hemiparesis and developmental regression were noted in 66.6%. There were no deaths in this series. Six went home completely recovered while 15 were discharged or transferred with residual complications. Discussion In spite of its 20 million population, Sri Lanka has shown to be a low prevalent country for TBM in children (1:20,000). The above low prevalence of TBM meningitis is probably related to its
high BCG vaccination rate.

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Infectious diseases

ICNC-0468: Neurological manifestations in pediatric leptospirosis
Objective: Leptospirosis is considered an important zoonosis and potentially fatal disease with protean manifestations. It is often underdiagnosed especially when the features are non specific, resulting in significant morbidity and mortality. The purpose of this retrospective clinical series is to further look into the disease hypothesis as well as studying the correlation between organ specific complications and its laboratory marker. The data will put emphasis on leptospirosis patients who presented with neurological symptoms and signs as primary manifestation. Method: Paediatric leptospirosis patients age 12 years and below who were admitted to our tertiary hospital at northern state of Kelantan, Malaysia from January 2014 to June 2015. All patients selected were labeled as Confirmed Case with MAT titer of > 1:400. Common clinical symptoms and organs involvement were all taken into account. Outcome of the patients recorded as either discharge or died in ICU. Results: 105 subjects were reviewed. Of these 11 (10.5%) presented primarily with neurological features, 7 of which (63.6%) came with encephalopathy manifesting as altered sensorium or seizure. 3 (27%) with acute flaccid paralysis in the form of acute demyelinating polyneuropathy (1 patient) and due to severe rhabdomyolysis (2 patients). These 2 patients had creatine kinase (CK) elevation > 500 folds. 1 patient had aseptic meningitis. 2 patients with encephalopathy died due to multiorgans failure, giving the mortality rate of 18% amongst the neurologically affected. Conclusion: Neuroleptospirosis are not uncommon in pediatric leptospirosis with relatively high mortality. Severe rhabdomyolysis resulting in paralysis is a rare but important manifestation.

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Infectious diseases

ICNC-0470: A case of Mild Influenza-Associated Encephalopathy with Biphasic Seizures and Late Reduced Diffusion in Korea
Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is one form of encephalopathy that has a biphasic clinical course and a typical magnetic resonance imaging (MRI) finding of reduced diffusion in the frontal or frontoparietal subcortical white matter, with sparing of the perirlandic region. There have been no previous reports of influenza-associated AESD in Korea, while approximately 20 cases per annum have been reported in Japan. We report a 24-month-old Korean female with a clinically, radiologically diagnosed mild form of AESD associated with influenza A. The patient had a complex partial seizure on the second day of fever, followed by a cluster of brief seizures on the fifth day of viral febrile disease. MRI showed diffusion restrictions on the subcortical white matter and cortex of both frontoparietal lobes. Influenza A was proven after her temperature had fallen. Her clinical symptoms improved gradually without using oseltamivir, and no other neurologic sequelae remained. This case report is the first reported mild form of influenza-associated AESD in Korea. The ethnicity and regionality of influenza-associated encephalopathy should be widely studied.

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Infectious diseases

ICNC-0471: Clinical features of pediatric enteroviral meningitis in a single medical center
Purpose: Human enterovirus is one of major causes of pediatric central nervous system infection. Our study aimed to examine the clinical predictors of enteroviral meningitis among pediatric patients who were diagnosed by RT-PCR. Method: We retrospectively reviewed the medical records of patients aged between 29 days and 18 years who were found positive for CSF enterovirus RT-PCR in Dankook University Hospital from January 2009 to December 2012. Mann-Whitney U test and Chi-square test were used by SPSS program (version 20.0). Results: A total of 124 patients were included in the study (male: female 1.88:1). Average age at admission was 2.77±3.75 years (median 0.26 years). Fever was the most common initial symptom (96.8%), followed by headache (32.3%), vomiting (26.6%), and neck stiffness (25.0%). Total duration of fever was 2.83±2.92 days. In CSF, mean white blood cell, neutrophils, protein, and glucose were 130.72/µL, 12.53%, 49.48 mg/dL, and 56.95 mg/dL, respectively. Pleocytosis was present in 69 patients (55.6%). Seventy-six (61.3%) were less than 2 years of age, and June to August was the most common months of admission. Most patients recovered completely, but meningoencephalitis with status epilepticus (n=2), ADEM (n=1), or prolonged recurrent seizures (n=2) developed in 5 patients. Longer duration of fever, abnormal brain images, and seizures were more frequent in the group with complications. Conclusion: Enteroviral meningitis occurred throughout the year. Most patients showed good outcome, but meningoencephalitis, ADEM, or prolonged recurrent seizures rarely
occurred. Therefore, detailed evaluation and close observation are important in management.

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ICNC-0805: Factors of occurrence of anxious behavior in adolescents after mass vaccination

INTRODUCTION: Conversion disorder has a complicated history that helps to explain the number of different names for it. Two eminent neurologists of the nineteenth century, Jean-Martin Charcot in Paris and Josef Breuer in Vienna were investigating what was then called hysteria, a disorder primarily affecting women (the term “hysteria” comes from the Greek word for uterus or womb). Women diagnosed with hysteria had frequent emotional outbursts and a variety of neurologic symptoms, including paralysis, fainting spells, convulsions, and temporary loss of sight or hearing.

METHODS: A cohort study of 300 teenagers after mass vaccination in one location. Among them were 97% girls and 3% boys. DESCRIPTION and results: we observed 300 cases with postvaccinal reaction after carrying out mass vaccination in 2015 in one region of Kazakhstan. 17 of them were admitted at our clinic. In clinical features prevailed panic attacks and anxious which led to vegetative (lack of air, dizziness, pain substernal, pale skin) and neurological symptoms including paralysis were observed. In this group the link of clinical features, social conditions and methods of vaccination were analyzed. CONCLUSIONS: It notes the importance of prior information of the population before the mass vaccination and strict adherence to the methodology of vaccination. in the event of panic and anxiety need to strictly observe the sequence of actions: the separation of patients from each other, from the parents, from the means of communication (phones, smart phones, Internet access) and daily individual counseling both teenagers and their parents.

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ICNC-0917: Reduced cortical and thalamic cerebral blood flow in adolescents with chronic post-concussive symptoms

Introduction: 14% of children with sports-related concussions (SRC) remain symptomatic 3 months after injury. Studies have shown regions of hypoperfusion in symptomatic patients in the chronic phase of mild TBI. In this study we used whole-brain spatial mapping and a voxel-wise statistical approach to investigate the extent and anatomical distribution of cerebral hypoperfusion in chronic symptomatic pediatric concussion subjects. Methods: 23 adolescents (15y) who previously sustained a SRC (3–24 months) and 13 controls (15y) were enrolled. Subjects were referred if they reported cognitive, behavioral, or emotional symptoms. Conventional 3D T1 weighted (T1WI) and DSC-perfusion weighted images were acquired (3.0T Siemens Tim Trio scanner). Relative CBF maps were generated and then deformably registered to the T1WI which was then deformably registered to a control T1WI template. Segmentation identified the regional cortical and thalamic structures. Voxel-wise analysis determined significant differences (p<0.05) in regional CBF. Results: We identified multiple areas of reduced CBF in cortical and subcortical regions, including the left medial temporal gyrus, left inferior frontal lobe, left posterior frontal lobe and left posterior cingulate cortex and bilateral thalami Conclusion: Our findings identified multiple cortical and subcortical regions of reduced CBF. We speculate that hypoperfusion in the temporal lobe, posterior cingulate cortex and thalamai may be implicated in cognitive deficits after SRC. Compared to our previous results [Bartnik-Olson et al., J Neurotrauma 2014;3:921-32] using ROI analysis, we detected a greater number of areas of hypoperfusion suggesting that whole-brain spatial mapping and voxel-wise analysis improved detection of CBF abnormalities.

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ICNC-0348: The headache in children with epileptic encephalopathy

Introduction. Epileptic encephalopathy - is a condition where abnormal electrogenesis of brain is the cause of disorders of the brain functions. In this condition the epileptic process itself leads to progressive brain damages. Aim of the study. To study the features of neurological status in children with epileptic encephalopathy and to find the characteristics of headache in paediatric patients with epileptic encephalopathy. Materials and Methods: We studied 120 children aged from 3 to 14 years, diagnosed with epileptic encephalopathy. We studied children using standard protocol: neurological examinations, Electroencephalography (EEG), and Magnetic resonance imaging. The results of the study. All of them were suffering by acute or chronic headache and symptomatic epilepsy. Preictal headache was present in 12 (10%) patients, postictal in 30 (25%) and interictal in 60 (50%) patients. Among the patients with postictal headache 10 (33.3%) had migraine, 15 (50%) tension-type of headache and 5 (16.7%) other headaches. The study of neurological patients with epileptic encephalopathy revealed the prevalence of cognitive impairment, decreased intelligence, memory and
Abnormalities in different types of headache revealed that there is an association between them. There was also a symptomatic epilepsy; it is often revealed the predominance of focal neurological symptoms. Co-prevalence of cognitive impairment, decreased intelligence, memory, and thinking. In neurological status of patients with (electroencephalography). Results The study of neurological patients with epilepsy. In this study, we used clinical, neurological, and instrumental methods of investigation such as EEG.

119 children aged from 3 to 14 years, 69

Abnormalities in children with symptomatic epilepsy on the background of headache. Materials and methods. We studied EEG abnormality is a prominent finding in children with headache. Aim The aim of this study was to evaluate EEG abnormalities in children with symptomatic epilepsy on the background of headache. Materials and methods. We studied 119 children aged from 3 to 14 years, 69 of them were diagnosed with epileptic encephalopathy and 50 with symptomatic epilepsy. In this study, we used clinical, neurological, and instrumental methods of investigation such as EEG (electroencephalography). Results The study of neurological patients with epileptic encephalopathy revealed the prevalence of cognitive impairment, decreased intelligence, memory, and thinking. In neurological status of patients with symptomatic epilepsy, it is often revealed the predominance of focal neurological symptoms. Comparing EEG abnormalities in different types of headache revealed that there is an association between them. There was also a

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Miscellaneous ICNC-0807: Tourette Syndrome and attention deficit hyperactivity disorders Background: Tourette syndrome (TS) and related tic disorders are commonly associated with obsessive-compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD). It has been argued, however, that any observed association between TS and these and other psychopathologies may be due to ascertainment bias in that individuals with multiple problems are more likely to be referred for medical evaluation. A tic is a sudden, uncontrollable movement which can occur anywhere in the body or be vocal. Tics are often very mild and may not be noticeable to others but tics can also be grandiose. It is common for some tics to normally occur in people, particularly children. Methods: In order to overcome the potential confounding by ascertainment bias, we conducted a community-based study of school children using direct interviews to determine the prevalence of tic disorders and any comorbid psychopathology. A standard psychiatric interview and standardized rating scales were utilized to diagnose childhood behavioral disorders. Results: Of the 325 children interviewed, 71 were identified as having tics. The following psychopathologies were found more commonly (p < 0.05) in the children with tics: OCD, ADHD, separation anxiety, overanxious disorder, simple phobia, social phobia, agoraphobia, mania, major depression, and oppositional defiant behavior. Conclusion: The behavioral spectrum of tic disorders includes OCD, other anxiety disorders, a mood disorder, and attention-deficit and disruptive behavior disorders.

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Miscellaneous ICNC-0808: Cognitive impairments in children with tic disorders and Tourette’s syndrome Introduction. Tics is the dominant form of hyperkinesis in children. The prevalence of tics child population is up to 6%. Tourette’s syndrome, occurs in 0.1% of cases and is characterized by multiple motor and vocal tics. It is proved that the close relationship between the motor disorders and attention deficit. Aim of The study of cognitive impairment was a combination of neurological and electroencephalographic techniques that allowed us to objectify pathogenetic features of Tourette’s syndrome and a differentiated approach to drug therapy. Methods. we studied 331 children to explore the semiotics of cognitive impairment in patients with tics and Tourette’s syndrome. Results It was found that during the period of acute illness disruption of the function of memory, attention, reading, and writing were revealed and disruption mainly localized in the fronto-temporal region of the dominant hemisphere. Patients with hereditary disorders ticks resistant auditory-verbal memory and reading correlate with the spectral power of the theta band in the temporal region of the dominant hemisphere, disorders of attention and memory - with high spectral power of the theta range in the frontal area of the dominant hemisphere. Conclusion. In patients with tic disorders cognitive impairments were identified with different severity depending on the severity of tics with topical localization the fronto-temporal areas of the dominant hemisphere. Cortical dysfunction fronto-temporal areas of the dominant hemisphere topically correlates to the pathological EEG rhythms. Combination therapy with neuroleptics and encephabol were effective in patients with tic disorders.

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Miscellaneous ICNC-0369: The relationship between headache and abnormal EEG patterns in children with Symptomatic Epilepsy Introduction. Epilepsy is one of the most complex medical and social problem at present time. Headache is a main symptom that occur before or after epileptic seizures. It has been stated that headache may represent an epileptic event. EEG abnormality is a prominent finding in children with headache. Aim The aim of this study was to evaluate EEG abnormalities in children with symptomatic epilepsy on the background of headache. Materials and methods. We studied 119 children aged from 3 to 14 years, 69 of them were diagnosed with epileptic encephalopathy and 50 with symptomatic epilepsy. In this study, we used clinical, neurological, and instrumental methods of investigation such as EEG (electroencephalography). Results The study of neurological patients with epileptic encephalopathy revealed the prevalence of cognitive impairment, decreased intelligence, memory, and thinking. In neurological status of patients with symptomatic epilepsy it is often revealed the predominance of focal neurological symptoms. Comparing EEG abnormalities in different types of headache revealed that there is an association between them. There was also a
Patients with moderate/severe (GCS score <13) or complicated mild (with hemorrhagic intracranial injury on CT) TBI were detected/quantified micro ........................................

Introduction: Susceptibility weighted imaging (SWI) is an advanced ICNC technique that improves the ability to detect/quantify micro- and macro-hemorrhagic lesions after TBI. There are few studies in children and most have been acute and not included repeated long-term imaging, combined with neurological or neuropsychological measures. We report the relationship of these acute lesions with one-year MRI, neurologic and neuropsychological outcomes. Methods: Patients with moderate/severe (GCS score <13) or complicated mild (with hemorrhagic intracranial injury on CT) TBI

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Miscellaneous
ICNC-0349: Episodic hypothermia, hyperhidrosis, and hypersomnmmia syndrome. A migraine precursor syndrome?

Objective: To describe the clinical findings, investigations, and outcome of 22 patients with episodes of hypothermia, hyperhidrosis, and hypersomnia (EHHH). Material: Retrospective review of 22 children with two or more episodes of EHHH. Hypothermia was defined as axillary temperature (AT) less than 35.3°C. The low AT, hyperhidrosis, and hypersomnia could not be attributed to any other recognized cause. Results: Median age was 3±4y, 13 children were male. AT ranged from 32.5 to 35.2°C, but rectal temperature was higher than 35°C in 20. Marked hyperhidrosis was the presenting symptom in all patients. Other symptoms were: Pallor (16), drowsiness (13), headache (5), bradycardia (5). The number of episodes ranged from 2 to more than 20 and episodes lasted between 15 minutes and 4 days. The episodes were in the awake state in 15. Twelve patients had a first-degree relative with periodic headache or migraine. Physical examination and cognitive assessment were normal. Brain CT scan (12) and MRI (15) were normal. EEG recordings during episodes were normal or showed slow waves. Routine blood investigations and cardiac evaluation were normal. Endocrine investigations disclosed hypothyroidism (1) and increased TSH (1). Because of the frequency and intensity of the episodes 7 patients were put on cyproheptadine with a favorable response in 5. Outcome of patients with a ≥4-year follow-up showed 9 symptom free and 4 with periodic headache. Conclusion: Considering the presence of headache during episodes and follow-up, the family history, and good response to cyproheptadine, EHHH may be considered either as another periodic syndrome or being associated with migraine.

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Miscellaneous
ICNC-0918: Early NAA reductions predict Neuropsychological outcomes after Pediatric TBI

Introduction: Advanced MRI methods are increasingly used to assess pediatric patients with traumatic brain injury (TBI) to predict outcome. Previous studies have been retrospective, lacked age-appropriate controls and have not included repeated long-term imaging, neurological or neuropsychological measures. We pre-sent our find-ings involving a pro-spective study of MR spectroscopic imaging (MRSI) in pediatric TBI patients studied acutely and at 1-year. Methods: Hospitalized patients (ages 4 to 18) were enrolled if they sustained a mild to severe TBI (GCS <13 or CT evidence of intracranial injury). Age-matched controls underwent identical imaging, neurological and neuropsychological testing. Subjects under-went 3T MRI with pro-ton 3D MRSI acutely (6-17 days) and at 1 year. Results: Regional MRS ratios (NAA/Cho, NAA/Cho, Cho/Cr) for the initial studies were correlated and regression analyses were done to determine which variables predicted neuro-logic (PCPCS) and neuro-psychological (memory, attention and intelligence) outcomes at 12 months. Results: We studied 68 children (ages 4 to 18); age 11.9 ±3.6yrs; initial GCS-Mild: n=25; Moderate=9; Severe=34) and 72 control children (ages 4 to 18); age 12.7±3.3 yrs. Initial studies were done at 12±4 days and follow-up studies at 12±1 months for TBI patients and 13±1 months for controls. Total and regional NAA/Cho and NAA/Cho ratios were significantly 1) re-duced initially com-pared to controls; 2) corre-lated with PCPCS, FSIQ, General Memory and General Attention scores; and 3) predicted dichotomized PCPCS (93%), FSIQ, General Memory and General Attention (p=.000). Conclusions: NAA reductions detected acutely are indicative of neuronal loss or dysfunction and predict long term neurologic and neuropsychologic outcomes [Supported by NIH/NINDS:R01-NS054001].

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Miscellaneous
ICNC-0919: Hemorrhagic MRI Brain Lesions are associated with one-year outcomes after Pediatric TBI

Introduction: Susceptibility weighted imaging (SWI) is an advanced MRI technique that improves the ability to detect/quantify micro- and macro-hemorrhagic lesions after TBI. There are few studies in children and most have been acute and not included repeated long-term imaging, combined with neurological or neuropsychological measures. We report the relationship of these acute lesions with one-year MRI, neurologic and neuropsychological outcomes. Methods: Patients with moderate/severe (GCS score <13) or complicated mild (with hemorrhagic intracranial injury on CT) TBI
underwent MRI (3T), acutely (6-18 days) and at 1 year. The number and volume of hemorrhagic brain lesions on SWI were compared to 1-year neurologic (PCPCS) and neuropsychological (memory, attention, IQ) outcomes. Results: We studied 75 children (54M/21F; mean age 12 years), who were injured in vehicle/bike accidents (48), falls (20), sports (6), or assaults (1). GCS scores were mild (28), moderate (11) or severe (36). Severely injured patients had the highest number or volume of brain lesions. Lesion number/volume showed significant negative correlations with one-year neurologic outcomes (p=0.000/p=0.001) and neuropsychological assessment related to memory (p=0.000/p=0.005) and attention (p=0.000/p=0.002). There was no significant correlation with IQ. 70 patients returned for follow-up MRI. ~50% of hemorrhagic lesions persisted at one year. Improvement in lesion volume correlated with improved one-year neurologic scores (p=0.000). Conclusions: The extent of hemorrhagic brain lesions on acute MRI correlate with one year neurologic and neuropsychological (memory and attention) outcomes. Although 50% of hemorrhagic lesions persisted, improvement in lesion volumes correlated with improved neurologic outcomes [Support from NIH/NINDS:R01-NS054001].

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Miscellaneous
ICNC-0350: Pseudotumour cerebri associated with sickle cell anemia
Introduction: Pseudotumour cerebri (PTC) is characterized by the presence of intracranial hypertension without evidence of lesion, hydrocephaly, or alteration of the composition of cerebral-spinal fluid (CSF). Method: case report of a child diagnosed with PTC secondary to sickle cell disease (SCD). Results: A 6-years-old girl with diagnosis of SCD-SS was in regular follow-up with pediatric hematologist. She presented with a two days history of bilateral headache, associated with photophobia, phonophobia and vomiting. At admission the physical examination, laboratorial exams and brain computer tomography (CT) were normal. She did not improve with analgesic treatment. On the 5th day she noted horizontal diplopia. Neurological examination revealed a stiff neck, bilateral papilledema, left relative afferent defect, best-corrected vision of 20/30 left eye and 20/25 right eye, visual field defect at right inferior quadrant, slight right sixth cranial nerve palsy. A lumbar puncture with an open pressure of 70cmH2O showed normal CSF analysis. Brain MRI showed stenosis of transverse cranial venous sinus, posterior flattening of the eyeball, and empty sella. Serum blood tests were normal. She was started on oral acetazolamide 10mg/kg/day, keeping asymptomatic. After two months opthalmologic examination showed reduction of the papilledema. Acetazolamide was then discontinued. Conclusion: PTC is rare in pediatric patients, usually secondary. Our case reinforces the link between PTC and SCD. These patients usually have good therapeutic response. Despite the high incidence of SCD in our country, this is the first reported case. Headache is a common symptom in SCD patients. Physicians must be aware of this rare etiology.

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Miscellaneous
ICNC-0792: Anterior Callosotomy in pediatric population: 7 year experience in a non reference center
Introduction: Corpus callosotomy is a surgical option for patients with medically uncontrolled seizures who do not have a unilateral, restricted epileptogenic focus. First introduced in 1940 by Van Wagenen and Herren. Objective: Evaluate the frequency and diagnosis of the subjects submitted to anterior callosotomy, rare for our institution. Methods: We reviewed the surgical preoperative plans scheduled in our institution for the past 7 years, and found that 3 callosotomies were performed, all by the same surgeon (AIT). Retrospective chart review an a descriptive analysis was done. Results: Three cases were found in the retrospective review, 2 females (66.6%), the most common diagnosis was Lenox-Gastaut Syndrome (66.6%) and the other case corresponded to a Rasmussen Encephalitis, originally thought to be an epilepsia partialis continua, but only after surgery final diagnosis was made, parents refuse hemispherectomy, because first surgery was successful. Mean follow-up for these subjects is 22 months, in which 2 subjects are classified as Engel II and one case as Engel IV in the Engel Outcome Score after epilepsy surgery, these 3 cases represent 0.81% of all the surgeries performed by the pediatric neurosurgeon in our institution (AIT) Discussion/Conclusion We found that even when our institution is not a reference center for pediatric neurosurgery, three cases is the expected for the population we attend in 7 years, and that results in seizure control are similar to those found in the larger series.

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ICNC-0351: Clinical, social and demographic profile of primary headache disorder in children
Introduction: Headache is the commonest neurological condition. In the Global Burden of Disease Survey 2010, headache was ranked as the third most prevalent disorder and seventh-highest specific cause of disability worldwide. Epidemiological studies conducted over the last 50 years have shown an increased incidence of primary headaches in children and adolescents, making this disease one of the most frequent reasons for child neuropsychiatric consultation. Recurrent headaches can negatively impact a child’s life in several ways. Due to significant paucity of data from developing countries, specific and lack of public and professional awareness of the headache disorders and their impact, this study was conducted. Methods: The data of all children attending the Headache Clinic were retrospectively reviewed. A total of 65 patients from June 2014 to August 2015 were selected. Data was collected from a predesigned questionnaire containing information on age, sex, social status, clinical features, ophthalmoscopic findings, management, and in selected cases imaging results. The diagnosis of headache type was made according to ICHD III criteria given by International Headache Society. Results: The mean age of headache in children was 12.23 years with relatively older age of presentation among girls (12.74 years vs 11.76 years). The sex ratio was 1.09:1 in favor of boys. Tension type headache (49.23%) and migraine headache (50.77%) were approximately equal in prevalence. Majority of children with headache present late for medical attention. Amongst children with migraine 33.37 % children had migraine with aura. 39.39% of migraine patients and 28.13% of TTH patients had been suffering from it for 1-2 years before reporting to the hospital. Headache was of moderate severity in 69.70%, whereas severe headache was experienced by 29.27% of the children with migraine. Whereas in tension type 46.88% had mild, 46.88% had moderate and only 3.13 % had severe intensity of headache. Throbbing character of headache (51.52%) was most common in migraine while children with tension headache had band/pressure (68.75%) as the commonest character of headache. The children commonly had nausea (66.67%), vomiting (69.70%), as well as photophobia (81.82%) as associated features with migraine headache which were rarely seen in tension type headache. Conclusion: Majority of the patients had waited for 1 to 3 years after onset of headache to seek medical attention. This study has highlighted the need of appropriate and timely diagnosis, effective treatment and prevention of primary headache disorders in children of developing countries.

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ICNC-0352: Botox therapy in pediatric chronic migraine
Introduction: Migraine in children occurs in approximately 6 percent of children and affects school work, extracurricular activities and quality of life. Chronic migraine (>15 headache days per month) is particularly devastating. Although botulinum toxin Type A (BoNTA) has been proven effective for treating chronic migraine in adults, little literature exists about its use in children (3,4). Here, we present the clinical characteristics and treatment response in children with chronic migraines treated with BoNTA at our institution. Method: Retrospective analysis of 27 consecutive migraineurs at a pediatric headache clinic who met IHS III-b criteria for chronic migraine treated with BoNTA injection according to the standardized adult protocol. Those under 18 with included in the analysis. Descriptive statistics and paired t-tests were performed. Results: Participants (n=19) were 15.7 ± 1.6 years old and 79% female. The headaches were precipitated by head trauma in 5 cases. All had failed standard pharmacotherapy including amitriptyline and topiramate. An average of 2.05 ± 1.3 BoNTA injection cycles were performed. Migraine severity decreased significantly from 7.7 ± .99 on a 10 point VAS to 4.84 ± 3.3 (p<.001) and headache frequency from 24.79 ± 7.38 painful days per month to 15.0 ± 11.97 painful days per month (p<.05). One patient developed nausea related to injection; all others tolerated it well with no side effects. Conclusion: BoNTA injection was safe and effective for chronic migraine in our cohort of children recalcitrant to medical therapy. Further research is warranted to evaluate for the long-term safety and efficacy in this population.

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ICNC-0814: Prevalence and incidence of febrile seizures in Korean children using the big data
Background: Febrile seizures (FS) are the most common seizures of childhood, occurring in 2 to 5 percent of children six months to five years of age. But there is no data for prevalence of FS in Korea. The aim of this study was to evaluate the prevalence and recurrence of FS in Korean children using the big data.Methods: The study data were collected from the Korea National Health Insurance Review and Assessment Service for 2009-2013. Patients who had febrile convulsion for main diagnosis were enrolled. The overall prevalence of FS less than 5 years old was estimated and the incidence and recurrence rate of FS was evaluated in children born in 2009. Results: The average prevalence of FS below 5 years old determined by hospital-visiting rate in Korea was 7.0%, 7.68% in boys and 6.28% in girls. The prevalence has a peak between the 2nd-3rd year of life with 27.51%. Monthly prevalence showed FS risk is higher during April to July as 42.3%
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**ICNC-0920: Experiences of Therapeutic Hypothermia for children with refractory intracranial hypertension in a pediatric intensive care unit**

**Background:** Nearly all acute brain damage cause intracranial hypertension and often result in severe neurological dysfunction or death. The use of therapeutic hypothermia (HT) had been recently reported to treat refractory intracranial hypertension in adult with cardiac arrest and neonate with asphyxia. However, the indications and effectiveness of HT in patient during childhood are still unclear. 

**Methods:** During 2013-2014, the severe neurological injured children who received HT in pediatric intensive care unit (PICU) of Kaohsiung medical university hospital were retrospectively analyzed. Clinical characteristics including age, gender, indications of PICU admission and methods of HT were recorded. Long-term sequels, brain imaging, electrophysiological study and mortality rate were also highlighted. 

**Results:** Based on the medical record, total 4 patients (mean age=6.8, SD=6.3) were enrolled. Indications of PICU admission were carbon monoxide intoxication, drowning, encephalitis and shaken baby syndrome. All the patients presented with raised intracranial pressure (IICP) and treated with osmotherapy immediately. HT was initiated while patients presenting refractory intracranial hypertension. All patient survived after HT and received outpatient clinic follow-up for over six months. All patients presented seizure and loss of consciousness during PICU admission. Only one of them developed epilepsy and require long-term anticonvulsants. Besides the patient during infancy, the intelligence (IQ) scores of our patients revealed normal. Brain imaging showed delayed encephalomalacia in most of the patients (3/4). Motor developmental delay were noted in patients during infancy and pre-school age. 

**Conclusions:** HT showed excellent effects in children with refractory intracranial pressure in our report. To our knowledge, this is the first report about the experience of HT for patients with drowning and carbon monoxide intoxication during childhood.
ICNC-0817: The development of an unique expertise system for children with handicaps, developmental disabilities, rare and chronic diseases in Croatia

Introduction: Following the WHO recommendation on need of creating social medical model for persons with disabilities, from the beginning of 2015, unique methodology of determining disability was introduced in Croatia. According to Croatian legislative, experts for measuring disabilities, representatives of medical professions and persons with disabilities generated national concept containing level of impairment, scale for measuring with assessment of functioning. This Regulation contains the separate part for children with handicaps, developmental disabilities, congenital, rare and chronic diseases.

Methods: Data, opinions of second degree of expertises and conclusions of 344 children, aged one to 21 years, were retrospectively elaborated, analysing diagnoses, functional impairments and disabilities.

Results: Between 344 children (47% >7 years of age), diagnoses were 51% congenital disorders, 2% developmental disorders, 9% solid tumours and haematological malignancies, 4% sense disorders, 6% mental disorders, 2% pervasive disorder and 26% acquired diseases. Severe disabilities had 15% of children, moderate 71%, disabilities had slight impact to functioning in 6% and no impact 8%. After expertise 59% of children received personal disability allowance, 10% child allowance, 10% status of a parent caregiver, 14% maternity and childbirth allowance, 7% allowance for assistance and care.

Conclusion: Analyses of second degree of expertises showed great utility and efficacy of this unique methodology in Croatia to help children with functional impairments and disabilities. Collaboration was good among people working in health, education and social service sectors. More effort must be done to obtain more precise medical and social data necessary for expertise that is more appropriate.

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ICNC-0818: Effect of elevated temperature on immediate neurodevelopmental outcome in term neonates with Hypoxic-ischemic encephalopathy

Background: Among term infants, hypoxic–ischemic encephalopathy due to acute perinatal asphyxia remains an important cause of neurodevelopmental deficits in childhood. Treatment is currently limited to supportive intensive care, without any specific brain-oriented therapy. Objective: To determine whether the risk of death or moderate/severe impairment in term infants with hypoxic-ischemic encephalopathy increases with relatively high skin or rectal temperature occurring between 12 and 72 hours of birth. Methods: This was an prospective observational study done in NICU of Dhaka Medical College Hospital and Dhaka Shishu Hospital, Dhaka. Asphyxiated newborns who came within 12 hours of birth was enrolled in this study. Both axillary and rectal temperatures were recorded 6 hourly for 72 hours and each infant’s temperature for each site were rank ordered. Then mean of all axillary and rectal temperature of each neonate was done. Outcomes were related to temperatures in logistic regression analyses for the elevated/relatively high temperatures and normal/low temperatures group, with adjustment of the level of encephalopathy and gender.

Results: The mean axillary temperature was 36.07 ± 6.10°C and 25.71%, 11.92% and 6.32% of all temperatures were >37°C, >37.5°C and >38°C respectively. The mean rectal temperature was 36.8 ± 60°C and 43.53%, 30.02% and 19.97% of all temperatures were >37°C, >37.5°C and >38°C respectively. Mean ambient temperature was 26.17°C. There was significant correlation between axillary and rectal temperature (r= 0.889). For elevated temperature, the odds of death or moderate to Severe impairment was increased 8.9 fold (CI 0.96 – 88.18 ) and the odds of death alone was increased 4.6 fold (CI 0.373 – 56.83). The odds of impairment was increased 1.84 fold (CI 0.45 – 7.50) . In multiple developmental domains, the odds of Primitive reflex, Gross motor, Fine motor, Cognition and Vision were increased 2.2, 2.27, 2.33, 2.28 and 1.97 fold respectively. Whereas the odds of Death , Hearing and Seizure were increased 3.66 (CI 1.04 – 12.90), 4.39 and 6.94 ( CI 1.75 – 27.41) fold respectively.

Conclusion: Relatively high temperature during usual care after hypoxic-ischemia in term neonates were associated with adverse neurodevelopmental outcomes. Early identification of NDIs and immediate intervention may reduce the severity of functional disability.

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ICNC-0819: Sleep duration at one year and intelligence scores at age six years

Introduction: Sleep is thought to be involved in brain plasticity and endogenous stimulation, therefore potentially playing a significant role in brain development. Identifying the relationship between sleep duration and intelligence scores is an important step towards understanding the mechanisms underlying these processes.

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role in child cognitive development. However, the association between the duration of sleep and intelligence among children is controversial. This study aimed to analyse the association between short sleep duration and performance in estimated intelligence scores among participants in a birth cohort. Methods: Of 4231 children recruited at birth, sleep duration at 1 year and intelligence scores at 6 years of age were available from 3433 children. Children who slept less than 11 hours per 24 hours at age 1 year were considered short sleepers. Estimated intelligence was measured through the Wechsler Scale. IQ scores were standardized into z-scores and low IQ defined as z < −1. Data were adjusted for socioeconomic and demographic characteristics. Results: Prevalence of short sleep duration was of 2.8% (95% CI 2.3-3.4), and that of low intelligence scores at age 6, of 17.6% (95% CI 16.3-18.9). In crude analysis, short sleepers at age 1 showed a 59% increase in risk of lower IQ at age 6 (PR=1.59; 95% CI 1.14-2.23; P=0.007). After adjusting for socioeconomic conditions, maternal schooling, child sex, skin colour, birth weight, gestational age at birth and duration of breastfeeding, the positive association remained at 56% (PR=1.56; 95% CI 1.09-2.23; P=0.015). Conclusion: In this longitudinal study of child health, short sleep duration at 1 year of age was associated with 56% increased risk of low performance in intelligence scores 5 years later.

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Miscellaneous

ICNC-0820: Mother-child bed-sharing and psychiatric disorders at the age of 6 years

Background: Little is known about the effect of bed-sharing with the mother over the child mental health. The objective of this study was to investigate the association of bed-sharing and psychiatric disorders at the age of 6 years. Methods: Population-based birth cohort conducted in Pelotas, Brazil. Children were enrolled at birth (n= 4231) and followed-up at 3 months and at 1, 2, 4, and 6 years of age. Bed-sharing was defined as ‘habitual sharing of the bed between the child and the mother, for sleeping, for part of the night or the whole night’. Trajectories of bed sharing were calculated using a group-based modelling approach. Mental health was assessed using the Development and Well-Being Assessment (DAWBA) instrument that generates psychiatric diagnosis according to ICD-10 and DSM-IV criteria. Strength of association was estimated by multivariate logistic regression. Odds ratios (OR) with 95% confidence intervals were calculated. Results: 3583 children were analyzed. Four trajectories of mother-child bed-sharing were identified: non-bed-sharers (44.4%), early-only (36.2%), late-onset (12%) and persistent bed-sharers (7.4%). In the adjusted analyses persistent bed-sharers were at increased odds of presenting any psychiatric disorder (OR= 1.7; 1.2-2.5) and internalizing problems (OR= 2.1; 1.4-3.1), as compared to non-bed-sharers. Among the early-only bed-sharers OR for any psychiatric disorder was 1.4 (1.1-1.8) and for internalizing problems 1.6 (1.2-2.1). Conclusion: Bed-sharing is a common practice in infancy and childhood in our setting and may impair the child mental health. Reasons for bed-sharing need to be uncovered in future research.

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Miscellaneous

ICNC-0821: Cardiac evaluation and iron state in children with breath holding spells

Objective: We aimed to non-invasively assess cardiac performance and iron state in infants and children with BHS and detect those at risk of arrhythmia or asystole. Methods: The study included 40 infant and children experiencing BHS and a group of age and sex matched control group. The work up done included lab investigations (Hb, S.Iron, TIBC), 12-lead ECG with calculation of QT, QT dispersion, P-wave dispersion and T- wave dispersion, echocardiography and 24hrs ECG recording . Results: Sixty five % of the studied children had cyanotic and 35% had pallid spells, lasting between 25-90 seconds and repeated once to 60/month. There was statistically significant lower Hb and serum iron levels and higher TIBC in the study group compared to control group. Also, higher QT dispersion and T-wave dispersion were recorded in patients with BHS. Dysrhythmia (PVC) and bradycardia developed in 4.8% of patients. Thirty seven episodes of BHS were recorded and there were statistically significant higher duration of bradycardia, lowest heart rate during attack and higher occurrence of dysrhythmia in cyanotic spells. Patients with prolonged or frequent spells seem to be especially at risk for arrhythmia or significant bradycardia. Conclusion: Our study supports the suggestion of autonomic dysfunction in BHS, whether pallid or cyanotic. Patients with BHS, especially those at risk, may require further evaluation for evaluation of life threatening events especially asystole and arrhythmia. Iron deficiency may play a role in this autonomic dysfunction.
and investigation for iron deficiency seems to be appropriate in patients with BHS.

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Miscellaneous
ICNC-0762: Efficacy and safety of everolimus treatment in tuberous sclerosis complex: Lithuanian experience

Introduction. Tuberous sclerosis complex (TSC) is characterized by non-malignant tumors in different organs, which can provoke life-threatening complications. The mammalian Target of Rapamycin (mTOR) inhibitor everolimus (Ev) is a new treatment option for patients with TSC which can help avoid surgical treatment and dangerous consequences of these tumors. Long-term treatment with Ev may be related to potential side effects. The aim of our study was to analyze the safety of everolimus use in children. Results. Eight patients are currently on Ev treatment due to subependymal giant cell astrocytoma (SEGA) and/or renal angiomyolipomas (AMLs) for the mean period of 16.75 (±10.78) months. Age at treatment initiation was 12.5 (±3.85) years. The maintenance Ev dose range was 2.5-7.5 (mean 5 ±1.89) mg, plasma levels 2.12.8 (5.58 ± 3.79) μg/L. Reduction of SEGA, AML and adrenal tumors have been observed while the size of hepatic and cardiac tumors remained unchanged. Self-limited 7 adverse events have been observed in 4 cases: stomatitis (1 case, twice), transient diarrhea soon after dose intake (1 case), acne (1 case, exacerbation twice). Frequent vomiting within several weeks possibly related to Ev has been observed in one female patient and resolved after dose decrease 4 months later. Dysmenorrhea requiring contraceptive use for 3 months (same patient) resolved successfully. Chronic hyperlipidemia was observed in 1 case, and fever for 3 days without any obvious source of infection (1 case). Conclusion. Treatment with Ev is related to transient and self-limited adverse effects.

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Miscellaneous
ICNC-0822: Childhood neurological disorders in a Child and Adolescent Mental Health (CAMH) Unit: Improving access to child neurology services through integration of child health services

BACKGROUND Childhood neurological disorders constitute an important cause of childhood morbidity and mortality. Dearth of child health services is a major contributory factor. Development of integrated child health services could enhance availability of services, facilitate access to these services and improve outcomes with these disorders. OBJECTIVE To assess the prevalence of childhood neurological disorders seen in a Child and Adolescent Mental Health (CAMH) Unit. METHOD A review of new attendees seen, between January 2014 and June 2015, at the CAMH unit of a psychiatric hospital. Attendees’ age, sex and diagnosis using the ICD 10 classification were assessed. RESULTS A total of 1,105 new attendees were seen during the study period with an age range of 0.5 years to 20 years. There was a male preponderance (638, 57.7%). Majority (338, 30.6%) were in the early adolescent (10-14 years) age group while under-fives (0-4 years) constituted the least (128, 11.6%) number of attendees. Most (857, 77.6%) of the attendees had childhood neurological disorders. Epilepsy was the commonest childhood neurological disorder (600, 70%) and commonest (600, 54.3%) diagnosis among the attendees. The other major diagnoses were schizophrenia (74, 6.7%), mental retardation (71, 6.4%), acute psychotic disorder (60, 5.4%), cerebral palsy (60, 5.4%), and attention deficit hyperactivity disorder (56, 5.1%). CONCLUSION Childhood neurological disorders constituted a majority of the disorders diagnosed among new attendees in the CAMH unit. This underscores the need to develop the integration of child neurology services and other related specialist services in order to improve availability and access to required services in settings such as ours.

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Miscellaneous
ICNC-0823: Neuroblastoma Mediastinal presented as Kinsbourne Syndrome (Opsoclonus myoclonus) in a child one year old

Summary A case is presented, a child one year 2 months of age with neuroblastoma that debuted with Kinsbourne syndrome (opsoclonus myoclonus), posterior mediatinal location, which improved significantly after surgical removal occurs. The frequency, location, format and treatment is discussed. Keys words: children, neuroblastome, thorax, Kinsbourne, opsoclonus, mioclonus
Due to personal and familial reasons and depression in October 2013, she ingested single simultaneously 80 pills.

In 2006, she had been diagnosed with Familial Mediterranean Fever, and managed from colchicine 0.5 mg three times a day.

Introduction: There are rare reports of acute poisoning with colchicine for suicide purposes. Main concern is, that the cases of deaths due to colchicine poisoning are caused by multiple organ failure. In cases of colchicine poisoning the target organ is also a neuromuscular system. Case Description: The patient was 17 years old female 40 kg weight, which in 2006 had been diagnosed with Familial Mediterranean Fever, and managed from colchicine 0.5 mg three times a day. Due to personal and familial reasons and depression in 2013 in October she ingested single simultaneously 80 pills.
colchicine (40mg). The patient was hospitalised into YSMU "Muratsan" University Hospital, Clinic of Toxicology and Pediatric Reanimation for further investigations and treatment. Results: The initial presentations were nausea, vomiting, diarrhea, abdominal pain, polyuria. After next days of admission clinic of toxicology she developed generalized tonic-clonic seizures, which were turned epileptic status due to hyponatremia. After develops aphthous stomatitis, myopathy (rhabdomyolysis), alopecia. Blood examination revealed a hyponatremia, alkalosis, thrombocytopenia, hyperenzymemia (ALT, AST, LDH, CPK), increased level of creatinine, ammonium, with an urine test was detected proteinuria, microhematuria. CT of the brain identified the presence of subcortical lesions, decrease of density in the frontal, temporal and occipital lobes. Conclusion: The patient was diagnosed intentionally colchicine poisoning due to suicidal purpose, multiple organ failure, alkalosis, epileptic status with generalized tonic-clonic seizures, hemostatic dysfunction - Disseminated Intravascular Coagulation. Obtained treatment of the patient - tracheal intubation with respiratory and cardiovascular measures control, stomach lavage every 6 hours with adopting charcoal, platelet transfusion 3 dose, fresh frozen plasma (FFP), intravenous thipental and phenobarbital injections, antibiotics, corticosteroids, symptomatic measures. After 15 days she was discharged home in stable condition, with antiepileptic continuous treatment.

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Miscellaneous

ICNC-0826: Febrile Convulsions - vit-d preventable condition
OBJECTIVE; Febrile seizures occur in young children at a time in their development when the seizure threshold is low, frequent during various bacteria , viral infections which results in higher temperature. A possible role of endogenous pyrogens, such as interleukin 1 beta, and vit-D by increasing neuronal susceptibility is documented. I have observed that children in 1-3 years of age group, who lack supplementation with oral VIT D, likely to suffer from febrile convulsive episodes then on regular supplementation with Vit D. Present life style drawback the urban populations with lacking sunlight exposure and increasing environment pollution ...

METHODS; 30 children from a community between the age group of 1-3 years were included in the Present study who had one or more episodes of febrile convulsions during last 6 months. The parents were interviewed about their general health, respiratory illnesses, food habits, vaccination status and supplementation with Vit D and parental attitude towards it were noted. RESULT; Parents of 3 (10%) of study group A, has given history that their kids were regularly given Vit D supplementation, Whereas 27 (90%) parents study group B were not aware and not been given any vit D supplementation. It was noted that in group A, ALL 3 (100%) of kids had mild flu like illness. Where as in group B, ALL KIDS had flu like symtoms but with medical intervention requirement. Non of children studied were immunized against flu. All children were from middle socio economic strata and healthy
CONCLUSION The hypothesis that cytokines network is activated by inyrtleukin 1 beta and role of Vit D as febrile seizures preventable is debatable. The present study suggests that incidence of febrile seizures is much less in children who has given Vit D supplementation Thus conclude that further elaborative and large studies may be helpful in establishing preventive role of Vit D

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Miscellaneous

ICNC-0355: Pediatric Mixed Headache - The relations between Migraine and TTH
Objective: To assess the relations between pediatric migraine and TTH. Methods: Children presenting with headache to three hospital's pediatric neurologic clinics in the last 5 years were assessed. 262 children, 5-18 years of age, who met the criteria for migraine were included. Results: Of 262 children (54% female) who had migraine, 26.2% had Migraine with aura. 59 children (24.5%) complaint that beside their Migraine headache, they had also headaches that met the criteria for TTH – Mixed headaches. Females were more than 2.8 times as likely to experience Mixed headaches compared to males (OR: 2.81, 95% CI: 1.43-5.54; p<.003). Multiple logistic regression analysis revealed that older age (p<.02), family history of aura (p<.02) and (lack of) TTH (p<.02). Children who had Migraine with aura were less likely to have mixed headaches than children who did not have aura (OR: 0.26, 95% CI: 0.11-0.63; p<.003). Conclusions: TTH and migraine without aura in children might be part of a continuum which can explain the high incidence of their co-occurrence as opposed to migraine with aura.

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ICNC-0961: Nitrazepam induced drooling and aspiration in children with infantile spasms

Objective: Nitrazepam is an antiepileptic drug used in several types of epilepsy, including Infantile Spasms (IS). Airway hypersecretion, especially in children, has been reported, and may cause aspiration and pneumonia. The objective of this study was to systematically evaluate the relationship of nitrazepam and airway hypersecretion in children with epilepsy.

Method: This was a retrospective study conducted at our University Hospital. Data was collected from clinical files and follow up visits. Inclusion criteria were: age younger than 18 years-old, diagnosis of IS, and current use of nitrazepam. The data was compared with a disease control group of epileptic patients without current use of any benzodiazepine.

Results: Eighteen patients were included (11 boys, age between 6 months and 6 years-old, mean = 2.5 years-old). The disease control group had 16 patients (11 boys, age between 1 and 6 years-old, mean = 3.3 years-old). Six (33%) patients in use of nitrazepam presented airway hypersecretion, as opposed to none in the control group. Conclusion: Hypersecretion is frequent in patients with IS in use of nitrazepam. The risk of serious pulmonary complications should be carefully evaluated before prescribing this drug.

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ICNC-0827: Development and validation of modified INCLEN diagnostic instruments for epilepsy and neuromotor impairments in children aged up to 18 years

Introduction: There is shortage of specialists for the diagnosis of children with epilepsy and neuromotor impairments, especially in resource limited settings. Existing INCLEN (International Clinical Epidemiology Network) instruments were validated for children aged 2-9 years. The current study validated modifications of the same including wider symptomatology and age group. Methods: The Modified INCLEN tools were validated by a team of experts by modifying the existing tools (2-9 years) to widen the age range from birth to 18 years and include broader symptomatology in a tertiary care teaching hospital of North India between January and June 2015. A qualified medical graduate applied the candidate tool which was followed by gold standard evaluation by a Pediatric Neurologist (both blinded to each other).

Results: A total of 197 children (128 boys (65%) and 69 girls (35%)) with a median age of 62.5 months (IQR:20-106 months), completed the study. The sensitivity, specificity, positive and negative predictive value, positive and negative likelihood ratio of the modified epilepsy tool were 91.5% (84.5-96.1), 88.6% (80.0-93.5), 89.7% (81.9-95.3), 90.8% (83.7-95.7), 8 (6.6-9.8) and 0.09 (0.07-0.12) respectively. The sensitivity, specificity, positive and negative predictive value, positive and negative likelihood ratio of the modified neuromotor tool were 90.4% (82.6-95.5), 94.5% (88.7-98.7), 95.5% (88.9-98.7), 90.3% (82.4-95.5), 19.9 (12.1-32.6) and 0.13 (0.08-0.12) respectively. Conclusion: The new modified diagnostic instruments for epilepsy and neuromotor impairments are simple, structured and valid instruments covering the entire pediatric age (from birth to 18 years) for use in resource limited settings with acceptable diagnostic accuracy.

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ICNC-0828: Validation and Indian adaptation of the adapted ASQ-3 (Ages and Stages Questionnaire) as a developmental screening tool as compared to reference standard tool (DASII- Developmental Assessment Scale for Indian infants) in at risk Indian children 2 to 24 months of age

Introduction: Studies indicate that parents can be reliable and valid sources of information regarding their child's current developmental status, when compared with professionally administered test.1,2 The Ages and Stages Questionnaire (ASQ) is a parent completed questionnaire used for estimation of the developmental status of infants and young children from four to sixty months of age. The aim of the current study was Hindi adaptation of ASQ in at risk Indian children under 2 years of age and evaluate its diagnostic accuracy compared to gold standard DASII (Developmental Assessment Scale for Indian Infants). Method: The study was conducted in a tertiary care teaching hospital in North India. In the first step, 13 age-wise questionnaires of the English version of Ages and Stages Questionnaire -3rd revision (ASQ-3) were translated into Hindi and their face validation was done by a panel of experts. Subsequently a total of 196 infants underwent assessment by ASQ followed by DASII. Those performing DASII were blinded to the scores of Indian...
adaptation of ASQ-3 and vice versa. Results Overall, Indian adaptation of ASQ-3 showed sensitivity, specificity, positive and negative predictive value, positive and negative likelihood ratio of 86.4%, 70.8%, 80%, 2.97 and 0.19 respectively. The overall diagnostic accuracy (percentage agreement) was 80%. Conclusion Indian adaptation of ASQ-3 is a valid parent completed questionnaire for identifying at risk children for developmental delay with an acceptable level of diagnostic accuracy.

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Miscellaneous

ICNC-0829: Role of ultrasound skeletal muscle in assessment of hypotonic children; a pilot study
Introduction Patients presenting with hypotonia is a common problem in paediatric neurology practice. Electrophysiological studies, used for diagnosis, are painful procedures which require active cooperation from the child which is difficult to obtain. Ultrasound muscle is a painless, quick, non-invasive and readily reproducible investigation. The current study assessed the feasibility of ultrasonogram skeletal muscle for screening hypotonic children. Methods The current study was conducted in a tertiary care teaching hospital in north India. A standard operating procedure (SOP) was developed for performing ultrasound of skeletal muscle in upper and lower limbs in 5 patients initially. Subsequently, in patients up to 12 years of age, presenting with hypotonia in whom a definitive topographical diagnosis has been reached, ultrasound skeletal muscle was done according to the SOP. The ultrasonologist was blinded to the diagnosis of the cases. Results Out of 65 children enrolled, 16 had central while 49 had peripheral hypotonia. Mean age of the patients was 6 ± 3.65 years. Thirty eight children with peripheral hypotonia had abnormal USG scans while the remaining 11 had normal USG scans. All 16 children with central hypotonia had normal USG scans. Muscle ultrasonography could differentiate between patients with central and peripheral hypotonia with a sensitivity of 77.55%, specificity of 100%, positive predictive value of 100% and a negative predictive value of 59.26%. Conclusions This pilot study established the feasibility of ultrasound skeletal muscle for screening children with hypotonia. Studies should be planned in future for assessing its role in individual subtypes of hypotonia.

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Miscellaneous

ICNC-0799: Is pulse Intravenous Methylprednisolone of benefit in the treatment of traumatic optic neuropathy?
Traumatic optic neuropathy (TON) is an uncommon cause of severe visual impairment. There is no consensus on treatment. We present two children with TON. Case 1 is a 7 year-old healthy boy that fell from a slide onto the left side of his head, 12 days before admission to our hospital. Vision loss was recognized by ophthalmologist 2 hours after injury. Brain computerized tomography (CT) scan was normal. Neurological examination revealed vision reduced to light perception in the left eye, weak pupillary light reflex and relative afferent pupillary defect (RAPD). Other neurological findings and orbito-cranial magnetic resonance imaging (MRI) study were normal. Case 2, a 9 year-old boy with a history of depression who fell from bike and hit the left side of his head 1 day before admission. Bilateral vision loss was recognized 15 minutes after injury. Neurological examination revealed total vision loss with no light perception, but weak pupillary light reflex with positive RAPD in the left eye. Brain CT and MRI were normal. Orbital MRI showed hyperintensity in left optic nerve on T2-weighted images. Pulse intravenous methylprednisolone (30 mg/kg/day) was administered to both patients for 5 days. After treatment, the first patient was able to count fingers from 30 cm; the second patient had light perception and normal visual evoked potentials Improvement in both patients’ vision, despite the long delay in case 1, may support the use of steroids in TON.

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ICNC-0764: Neurologic complications of CD19 chimeric antigen receptor (CAR) T cell therapy in pediatric B-cell ALL patients

CAR T cell therapy treats cancer by modifying the patient’s own T cells with a chimeric antigen receptor designed to target the malignant cells. CAR T cells directed against the B cell antigen CD19 are in promising clinical trials for B cell malignancies, but a high frequency of neurologic complications has been noted. We conducted a retrospective chart analysis of all pediatric patients treated at a single center from 2013 to 2015 as part of a clinical trial of CD19 CAR-T cells for refractory or relapsed B cell acute lymphoblastic leukemia (ALL). CSF and serum from patients with neurologic complications was analyzed for CAR T cell persistence and cytokine levels. 18/36 patients (50%) had neurologic complications such as delirium, headache, seizures, and altered consciousness. 60% of patients who had MRIs showed abnormal imaging findings, most frequently increased T2 signal in the periventricular or subcortical white matter, brainstem, and cerebellum. CAR T cell persistence in the CSF was common, and the peak of neurologic symptoms coincided with the peak in inflammatory markers. The novel pattern of neurologic dysfunction, imaging findings, and cytokine elevations as a complication of CAR T cell therapy overlaps with other inflammatory syndromes that can affect the CNS, such as sepsis associated encephalopathy, macrophage activation syndrome/hemophagocytic lymphohistiocytosis, as well as posterior reversible leukencephalopathy syndrome. Understanding the biology of the complications in CAR T cell therapy may be a step toward targeted therapies.

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ICNC-0921: Impact of selective glucocorticoid receptor blockade on hippocampal neurotrophic response to micro-Fluid Percussion Injury and on histological and cognitive outcome

Impact of selective glucocorticoid receptor blockade on hippocampal neurotrophic response to micro-Fluid Percussion Injury and on histological and cognitive outcome Background: TBI is a major cause of mortality and morbidity. Cognitive sequelae have been attributed to hippocampal selective vulnerability. Interactions exist between glucocorticoid and hippocampal neurotrophin responses that may be neuroprotective. Aim: To investigate the impact of pre-injury blockade of Mineralocorticoid (MR), and Glucocorticoid (GR) receptors on neurotrophic response and histopathological and cognitive outcomes post-TBI. Methods: Adult Male Wistar rats were pre-treated with MR antagonist, Spironolactone; GR antagonist, Mifepristone; or Vehicle, one hour before micro-fluid percussion (MFP) or sham-injury. Four hours post-MFP, expression of mRNA to Brain Derived Neurotrophic Factor (BDNF), Neurotrophin-3 (NT-3), Neurotrophin-4/5 (NT-4/5), and receptors TRK-B, TRK-C and p75NTR, was assessed by in situ hybridization. Histological outcome was assessed 48 hours post-MFP by H&E & TUNEL staining and antibody testing to apoptotic (Caspase-3, PARP-1) and anti-inflammatory (Annexin-1) mediators. Semi-quantitative analysis was performed by two blinded observers. Spatial memory was assessed by T-Maze. Results: In situ hybridization studies (n=36) demonstrated FPI increased ipsilateral hippocampal BDNF, NT-4/5 and TRK-B mRNA (p<0.001;p=0.041;p<0.0001) and reduced NT-3 mRNA (p=0.01), especially in dentate gyrus (DG). Significant injury-drug interaction for BDNF mRNA was seen in DG (p=0.009), Mifepristone attenuating FPI-induced up-regulation. Histopathological analysis (n=72) demonstrated neurodegeneration in ipsilateral hippocampal sub-regions CA1, CA3/2, CA3c, inferior DG (iDG), superior DG (sDG) and dentate hilus (DH) post-MFP, compared to sham-injury (p=0.008;p=0.059;p=0.015;p=0.002;p=0.001;p=0.002). Histopathological studies showed little hippocampal apoptotic change, but FPI-induced apoptotic changes and increased Annexin-1 were seen in ipsilateral cortex. Neuronal degeneration was significantly lower in FPI/Mifepristone rats, compared to FPI/Vehicle, in CA3/2 (p<0.001), CA3c (p<0.001), iDG (p=0.03), and sDG p=0.01). Cortical neuronal degeneration was significantly higher in FPI/Spironolactone rats than other groups (p=0.015). FPI impaired T-Maze performance 24 and 48 hours post-injury (p=0.001;p=0.02). Mifepristone rats performed better than other FPI groups, but differences were non-significant. Conclusions: Mifepristone significantly reduces hippocampal neurodegeneration post-FPI, not explained by neurotrophin up-regulation.

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ICNC-0830: Efavirenz as a cause of Ataxia

Introduction: Acute ataxia in childhood is often caused by toxin ingestion. With the increasing number of paediatric patients on antiretroviral medication we are seeing more side effects of these drugs. We report two separate cases of efavirenz toxicity causing ataxia. Methods / Case Description: Two case reports of patients who presented with an acute onset of ataxia. Both children where HIV positive and had been on ART for the past year. Both cases were investigated
for possible causes of ataxia but the persistent ataxia, with no cause identified, made us consider possible medication toxicity. CNS symptoms are the most frequently reported side effects in HIV positive patients on efavirenz. Although ataxia has not previously been described, we did efavirenz levels in light of the CNS propensity of the drug. Results: Efavirenz level was 69,110 ng/mL for the first case and 16,274ng/mL for the second (Ref 1,000ng/mL – minimum target trough concentration). Analysis was performed using liquid chromatography–tandem mass spectrometry. Conclusion/Discussion: A child presenting with ataxia may pose a diagnostic dilemma. After excluding the common causes, including toxins, infection and tumours, one needs to look more carefully for a possible genetic cause. We conclude that the cause of ataxia in both of our patients was attributable to the high plasma concentration of efavirenz. In both cases, the efavirenz level was at least 4 times greater than the toxic level (4,000ng/mL) described by Manzoni et al and the ataxia improved when the drug was discontinued.

Marc Hauptfleisch

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ICNC-0765: Lower SNAP25 level detected by multiple microarray systems and its functional significance in Medulloblastoma

Medulloblastoma (MB) is the most common pediatric malignant brain tumor and patients with a high-risk or recurrent MB respond poorly to current therapies, with higher related mortality. Potential molecules related to MB must be identified to develop targets for therapeutic development. In the present study, we compared MB microarray data obtained using different microarray systems and significant targets were selected by gene annotation and enrichment analysis. Genes for soluble Nethylmaleimide-sensitive factor attachment protein receptors (SNAREs) annotated with the function “vesicle” were identified and one of these proteins, synaptosomal-associated protein 25 (SNAP25), had significantly lower expression levels in MB. In addition, SNAP25 was detected in a very low number of MB cells according to western blot analysis and immunohistochemical analyses of archived and formalin-fixed/paraffin-embedded human MB specimens. We found that SNAP25 could increase the dendritic spike density and the chemotherapeutic effect of arabinofuranosyl cytidine (Ara-C) on SNAP25-expressing MB cells. In conclusion, a SNARE complex that includes SNAP25 is crucial for normal neuronal functions and impaired neuronal functions may impede targeted chemotherapy. The detection of SNAP25 expression in MB cells may be essential for the chemotherapeutic application of Ara-C.

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ICNC-0831: Type I interferon response induced by transfected self DNA

[Introduction] Viral nucleic acids are recognized by RNA or DNA sensors and trigger type I interferon (IFN) responses. In contrast to well-characterized RNA sensors, the mechanisms underlying DNA sensing are relatively obscure. In addition to membrane-bound Toll-like receptors, many intracellular DNA sensors have been identified and include molecules associated with DNA damage repair such as meiotic recombination 11 (MRE11). In previous reports, exogenous DNA or synthetic DNA has been used as a ligand, but our study presents the type I IFN production by transfection of genomic DNA. [Methods] Genomic DNA was extracted from immortalized mouse microglia cell line (MG6) and dsDNA was transfected with lipofectamine into MG6. Type I IFN production was analyzed by quantitative-PCR, ELISA and cell viability by cytotoxicity assay and flow-cytometric detection of annexin-V and 7-AAD. [Result] While naked DNA showed no response, DNA transfected by lipofectamine into MG6 induced production of CXCL10 in a dose-dependent manner and expression of IFN- stimulated genes including OASL2 and RSAD. DNA transfection also caused decreasing living cells and increasing LDH and number of apoptosis cells. Chemical inhibitors of ATM and MRE11 did not affect CXCL10 production from MG6. [Conclusion] These results suggest that transfected DNA is recognized by intracellular DNA sensors. Not only pathogen-derived but also improperly localized self DNA triggers type I IFN response. Both ATM and MRE11 do not seem to play central roles in DNA sensing.

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ICNC-0833: Post herpes NMDAR encephalitis in a 8th month old girl

Introduction: Patients with Herpes Simplex Virus Encephalitis can relapse with a second phase of encephalopathy with
fever, seizures and often with a florid choreoathetoid movement disorder. It is a true relapse only in one fourth of cases and an autoimmune encephalitis in greater majority. There is a myriad of symptoms namely psychiatric symptoms, seizures, movement disorders and autonomic instability having phenotypic similarities to the choreo athetosis in relapsing HSVE.7 N-methyl-D-aspartate receptor (NMDAR) antibody encephalitis, a well characterized encephalopathy syndrome is the most likely culprit Case Report: A previously healthy 8 month old child presented with fever and seizures. On examination, she was afebrile with low GCS and had partial seizures over her left arm intermittently. LP done showed a TLC of 10 with predominantly lymphocytosis and raised proteins. Herpes PCR was positive for HSV 1. MRI Brain was abnormal showing diffuse involvement. A working diagnosis of acute necrotizing encephalomyelitis was made. Acyclovir was added along with AEDs. She was administered IVIG for two consecutive days. Condition started improving; after almost 2 weeks of therapy she suddenly developed choreoathetoid movements and started going downhill clinically. Repeat MRI showed progression of disease and repeat CSF after three weeks of Acyclovir had Herpes PCR negative but was positive for NMDAR antibodies. Acknowledgement: Dr Josep Dalmau and Dr Thais Armanegue Salvador Key Words: autoimmune encephalitis NMDAR encephalitis HSV

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Miscellaneous

ICNC-0766: Vincristine induced peripheral neuropathy – clinical course and early insights into natural history and pathophysiology
Vincristine induced peripheral neuropathy – clinical course and early insights into natural history and pathophysiologyIntroduction: Peripheral neurotoxicity is a well described adverse effect of vincristine, a chemotherapeutic agent frequently used to treat childhood cancer. While there is evidence to suggest that vincristine induced peripheral neuropathy (VIPN) can be long lasting 1-3, very little is understood about its natural history or pathophysiology.Methods: Prospective, longitudinal follow up of patients on vincristine aged 2-18 years, newly diagnosed with Acute Lymphoblastic Leukaemia, were undertaken. Each patient had comprehensive neurotoxicity assessments, at baseline and at multiple pre-determined time points during their treatment, with clinical and neurophysiological measures utilising novel nerve excitability techniques. Results: 10 patients aged between 2 and 14 years had a minimum of four neurotoxicity assessments during the intensive phase of their chemotherapy treatment. Patients received a median of 8 doses of vincristine (total 12mg/m²), frequently co-administered with corticosteroids. 90% of patients developed early motor deficits by the second assessment (fourth dose of vincristine) and 40% became non-ambulant. Only 20% articulated sensory symptoms. Suppression or absence of lower limb deep tendon reflexes was seen in 80%. All patients had concurrent alterations in their sensory and motor axonal excitability parameters of threshold electrotonus and subexcitability without any significant change in sensory or motor amplitudes. Clinical and neurophysiological changes were more evident during periods of high vincristine dose density.Conclusion: Clinical and electrophysiological changes in nerve function occur early during treatment with vincristine with a prominent motor manifestation in the paediatric age group. The pattern of changes in axonal excitability may provide insights into the underlying mechanisms for VIPN.

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Miscellaneous

ICNC-0356: A study of headaches in children admitted to Hospital (RHSC)
BackgroundHeadaches are common in children aged 0-15 years¹. Management of paediatric headaches has been deterred by differences in presentations and classification, which causes delayed diagnosis, unnecessary investigations and poor outcome². There are few studies published about headaches involving children admitted to hospital.ObjectivesTo identify correlating clinical presentations of headaches, based on subsequent investigations undertaken, and treatment outcomes in an in-hospital population.MethodsA retrospective study was conducted on children with headache admitted to the RHSC in 2012. Electronic TRAK records were analysed to determine patient demographics, clinical presentation, investigations conducted and management for each individual patient. Statistical analysis was carried out using Fisher’s exact test, odd’s ratio and confidence interval measurements. ResultsAverage age of diagnosis was 11.4 years, with increasing incidence at older age groups. Headaches affected males in the younger age
group compared to females in the older agegroup. Co-morbidity was associated in 58.4% of children, commonly presenting with either spina bifida (9.68%) or hydrocephalus (16.1%). Nausea and vomiting (47.2%) were commonly associated with symptoms of headaches. Headaches were investigated with the use of MRI imaging (34.0%). The most commonly preferred treatment was propranolol alone or a combination of pizotifen and propranolol.

Discussion/Conclusion The audit on headaches clearly identified gender differences, its distribution among varying age groups, associated co-morbidities and common symptoms, in the patient population admitted to hospital with a headache. Guidelines can be developed by analysing the outcome following the initiation of the commonly used treatment in headaches. (244 words)


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Miscellaneous

ICNC-0835: Hypoglycemia in a child with episodic spontaneous hypothermia

Introduction: Episodic spontaneous hypothermia is a rare condition, occurring in isolation or associated with corpus callosum agenesis. Hypothermia seems to be the hallmark, followed by hyperhidrosis and autonomic symptoms. Case report: We report the case of 4-year-old male with episodic spontaneous hypothermia with hyperhidrosis and pallor responsive to sugar replacement. Initially, the episodes would occur twice a year with each lasting 3-4 hours and were self-limited in nature. Patient had normal EEG, EKG, ECHO, hormonal and metabolic studies in between episodes. Episodes resolved until 6 years, when they recurred at higher frequency. Triggers included beginning of the school year with stress and emotional disturbance. During the hypothermia, body temperature dropped to 35°C and blood glucose was measured in 20-33 mg/dl, returning to normal after the episodes. Repeat hormonal studies, abdominal US and brain MRI were normal. During the next few episodes, patient was given a tablespoon of honey diluted in the water, which aborted the spell or significantly shortened the duration of these episodes. At age 10, patient continues to do well with rare episodes and normal neurodevelopment. Summary: Our pediatric patient with episodic hypothermia had classic features with hyperhidrosis and autonomic symptoms. In addition, hypoglycemia was also found during the attacks, though unclear if this was primary or secondary in origin. Hyperinsulinaemia as a potential mechanism has been reported in the literature. At 5-year follow-up, our patient has the favorable response to the treatment with sugar replacement and normal development. Neurological Outcomes in Critically Ill Infants with Seizures Anna Mrelashvili 1, MD, Eileen Broomall 2, MD, Katherine C. Nickels 3, MD, Lily C. Wong-Kisiel 3, MD, William A. Carey 4, MD, Suresh Kotagal 3, MD, Elaine C. Wirrell 3, MD, Eric C. 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Payne 3, MD 1 Division of Pediatric Neurology, University of South Carolina, Columbia, SC, USA 2 Division of Neurology, University of Cincinnati, Cincinnati, OH, USA 3 Division of Child and Adolescent Neurology, Mayo Clinic, Rochester, MN, USA 4 Division of Neonatal Medicine, Mayo Clinic, Rochester, MN, USA Neurological Outcomes in Critically Ill Infants with Seizures Anna Mrelashvili 1, MD, Eileen Broomall 2, MD, Katherine C. Nickels 3, MD, Lily C. Wong-Kisiel 3, MD, William A. Carey 4, MD, Suresh Kotagal 3, MD, Elaine C. Wirrell 3, MD, Eric C. Payne 3, MD 1 Division of Pediatric Neurology, University of South Carolina, Columbia, SC, USA 2 Division of Neurology, University of Cincinnati, Cincinnati, OH, USA 3 Division of Child and Adolescent Neurology, Mayo Clinic, Rochester, MN, USA 4 Division of Neonatal Medicine, Mayo Clinic, Rochester, MN, USA Background: Continuous video-electroencephalography monitoring (cEEG) remains the gold standard for seizure diagnosis and quantification in infants with critical illness, and may help to predict long-term neurological outcomes. Aim and Methods: We reviewed critically ill infants (0-4 months) who underwent cEEG at Mayo Clinic between 2010 and 2013. We sought to evaluate predictors of favorable long-term neurodevelopment, including seizure freedom. Results: Of 72 patients identified, 45 (62%) were male. At the time of cEEG, their median conceptional age was 40 weeks (IQR 38.5-42.0). The median duration of cEEG monitoring was 45 hours (IQR 23.0-86.2). Forty-nine (68%) infants were monitored in the neonatal ICU and 23 (32%) in the pediatric/cardiac ICU. The most common etiologies included ischemic or hemorrhagic stroke (n=18, 25%) and acute hypoxic-ischemic encephalopathy (n=18, 25%). Forty-two patients (58%) had electographic seizures and 19 (26%) had status epilepticus. The majority of patients with a clinical correlate (n=28, 67%). Seizures were identified within the initial 30 minutes of cEEG recording in 33 (79%) infants. Among infants who experienced seizures, 37 (88%) underwent follow-up.
with a pediatric neurologist at a median of 23.0 months (IQR 9.0-37.0). Thirty- one (84%) were seizure-free and 26 (70%) were off all antiepileptic medications. Normal neurodevelopment was only reported in 13 (35%) infants. Motor (n=xx, xx%) and cognitive (n=xx, xx%) deficits were frequent. Discussion: Seizures were common among our critically ill infants and cEEG was essential to their diagnosis. However, most infants were seizure-free and off antiepileptic drugs at last follow-up, although most had suffered long-term neurodevelopmental sequelae Neurological Outcomes in Critically Ill Infants with Seizures Anna Mrelashvili 1 , MD, Eileen Broomall 2 , MD, Katherine C. Nickels 3 , MD, Lily C. Wong-Ksisel 3 , MD, William A. Carey 4 , MD, Suresh Kotagal 3 , MD, Elaine C. Wirrell 3 , MD, Eric C. Payne 3 , MD 1 Division of Pediatric Neurology, University of South Carolina, Columbia, SC, USA 2 Division of Neurology, University of Cincinnati, Cincinnati, OH, USA 3 Division of Child and Adolescent Neurology, Mayo Clinic, Rochester, MN, USA 4 Division of Neonatal Medicine, Mayo Clinic, Rochester, MN, USA Background: Continuous video-electroencephalography monitoring (cEEG) remains the gold standard for seizure diagnosis and quantification in infants with critical illness, and may help to predict long-term neurological outcomes. Aim and Methods: We reviewed critically ill infants (0-4 months) who underwent cEEG at Mayo Clinic between 2010 and 2013. We sought to evaluate predictors of favorable long-term neurodevelopment, including seizure freedom. Results: Of 72 patients identified, 45 (62%) were male. At the time of cEEG, their median conceptional age was 40 weeks (IQR 38.5-42.0). The median duration of cEEG monitoring was 45 hours (IQR 23.0-86.2). Forty-nine (68%) infants were monitored in the neonatal ICU and 23 (32%) in the pediatric/cardiac ICU. The most common etiologies included ischemic or hemorrhagic stroke (n=18, 25%) and acute hypoxic-ischemic encephalopathy (n=18, 25%). Forty-two patients (58%) had electrographic seizures and 19 (26%) had status epilepticus. The majority experienced electrographic seizures without clinical correlate (n=28, 67%). Seizures were identified within the initial 30 minutes of cEEG recording in 33 (79%) infants. Among infants who experienced seizures, 37 (88%) underwent follow-up with a pediatric neurologist at a median of 23.0 months (IQR 9.0-37.0). Thirty-one (84%) were seizure-free and 26 (70%) were off all antiepileptic medications. Normal neurodevelopment was only reported in 13 (35%) infants. Motor (n=xx, xx%) and cognitive (n=xx, xx%) deficits were frequent. Discussion: Seizures were common among our critically ill infants and cEEG was essential to their diagnosis. 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Forty-nine (68%) infants were monitored in the neonatal ICU and 23 (32%) in the pediatric/cardiac ICU. The most common etiologies included ischemic or hemorrhagic stroke (n=18, 25%) and acute hypoxic-ischemic encephalopathy (n=18, 25%). Forty-two patients (58%) had electrographic seizures and 19 (26%) had status epilepticus. The majority experienced electrographic seizures without clinical correlate (n=28, 67%). Seizures were identified within the initial 30 minutes of cEEG recording in 33 (79%) infants. Among infants who experienced seizures, 37 (88%) underwent follow-up with a pediatric neurologist at a median of 23.0 months (IQR 9.0-37.0). Thirty-one (84%) were seizure-free and 26 (70%) were off all antiepileptic medications. Normal neurodevelopment was only reported in 13 (35%) infants. Motor (n=xx, xx%) and cognitive (n=xx, xx%) deficits were frequent. Discussion: Seizures were common among our critically ill infants and cEEG was essential to their diagnosis. However, most infants were seizure-free and off antiepileptic drugs at last follow-up, although most had suffered long-term neurodevelopmental sequelae

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hippocampus. Results: Two days after KA administration, few clusterin-immunoreactivity (IR) was detected in the hippocampus of the KD-fed mice, while strong clusterin-IR was found in the ND-fed mice. By Western blotting, we also found that KD diminished nCLU protein accumulation in the hippocampal neurons (relative density 0.98 ± 0.17 vs. 4.16 ± 0.84 A.U., P < 0.01). Conclusion: These results suggest that KD has neuroprotective effects via preventing the apoptotic death signals through diminishing the nCLU accumulation in the KA-induced seizure mouse model.

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Miscellaneous
ICNC-0358: Predicting responsiveness to Topiramate as preventive treatment for pediatric Migraine
Introduction: The purpose of this study is to find factors related to response of Topiramate as a preventive medication for pediatric migraine.Method: One hundred-thirteen patients who were 7 year-old and older that received topiramate for longer than 3 months as a preventive treatment for migraine, were included. Response to treatment was defined as decline of headache frequency more than 50% compared to that of pre-treatment period. Factors including intensity, frequency, duration, sex, pre-treatment duration, associated symptoms, family history, significant disability in everyday life, were assessed.Results: Seventy patients (62%) showed good response to topiramate. Patients who reported significant disability in everyday life, responded better (73% vs. 52%, p=0.035). Sex, intensity, frequency, duration, pre-treatment duration, onset age, treatment duration, and presence of associated symptoms did not show statistically significant correlation to treatment response. Headache was more intense (p=0.035) and nausea (p=0.027), photophobia (p=0.028), and visual symptoms (p=0.033) were more frequent in patients who reported significant disability in daily activity.Discussion: Migraine characteristics and associated symptoms were not related to treatment response with topiramate in patients with pediatric migraine. However, patients with significant disability in everyday life showed better response even though their limitation to daily activity was more severe. These patients should be actively considered for prophylactic treatment with topiramate.

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Miscellaneous
ICNC-0359: EEG characteristics and diagnostic value in childhood headache-multi-center study
Introduction Epilepsy and migraine are frequently observed in comorbidity, with the occurrence of one disorder increasing the probability of the other. If patients with headache have visual aura, EEG is performed to differentiate from occipital lobe epilepsy. The authors evaluated the characteristics of EEG depending on the type of headache and the usefulness of EEG in patients with headache Method We conducted a retrospective analysis by reviewing medical records of 259 patients who visited the department of pediatrics of Pusan, Yonsei, Hyallym, Chonnam, and Chosun University hospital from April 2011 to March 2013. The headaches were classified according to the ICHD- II. We evaluated clinical characteristics of headache such as type of headache, frequency, duration, location, severity, and family history. EEG was analyzed in relation to the type of headache Results There were significant differences in the frequencies of abnormal EEG findings according to the type of headache. Migraine with aura patients had the most frequent abnormal EEG findings (24.4%) comparing with other headache types. Overall, there were normal EEGs 228 (88%) and 31 (12%) abnormal. Epileptiform discharges were noted in 17 of 31 abnormal EEG studies. Of the 17 patients with epileptiform discharges, 9 patients had focal spikes and 8 patients had generalized spikes respectively. Finally, only one patient was diagnosed as focal epilepsy. Conclusion We concluded that headache patients selectively need to undergo EEG examination, especially patients who have atypical aura, to differentiate from focal epilepsy.

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Miscellaneous
ICNC-0357: Headaches in the pediatric emergency departments in Cheongju, Korea
Seventy four children visiting the ED in the tertiary care hospitals in Cheongju, Korea were enrolled from October 1, 2013 to September 30, 2014. There were 34 boys (45.9%) and 40 girls (54.1%). Their ages ranged from 3 to 18 years with the
mean age being 13 years. There were 34 migraines (45.9%), 27 tension headache (36.5%), 3 secondary headache (4.1%), 2 seizure-related headache (2.7%), 1 headache with hydrocephalus (1.4%), 1 concussion (1.4%), and 1 headache with subdural hematoma (1.4%). Twenty eight children (37.8%) had 1 headache symptom and 28 children (37.8%) also had 2 headache symptoms. Duration of symptoms within 2 hours had the highest number of patients, which were 31(41.9%), and then, 11 pediatric patients (14.9%) had within 2-4 hours. Twenty nine patients (39.2%) had a headache once in a month, 20 patients (27.0%) had 1 to 14 headaches per month, 4 patients (5.4%) had more than 15 headaches per month. Forty three children (58.1%) took nonsteroidal anti-inflammatory drug (NSAID) for treating headache, 3 children (4.1%) took antiepileptic agent. Average strength of headache is 7.37±1.79. Children with migraine took NSAID (34 patients; 45.9%), acetaminophen (19 patients; 25.7%), and Topiramate (1 patient; 1.4%). There were 23 children (31.1%) with headache from parieto-occipital area, 16 children (21.6%) from occipital area, 9 (12.2%) from frontal area, 4 (5.4%) from global area, and 6 (8.1%) from uncertain location. There were 31 (41.9%) with pulsating headaches, 18 (24.3%) with squeezing headaches, 5 (6.8%) with stabbing headaches, and 11 (14.9%) with uncertain nature.

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Miscellaneous

ICNC-0360: Two cases of an unusual cause of headache and papilledema not to be missed

Introduction: Chronic headache is a frequent reason for referral to pediatric neurologists. Rarely, but important, history and clinical findings can lead to the diagnosis of a genetically determined, treatable form of headache caused by chronic meningitis/inflammation. Case description: 2 children aged 5-6 years presented with chronic headache, spontaneously resolving fever periods and papilledema. One child, furthermore, had a chronic monarthritis of the left knee (bacterial arthritis/osteomyelitis excluded), the other child showed a non-pruritic rash and wakening since birth. Both children had elevated cerebrospinal fluid opening pressures (CSFOP) with 30 cm H2O and 32 cm H2O, respectively. In one child, audiological investigations showed a mild to moderate sensorineural hearing impairment. Molecular genetic testing for periodic fever syndromes revealed mutations in the NLRP3-Gene in both. Both patients responded to treatment with acetazolamide and canakinumab with disappearance of headaches, normalization of CSFOP and hearing impairment. Conclusion/discussion: In both patients with slightly different phenotypes, the diagnosis of chronic infantile neurologic, cutaneous and arthritis syndrome (CINCA), the most severe form of the cryopyrin-associated periodic syndromes (CAPS), was confirmed. Affected patients may present with chronic central nervous system and inner ear inflammation, episodic fever, a neutrophilic rash and arthritis. CINCA typically occurs sporadically with de novo mutations of the NLRP3-gene, which encodes for a protein involved in IL-1β-activation. In attempt to prevent end organ damage with IL-1β-blocking therapy, early diagnosis of CINCA in patients with headache and/or papilledema is crucial.

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Miscellaneous

ICNC-0768: Neurologic manifestations of systemic childhood malignancy

Neurologic manifestations and complications are often observed in non-neurologic malignancies in children. Objective: To study the relative prevalence, type, etiology and outcome of neurologic manifestations in systemic malignancy. Methods: A prospective follow up of new patients over one year and retrospective analysis of case records of last 5 years was done at a Pediatric Oncology centre treating all systemic (non neurologic) malignancies which is part of national retinoblastoma registry. Results: A total of 1572 patients (311 prospective, 1261 retrospective) of pediatric malignancies were enrolled. The most common malignancies seen were acute lymphoblastic leukemia (ALL=461; 29.3%), retinoblastoma (198, 12.6%), renal tumours (145, 9.2%), acute myeloid leukemia (AML = 144, 9.2%) and Hodgkin’s disease (129, 8.2%). Neurologic manifestations were seen most commonly in retinoblastoma (17.1%), AML (16.6%), neuroblastoma (16.6%), Ewing’s Sarcoma (16.1%) and Langerhans Cell Histiocytosis (14.2%). Although ALL had 9.1% patients with neurologic involvement, they accounted for the largest number (42). The common neurologic diagnoses in ALL were intracranial bleed (6), chemical meningitis (6), central nervous system relapse (6), cerebral (3) or cerebellar (1) atrophy, neuropathy (3), neurocysticercus granuloma (2), reversible posterior leuocencephalopathy (1) and brain abscess (1), while in 12 patients no diagnosis was reached. In retinoblastoma the common neurologic diagnoses were brain metastasis and intracranial extension. Spinal metastases were common in neuroblastoma, Ewing’s and AML.

Conclusions: Neurologic manifestations in malignancy can be unrelated to the disease (as in neurocysticercus granuloma), or of obscure etiology (as cerebral atrophy), due to infection or secondary to treatment.

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Miscellaneous

ICNC-0837: Epidemiology and neurodevelopmental correlates of Vitamin B12 deficiency in north Indian infants
Vitamin B12 deficiency has been associated with neurodevelopmental disorders in infants and vegetarianism in mother.
Objective: To compute prevalence of vitamin B12 deficiency in hospitalized children 2 -24 months of age and compare
demographic, clinical, dietary and developmental status between those found deficient and sufficient. Methods: The first
3 children aged 2 - 24 months, hospitalized on a predecided weekday were enrolled for study and subjected to a
proforma driven work up. Those on vitamin supplements in the last 2 months were excluded. Vitamin B12 and folate
levels were measured by chemiluminiscence method. Vitamin B12 cut off value <200 pg/ml and folic acid cut off value <3
ng/ml were considered deficient. Neurodevelopmental status was assessed by Vineland Social Maturity Scale.
Demographic data, dietary history of mother and child, anthropometry, clinical features and neurodevelopmental status
were compared between the 2 groups. Results: A total of 91 children (mean age 9.64 +/- 4.42 months; 57.1% male) were
enrolled, of which 17 (18.7%) were deficient. No child was folic acid deficient. Vitamin B12 deficient children were
statistically more likely to be rural, lower socioeconomic status, exclusively breast fed infants of vegetarian mothers with
higher prevalence of anemia and higher mean corpuscular volume but lower mean platelet count. They also had higher
odds of social quotient < 70 (OR=7.8; 95% CI 2.4-24.8; p=0.000) and significantly lower mean DQ (p=0.018).
Conclusions: Clear association of vitamin B12 deficiency with maternal and infant diet and impaired neurodevelopmental
status was found.

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Miscellaneous

ICNC-0922: PGC-1α, a new therapeutic target to resist muscle atrophy after peripheral nerve injury
Introduction: Muscle atrophy is the leading cause of disability after peripheral nerve trauma (PNT). Annual incidence is
approximately 45 cases per 100000, similar to the incidence of epilepsy. (1) To retard the atrophy on going is an important
work for the clinical physicians. The transcriptional coactivator peroxisome proliferator-activated receptor γ coactivator-1α
(PGC-1α) is one of the best recognized regulators of mitochondrial biogenesis. (2,3) In this work, we investigated
the involvement of PGC-1α in sciatic nerve axotomy-mediated skeletal muscle wasting. Furthermore, we investigated
whether the administration of Pyrroloquinoine quinone (PQQ), PGC-1α activator, prevented denervation-induced protein
degradation. Methods: The C57BL6/J mouse was subjected to a hindlimb sciatic axotomy. APQQ-containing osmotic
pump was implanted subcutaneously into the right lower abdomen of the mouse. In the time course study, the mouse was
sacrificed and the gastrocnemius muscle was prepared for analysis. Results: We observed that PQQ administration abolished
the denervation-induced decrease in muscle mass and reduced mitochondrial activities, as evidenced by the reduced
fibersize and the decreased expression of cytochrome c oxidase and NADH-tetrazolium reductase. The protein levels of
PGC-1α and the electron transport chain (ETC) complexes were also increased by treatment with PQQ. Bioenergetic
analyses demonstrated that PQQ reprogrammed the denervation-induced increase in the mitochondrial oxygen
consumption rate. Furthermore, PQQ administration highly enhanced the expression of oxidative fibers and maintained
the type II glycolytic fibers. Conclusion: This pre-clinical in vivo study suggests that PQQ may provide a potent therapeutic
benefit for the treatment of denervation-induced atrophy by activating PGC-1α and maintaining the mitochondrial ETC complex in skeletal muscles

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Miscellaneous

ICNC-0838: The clinical characteristics of Syncope in children
Purpose: It is important but difficult to determine the cause of syncope with loss of consciousness (LOC) in children who
visit ER or outpatient clinic. The aim of this study is to identify the causes and the clinical features of syncope. Methods:
This is a retrospective study of patients who visited ER or pediatric neurology outpatient clinic with symptoms of syncope
with LOC. A search of medical record from March 2009 to February 2015 at Catholic University of Korea, Seoul St.
Mary’s Hospital was used. Patients with underlying disease or patients whom did not take the exam were excluded. The electroencephalogram (EEG), head up tilt test (HUTT), Brain MRI, electrocardiography (ECG), chest x-ray and lab results were analyzed. Results: A total of 106 patients, with a mean age of 13.05 ± 2.30 years (range, 8-18 years), was included in the study. Out of 106 patients, 46 patients (43.4%) were male and 60 (56.6%) patients were female. The causes of syncope were identified; 46 patients (43.4%) with unknown causes, 28 patients (28.3%) with vasovagal syncope (VVS), 22 patients (20.8%) with abnormal EEG findings, 4 patients (3.8%) with cardiovascular problem, 2 patients with neurovascular, 2 patients with systemic disease, and 2 patients with both VVS and EEG abnormal findings. Patients with unknown causes had suspicious history of psychologic problem, migraine, BPPV. Among 28 VVS patients, 19 patients showed mixed type in HUTT, 7 with vasodepressor type and 2 with cardioinhibitory type. Among 22 abnormal EEG group, 19 showed partial seizure and 3 with generalized seizure. 6 of 22 abnormal EEG patients were diagnosed as epilepsy and had AED treatment. There was no significant difference in etiology between ER and outpatient clinic. Brain MRI showed normal in 82 patients (77.4%). Conclusion: HUTT and EEG are simple, noninvasive diagnostic tools for distinguishing syncope from epilepsy in children and should be considered early in the diagnostic plan. Children with abnormal EEG findings can be easily misdiagnosed as epilepsy, therefore, regular follow up and observation are necessary. There was no significant difference in etiology between ER and outpatient clinic. Moreover, there was no significant difference in duration of LOC and associated symptoms before syncope between VVS and abnormal EEG. Brain MRI does not help in determining the causes of syncope.

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Miscellaneous

ICNC-0839: Polysomnographic analysis of sleep problems in children with epilepsy
Introduction: Patients with epilepsy frequently report sleep problems and sleep disorders are known to be more common in the patients than general population. There have been few studies investigating sleep disorders in children with epilepsy based on polysomnography. Purpose: The objective of this study was to identify the characteristics of sleep disorders in children with epilepsy complaining of sleep problems, and find out sleep-related factors influencing on the prognosis of epilepsy. Methods and Patients: We retrospectively reviewed medical records and polysomnographic data of 94 children (mean age 13.7 ± 3.8 years), who visited tertiary university hospital for epilepsy between March 2001 and December 2014. The patients were evaluated with polysomnography and questionnaire of sleepiness. We compared the clinical characteristics between the patients with and without sleep disorders. We analyzed the difference of sleep parameter between the prognostic groups of epilepsy. Results: The patients enrolled in this study complained of various sleep problems, such as snoring, mouth-breathing, excessive daytime sleepiness, and insomnia. Sleep disorders were diagnosed in 46 patients (48.9%). Obstructive sleep apnea was the most common sleep disorder (n=26), followed by narcolepsy (n=8), periodic limb movement disorder (n=8), and delayed sleep phase disorder (n=6). Patients with poor prognosis showed decrease of stage 3-4 NREM sleep (p=0.010). There was no significant difference in the prognosis of epilepsy between the presence of sleep disorders and seizure control (p=0.053). Conclusion: Various sleep complaints and sleep disorders are commonly found in children with epilepsy. Active evaluation of sleep problems adopting screening sleep problems and diagnostic test with polysomnography is needed in all pediatric patients with epilepsy.

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Miscellaneous

ICNC-0769: Cerebellar medulloblastoma. Clinical case
Background: Medulloblastoma is a most common pediatric malignant primary brain tumor originating in the part of the brain that is towards the back and the bottom, on the floor of the skull, in the cerebellum or posterior fossa. Methods: Clinical case. Clinical, neurological and neuroradiological studies were conducted. Results: a girl, 5 years old was admitted to the hospital in the NICU with complaints of impaired consciousness, fever, cough, shortness of breath, noisy breathing, vomiting. From the age of four she became irritable, moody. Constipation and occasionally vomiting were evaluated for pathology of the gastro-intestinal tract. She was twice admitted to hospital to the gastroenterology department with the diagnosis: "Chronic widespread gastritis, acetonemic vomiting syndrome". Girl's condition worsened: vomiting became more frequent, appeared general weakness, cough, noisy breathing, shortness of breath. She was urgently taken to hospital in the NICU. Neurological status: consciousness, soporous, sluggish response to the inspection. Nystagmus in extreme abduction more to the left. Brain MRI: a giant formation of the posterior cranial fossa with obstructive hydrocephalus. The diagnosis: "Cerebellar medulloblastoma". Conclusions: children are often arrive in neurological and neurosurgical hospital in the late stage of the disease when the tumor is large. Such children before admission to a specialized hospital are screened in somatic hospitals about gastritis, hepatitis, worm infestation, rickets, hydrocephalus, meningitis, meningoencephalitis. We need to take into account symptoms such as unreasonable irritability, moodiness, lack of communication, change in nature and the most important thing you need to properly
differentiate vomiting of central genesis.

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Miscellaneous

ICNC-0923: Severe brain trauma increases pneumonia susceptibility in children requiring intensive care
Introduction: Emerging evidence suggests extra-thoracic trauma may alter the lungs’ responses to infection, increasing the risk of developing pneumonia. It remains unclear if brain trauma increases the risk of pneumonia in children. Aim: To determine the incidence of pneumonia in children with brain trauma requiring intensive care. Methods: A retrospective study was conducted in a single paediatric intensive care unit (PICU) over a 3 year period (01/04/2011 to 31/03/2014). 26 patients were admitted to the PICU with isolated brain trauma over this time. A pre-designed pro forma was used to collect data which included GCS at the scene and in the Emergency Department, duration of stay in the PICU, duration of ventilation, evidence of pneumonia and its timing in relation to the injury, CT head findings, requirement for invasive intracranial pressure (ICP) monitoring and evidence of seizure activity while in the PICU. Results: Median age on admission was 6 years (range: 18 days – 14 years 7 months). Median length of stay was 6.5 days (range: 2 – 16 days). Of the 26 patients studied, 13 had evidence of pneumonia. All of the patients with evidence of pneumonia had stayed in the PICU more than 3 days (p<0.05, Fisher’s exact test). 15 children had ICP monitoring. 11 of those with ICP monitoring developed pneumonia. Conclusion: Significantly more brain trauma patients who stayed over 3 days in the PICU or had ICP monitoring developed pneumonia. Further study is required to determine the reasons that these patients are more prone to developing pneumonia.

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Miscellaneous

ICNC-0840: Response inhibition is altered in extremely preterm children studied with Magnetoencephalography
Introduction: Neuronal sensorimotor alpha-oscillations are thought to reflect changes in the excitability of the sensorimotor cortex: lower oscillation levels indicate increased and higher levels decreased cortical excitability. We studied with magnetoencephalography (MEG) how a go/no-go task with tactile stimulation of fingers affects sensorimotor alpha-oscillations in 6-year-old extremely preterm (EPT) children. Methods: Whole-head MEG of 23 EPT children (gestational age <28 weeks) and 23 fullterm (FT) children (gestational age 37-42 weeks) was recorded during semi-random tactile stimulation to left index or little finger in two conditions. In the TASK-condition subjects squeezed a toy with the right hand after little finger stimulation (go) and retained from squeezing after index finger stimulation (no-go). In the REST-condition they ignored the stimuli and listened to a story. The amplitude level of sensorimotor alpha-oscillations in three post-stimulus time-windows within 1700 ms was calculated for analysis. Results: Both groups showed post-stimulus suppression of the sensorimotor alpha-oscillations similar to that reported in adults, in the right (contralateral-to-stimulus) hemisphere in both conditions. In the FT group, the effect of retaining from squeezing after the index finger stimulation in the TASK-condition was reflected in enhanced oscillation level compared with the REST-condition in the left (contralateral-to-squeeze) hemisphere, especially during the later time-windows (p<0.05). Interestingly, the EPT group did not show this effect. Discussion: We suggest that the enhanced sensorimotor oscillations in the left hemisphere when retaining from squeezing reflect motor response inhibition. The lack of this effect in EPT children may reflect altered brain mechanisms underlying active response inhibition.

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Miscellaneous

ICNC-0362: Exome sequencing in two family trios to identify relative importance of novel genes and to explain migraine inheritance
Introduction: Migraine is common neurological disorder that affects ~10% of world’s population. The etiology of migraine is extremely complex; most likely caused by combination of genetic and environmental risk factors. Increased prevalence of migraine in women could be partly caused by genes located in X-chromosome. Several potential autosomal and X-linked genes for migraine have been suggested using GWAS, unfortunately it often explains a small percentage of heritability of common diseases. The aim of this study is to discover possible novel genetic risk factors; also to some extent describe the inheritance pattern. Methods: Family-based design is used in this study to locate genes that underlie
migraine. Two family trios (proband and two first-degree relatives – biological parents) were included in study. Both probands (one diagnosed with migraine with aura, another migraine without aura) and both female relatives have been diagnosed with migraine according to International Classification of Headache Disorders III. Male relatives are healthy individuals without migraine. The exomes of all six participants are sequenced and analyzed. Results: As current study is ongoing, the results are yet to be confirmed. However, we expect to obtain one or few possible novel potential genetic risk factors for migraine and to explain possible relationship between migraine and inheritance. Discussion: Since migraine is known to have a genetic component, any novel genes found could advance the understanding of this disorder. As family-based exome sequencing on migraine has not been used extensively, any this kind of studies could help us comprehend X-chromosome’s part in migraine.

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Miscellaneous

ICNC-0841: Clippers Syndrome: A case report in child

Introduction: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) represents a rare central nervous system (CNS) inflammatory disorder, of unknown etiology, was initially described in 2010. This work aims to report the case of a child with CLIPPERS syndrome. Case description: An 11-year-old male child, developed progressive gait ataxia, dysarthria, diplopia and weakness over the course of four months, after Epstein-Barr infection. Cerebrospinal Fluid Examination without leukocytes, with elevated protein (85 mg/dl) and positive for oligoclonal bands. Flow cytometry had normal CD4 and CD8, and low CD19 and natural killer cells. Serum immunoglobulin levels features Selective immunoglobulin M (SlgM) deficiency. Antinuclear Antibody and Anti-neutrophil cytoplasmic antibodies (ANCA)s test were negative. Magnetic resonance imaging (MRI) showed the typical pattern of the Clippers Syndrome. It was initiated in February 2014 short course of high-dose intravenous methylprednisolone followed by oral glucocorticosteroids (GCS) with clinical improvement, but without total remission of symptoms. Six months later, due to worsening of the radiological lesions and occurrence of repeated infections (including herpes zoster), monthly immunoglobulin was associated with oral steroids resulting in radio-clinical improvement. Conclusion: CLIPPERS pathogenesis remains poorly understood, its risk factors or triggers need to be further assessed. It is also a recent disease that has been investigated. We believe that our case report could help because it is a paediatric case with some comorbidities that could lead to a better understanding of the disease.

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Miscellaneous

ICNC-0843: Steroid therapy ameliorated cataplexy in three children with recent-onset of narcolepsy

Introduction: Autoimmune mechanism has been hypothesized to underlie the pathogenesis of narcolepsy. Here we reported favorable effects of steroid therapy on three recent-onset children who suffered from narcolepsy with cataplexy. Patients and Methods: Three children showed excessive daytime sleepiness and cataplexy, and were diagnosed as narcolepsy by undetectable hypocretin 1 levels in the cerebrospinal fluids (CSF) and the presence of sleep onset rapid eye movement (REM) period. They are aged from five to thirteen. Polysomnography and multiple sleep latency test (MSLT) were studied in two patients. Prednisolone (1mg/kg/day) was given continuously for 2 or 3 weeks, and tapered gradually. Parents of three patients gave the written informed consent to the unauthorized use of steroids in children with narcolepsy, which was approved by ethics committee. Results: After the treatment with steroid, the sleepiness and cataplexy were ameliorated, though the CSF hypocretin-1 levels unchanged. There were no side effects of steroid except temporary and mild increase of intraocular pressure. Efficacy of steroid lasted for at least one year. The titers of Trib2-specific antibody, one of antibodies which has been reported to be related to the pathogenesis of narcolepsy, were not elevated in all of our patients. We suspected the possibility that steroid effect immune systems and/or hypothalamic-pituitary-adrenal axis. Conclusion: Steroid therapy may be one of the effective treatment for recent onset children with narcolepsy.

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INTRODUCTION The aim of this review is to evaluate the physical, endocrinological disturbances and neuropsychological sequelae in children with posterior fossa tumors (PFT). METHODS We performed a retrospective study reviewing a cohort of patients under 18 years of age diagnosed with PFT over the last five years (2010-2015) in a reference pediatric hospital in Spain. We describe the presence of functional motor impairment, endocrinological disturbances and neuropsychological sequelae. Neuropsychological assessment included four distinct categories: disturbances of executive function, impaired spatial cognition, personality change and linguistic difficulties. RESULTS 64 patients with posterior fossa tumors were included, 47% female and 53% male subjects, diagnosed between one month and 18 years of age. Medulloblastoma accounted for 37% of the patients, followed by low-grade astrocytoma (36%) and ependymoma (20%). There was an 85% survival rate. Functional motor impairment
sequelae were found in 61% of survivors, 27% displayed endocrinological disturbances and 45% exhibited some degree of neuropsychological deficit in at least one the four evaluated categories. DISCUSSION As long-term survival in children with PFT has increased over the last decades, neurological and neuropsychological deficits have become more relevant in terms of functional impact. Endocrinological disturbances also contribute to long-term quality of life. Complete neuropsychological assessment is required to identify cerebellar cognition affective syndrome and provide adequate therapeutic intervention to achieve the best possible outcome for survivors.

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**Miscellaneous**

**ICNC-0846: Septo-optic dysplasia- clinical variability**

The septo–optic dysplasia, also known by Morier syndrome (MS), is a rare congenital entity, with an incidence of 1:10,000. Main findings are hypoplasia of one or both of the optic nerves, brain malformations of the midline and hypothalamic– pituitary dysfunction. Early diagnosis and the establishment of hormone replacement treatment are crucial. This paper describes the clinical findings of five children with septo–optic dysplasia. Clinical cases. We present 5 cases with ages ranging from the first year of life to 17 years with different forms of clinical presentation and neuroimaging (MRI). Further to ophthalmology and endocrinology manifestations, three children had psychomotor retardation and epilepsy. Two of them had no evidence of neurological disease. Only one was diagnosed during pregnancy. Discussion: MS diagnosis is confirmed through blood tests and neuroimaging. Different forms of clinical presentation may be observed. Unfortunately these children are usually diagnosed late in life.

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**Miscellaneous**

**ICNC-0365: Serum pentraxin-3 levels in pediatric migraine patients**

Introduction: Migraine is the most common episodic headache in children. Neurogenic inflammation is the suggested pathogenesis. Pentraxins have been shown to be related to immunologic response in inflammatory diseases. Relationship between migraine and pentraxin-3 has been studied in a few studies. In this report we aimed to analyze the association between clinical and laboratory features of migraine and serum pentraxin-3 levels in pediatric population. Methods: Children with migraine were recruited. Healthy subjects with no headache history served as controls. Patients with known morbidity including anemia, hypertension, hyperlipidemia, diabetes mellitus, obesity were excluded. Serum samples were obtained. The association between serum levels of glucose, insuline, complete blood cell count, CRP, pentraxin-3 and clinical features including age, sex, BMI, disease duration, attack frequency, attack duration, analgesic use, family history, PEDMIDAS score were evaluated. Results: We assessed samples from 31 children(11 boys, 21 girls) with migraine and 20 healthy control(8 boys, 11 girls). There were no significant differences between groups regarding age and gender( p=0.609 and p=0.765 respectively). We found significantly higher pentraxin-3 levels and insuline resistancy in patients with migraine(p=0.001 and p=0.008 respectively). Pentraxin-3 levels were higher in patients with migraine patients than probable migraine patients(p=0.037). Attack duration and pentraxin-3 levels were higher in patients with family history of migraine(p=0.020 and p=0.048 respectively). Other laboratory tests and clinical features did not indicate any statistically significant differences. Conclusion: Pentraxin-3 level measurement in peripheral blood may give help in diagnosing migraine as a biological marker. Future researches in larger patient population are needed.

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**Miscellaneous**

**ICNC-0847: Psychomotor development of infants in treatment for congenital hypothyroidism in the second quarter of life**

Introduction: Congenital hypothyroidism (CH) is an endocrine disorder caused by a hormonal deficiency of the thyroid gland upon birth that can lead to developmental deficits when not treated adequately. The aim of the present study was to analyze cognitive, motor and language performance among infants aged three to six months in treatment for CH. Methods: An observational, cross-sectional study was conducted involving 75 infants: 36 in treatment for CH (mean age: 4±0.9 months) and 39 in the control group (mean age: 5±0.43 months). The CH group was subdivided into ≤28 days and >28 days to investigate the influence of the onset of treatment. The confirmatory serum TSH level was used as the
indicator of CH severity: ≤30uIU/ml and >30uIU/ml. The Bayley Scales of Infant and Toddler Development Third Edition were used for the evaluation of motor, cognitive and language development. The significance level was set to 5%. Results: Significant differences were found between the CH and control groups regarding performance in cognition (p=0.039) and language (p=0.002). Moreover, language was significantly associated with age at the onset of treatment (p=0.008) and confirmatory TSH level (p=0.008). No significant differences between groups were found regarding cognition and motor skills for either of the two variables studied. Treatment in the majority of severe cases was initiated in the neonatal period. Conclusion: Language in infants in treatment for CH was influenced by age at the onset of treatment and confirmatory serum TSH levels.

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Miscellaneous

ICNC-0832: A rare encounter of foot drop as a presenting feature of Type 1 diabetes in a child
Introduction: To describe a case of newly diagnosed diabetic child who presented with a foot drop. Case: A 12 years old girl presented with 10 days history of foot drop to Children assessment unit. There was no history of trauma preceding the foot drop. On detailed history it became evident that she had history of polyuria, polydipsia and weight loss over the period of last 2 months. Her initial assessment showed inability to dorsiflex her right foot with normal planter flexion and no sensory involvement. Her reflexes were normal including ankle reflexes. The rest of her neurological examination was unremarkable. Her blood glucose was 28 mmol along with glucosuria. She had confirmed diagnosis of Type 1 diabetes and was started on subcutaneous insulin. The examination finding was suggestive of Common Peroneal nerve palsy which was confirmed on Nerve Conduction Study. As there is no history of trauma, the most likely reason for her foot drop is Peroneal neuropathy following diabetes. After starting on insulin she started showing improvement for her foot drop. Results: Foot drop commonly presents after trauma in paediatrics population and to our knowledge this is a first case report of type 1 diabetes presenting as a foot drop in Paediatric population, although foot drop is a well recognised presentation of Diabetes in adults. Conclusion: This case highlights the importance of screening for Diabetes in Paediatrics population who presents with isolated foot drop especially when there is no clear history of trauma or any other autoimmune disease.

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Miscellaneous

ICNC-0771: Pediatric Cavernous Meningioma presenting with Ptosis: A case report
To present a case of cavernous meningioma in a young, female. A 1.10 year-old female from Palawan, Philippines who presented with left ptosis. This was followed by inability to move the left eye noted 6 months prior to admission. Magnetic resonance imaging (MRI) with contrast administration revealed a lobulated enhancing mass involving the lateral aspect of left cavernous sinus. The tumor arising from the lateral wall of the cavernous sinus was partially removed via frontotemporopolar craniotomy. The histopathological diagnosis was meningioma WHO grade 1. Repeat MRI displayed partial tumor removal, 5 months after surgery. Intracranial meningiomas in children are rare, representing 1–4.2% of central nervous system tumors and 1.5–1.8% of all intracranial meningiomas. Meningiomas arising from the lateral wall of the cavernous sinus account for less than 1% of all intracranial meningiomas. At present, only two cases of a meningioma arising from the cavernous sinus has been reported in childhood. Though the tumor is slow-growing and progressive. The majority of recurrences are thought to be due to residual tumor in the operative bed, which happen because of fear of causing severe functional deficits, were resection attempted. Meningiomas of all locations have a recurrence rates ranging from 10 to 23%.

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Miscellaneous

ICNC-0366: Effectiveness of Intravenous Dihydroergotamine for treatment of pediatric chronic headache
Text: Introduction: Chronic pediatric headache is a disabling disorder that at times may require inpatient care.1
Intravenous dihydroergotamine (IV-DHE) has emerged as an effective treatment for chronic headache disorders. Positive outcomes were also found in a study examining the efficacy of IV-DHE in pediatric populations. This study provides a further assessment to supplement the literature on the efficacy of an inpatient trial of IV-DHE in pediatric patients.

Methods: A retrospective chart review was conducted on patients admitted for treatment with IV-DHE. 33 patients, age 8-20 years and 81.8% female, accounted for 38 admissions. Discharge status, pain score (VAS), and adverse events were collected. Results: The average VAS at admission was 6.9/10, which decreased to 3.6/10 at discharge. A significant paired difference of 3.3/10 was found (p < .001). At discharge 68% (n = 26) of patients were assigned a status of "improvement," with 26.3% of all patients headache pain-free (i.e. VAS of 0/10) upon discharge. There were no differences in outcomes by headache diagnosis or gender (p > .05). Only one significant adverse event occurred: a visual hallucination in association with the fourth of five doses, however, the patient tolerated the final dose with no adverse events. A majority of patients (65.8%) did experience nausea/vomiting, which was successfully managed by antiemetics.


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**Miscellaneous**

**ICNC-0367: Headache-related disability among school children: A population-based study**

Introduction: Headache is a frequent neurological symptom at school age and recurrent headache have a significant disabling occurrence in children and adolescents such as school absenteeism, decreased extracurricular activities, and poor academic performance, as shown in many studies. In Korea, there have been not population-based studies of headache-related disability in children and adolescents. Objectives: To estimate the headache-related disability and to investigate the relevant predictors of disability due to headaches among school children in South Korea.

Methods: This is a cross-sectional school-based study. We surveyed 5,039 (boys 2405, girls 2634) students aged 6-18. The questionnaires collect demographic data, in addition to specific questions about headache according to International Classification of Headache Disorder criteria, 2nd edition. The disability to participate in desired activity evaluated by using the 6-question Pediatric Migraine Disability Assessment (PedMIDAS). Results: Six hundred sixty six school children and adolescents with headaches (boys 225, girls 441) completed all questionnaires. The percentage of headache sufferers with grade 1 disability was 88.6%. The mean PedMIDAS score was 5.11 ± 11.17. There was a trend towards more severe disabilities in older age groups, especially in the 16-18 year-olds. The migraine students have the highest PedMIDAS scores (6.69 ± 10.66), whereas, the other headache students have the lowest scores (3.81 ± 7.52). The predictors of headache-related disability are intensity (P = 0.028), frequent headache (P = 0.003), and longer duration of symptom before presentation (P = 0.008). Conclusions: There was a trend towards more severe disabilities in older age group. School children with migraine have the greatest headache-related disabilities. The predictors of headache-related disability are intensity, frequent headache, and longer duration of symptom before presentation.

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**Miscellaneous**

**ICNC-0772: Diamond Blackfan Anemia with cerebral germinoma: case report**

Introduction: Diamond Blackfan Anemia (DBA) is a rare genetic disorder characterized by red cell aplasia and congenital anomalies including facial malformations and triphalangeal thumbs. Predisposition to cancer occurs including acute myeloid leukemia (AML) and solid tumors. In 50% of the cases there is a mutation affecting a ribosomal protein gene. We report a unique case of DBA with a cerebral germinoma.

Case report: 13 year-old boy diagnosed at age of 6 months with BDA. Two weeks before admission he complained of headache and vomiting. MRI revealed an enhancing nodular calcified mass in the pineal region. Neuroradiological exam revealed germinoma.

Discussion: Report from de DBA Registry disclosed in 608 patients 18 cases of cancer including 2 AML, 3 adenocarcinomas of the colon, 2 osteogenic sarcomas, 2 breast cancers, 2 squamous cell carcinomas, and one patient each with non-Hodgkin lymphoma, soft tissue sarcoma, uterine cancer, cervical cancer, testicular cancer, choroid meningioma of the lung, and melanoma. So far, about 30 cases of cancer in patients with DBA have been recorded. There were no brain tumors. DBA pathogenesis is linked to mutations of ribosomal protein genes resulting in defective ribosome biogenesis with activation of p53 pathway and consequent apoptosis and cell cycle arrest. Cancer formation from these scheme is somewhat paradoxical and the mechanism for cancer formation is unclear. It is worth mentioning that p53 gene is not mutated in cerebral germinomas. Conclusion: this is the first reported case of germinoma linked to DBA.

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evaluate BPVC diagnostic stability after exhaustive workup. Patients who initially meet International Headache Society (IHS) criteria can change the diagnosis after follow-up. AIM: to evaluate BPVC diagnostic stability after exhaustive workup and during follow-up. MATERIAL AND METHODS: 1)
retrospective study of 37 children with positive BPVC-IHS criteria whose follow-up was three years or more. 2) Initial evaluation: MRI, EEG and BERA with hearing thresholds. 3) Extended evaluation: neurotological periodic exam and as appropriate angioMRI, EEG, multifrequency BERA, inner ear CT, caloric test, cVEMP or otoacoustic emissions.

RESULTS: 1) 9 of 37 patients (24%), 5 men, range 3-7 years, modified initial diagnostic. 2) Newly diagnosis: enlarged vestibular aqueduct 5, focal epilepsy with vestibular symptoms 2, neurovascular compression 1, progressive vestibular failure of unknown etiology 1. 3) Warning signs and symptoms: no migraine history, hyperacusis, positional triggers, multiple daily events, asymmetry rotatory nystagmus, and positional nystagmus. CONCLUSION. Since a minor proportion of initially diagnosed as BPVC children can have alternative diagnosis, a comprehensive neurotological evaluation and carefully follow up may be necessary.

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Miscellaneous

ICNC-0953: Neurologic manifestations at the onset of neurogenic tumors in children

Introduction Neuroblastoma (NB) is the most common extracranial solid tumor of childhood and may cause neurological signs at diagnosis. To provide the analysis of the type and frequency of neurological symptoms at diagnosis in a cohort of the patients with NB treated in federal center in Russia. Methods 244 patients with neurogenic tumors (NB, ganglioneuroma (GN) for the period of 01.2012-12.2014 (36 months) have been analyzed. Neurologic status have been analyzed for all the patients at the time of admission and additional tests were done if it was needed. Results NB was diagnosed in 236/244 (96.7%), GN in 8/244 (3.3%) cases. The median age at diagnosis was 17.8 months (range 0.5-189.3). Male to female ratio was 1:1.1. Epidurial compression (EC) was the most common neurological manifestations (15/244, 6.1%). Opsoclonus myoclonus syndrome (OMS) was the second common presentation (13/244, 5.3%). 8/244 (3.3%) patients had segmental disorder of the autonomic nervous system (Horner's syndrome, local temperature changes). 3/244 (1.2%) of the patients had bilateral blindness associated with optic nerve compression. In 3/244 (1.2%) cases peripheral nerve palsy due to compression of the nerve roots/plexus was noted. Combined disorders were observed in 3/244 (1.2%). 1/244 (0.4%) patient had initial brain metastases (stage 4 NB). Conclusion Neurological symptoms was observed in 46/244 (18.7%) cases with neurogenic tumors at the time of the onset of the disease. The most common symptoms were EC and OMS. Multidisciplinary approach with inclusion of neurologists and neurosurgeons is strongly required in order to provide the most appropriate care.

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Miscellaneous

ICNC-0856: Understanding the gap between developed and resource-poor countries impression of a trainee

Introduction Scientific strides in pediatric neuroscience in developed countries have not been matched by resource-poor countries which bear 80% of the global burden of pediatric neurological disorders. Methods This study reflects the experience of a trainee during a month (January-February, 2015) of attachment at the Pediatric Neurology Unit of a tertiary care hospital in North India. Result: The Pediatric Neurology OPD was a walk-in clinic twice a week, with an average of 300 children per clinic, with all sorts of neurological diseases from all over North India and some cases from East and South India, spanning hundreds/thousands of miles. Three Pediatric Neurologists with a team of 15-20 residents managed all these cases. Cerebral Palsy (CP), developmental delay and epilepsy constituted the major chunk. Majority of these occurred secondary to preventable causes, particularly CNS infections and perinatal complications – including kernicterus and severe birth asphyxia. Neurological emergencies constituted a significant proportion of emergency admissions. While neuroimaging was easily available, genetic and metabolic tests were extremely expensive. The neurologists and the DM trainees did both - clinical work and laboratory procedures. This was a huge contrast from the U.S. where children are brought to sub-specialty clinics and several technicians conduct laboratory procedures. Conclusion There is a huge gap between developed and developing countries. Whereas most patients are in developing countries, investigative and management facilities are in developed countries. The gap could be bridged by facilitating the training of child neurologists from resource limited countries and increasing international collaboration in educational and research activities.

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Miscellaneous

**ICNC-0761: A rare cause of chronic Ataxia in childhood: Ganglioneuroma**

Introduction: Ganglioneuroma is a benign neurogenic tumor that is mostly asymptomatic. Opsoclonus-myoclonus-ataxia syndrome is the most common paraneoplastic neurological syndrome in childhood. On the other hand, only chronic ataxia is very rare. Method: Case presentation.

Case Description: A four year old boy presented with wide-base gait for two years. Neurological examination was revealed gait ataxia. He had no opsoclonus and myoclonus on physical examination. Metabolic screening, electromyelography, cranial neuroimaging findings and apraxia and senataxin gene analysis were normal. As spinal MRI was revealed a mass lesion on right surrenal gland, we obtained abdominal MRI. Abdominal MRI showed the mass lesion with 21x18 mm in diameter with contrast enhancement. Results: After resection of the tumor completely, his gait ataxia resolved in a few days. Pathological examination was revealed as ganglioneuroma.

Conclusion: Although childhood paraneoplastic neurogenic tumors cause acute or subacute ataxia, or other clinical syndromes such as opsoclonus and myoclonus with or without ataxia, ganglioneuroma should be considered in differential diagnosis of chronic childhood ataxias.


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**ICNC-0796: Cortical brain mapping during removal of the tumors located in the central gyrus**

Introduction: To evaluate the effectiveness of the Cortical stimulation mapping (CSM) during the removal of brain tumors, located in the central gyrus.

Methods. CSM was performed to 7 pediatric patients with neoplastic process located in the central gyrus. 5 patients present pathological process located in the precentral gyrus, the rest in postcentral gyrus during the period from 01.01.2015 to 01.09.2015. Intraoperative neurophysiological monitoring was performed by the technique of direct cortical stimulation on with the help of ISIS IOM System (Inomed, Germany) using the SDN electrodes.

Results. Histologically, low-grade gliomas (LGG) were in 5 cases while 2 cases were with high grade gliomas. Mapping of the motor cortex and identification of the pyramidal tract in the area for surgical intervention was performed in all cases. In 4 patients with tumors located in the precentral gyrus were identified parts of the brain responsible for motor function of the body and face which implemented safe approach and its removal. In patients with tumors located in postcentral gyrus, motor responses were not registered. In all cases, the tumor was removed totally, which was confirmed by postoperative MRI/CT. Temporary neurological deficit as mild weakness in the hand occurred in one patient with LGG located in the precentral gyrus. Conclusion. CSM represents a reliable method for removing tumors located in the functionally important areas of the brain, which allows to safe and improve the quality of life.

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**ICNC-0368: Evaluation of Autonomic Dysfunction in pediatric migraine patients**

Introduction: The most important and frequent cause of primary childhood headache is migraine. The pathophysiologic mechanisms of migraine are yet to be understood. The aim of this study is to investigate autonomic dysfunction in pediatric migraine patients.

Methods: Thirty pediatric migraine patients followed in Dokuz Eylul University, School of Medicine, Pediatric Neurology Department and twenty healthy controls were included in the study. In order to evaluate autonomic functions, orthostatic test, 30:15 ratio, cold pressor test, heart rate responses to deep and normal breathing, valsalva ratio, blink reflex, sympathetic skin response tests were used. Results: There were no statistically differences between groups regarding age and sex. Consistently with sympathetic hypofunction, more frequent orthostatic hypotension (p=0.019), negative correlation between average disease duration and orthostatic tests and negative correlation between migraine attack duration and orthostatic tests were found. In consistency with parasympathetic hyperfunction, migraine group had higher valsalva ratio (p=0.035). Regarding the blink reflex, positive correlation between average disease duration and blink reflex R2 and R2' latency was found in the migraine group.

Conclusion: Our study revealed that autonomic nervous system functions are affected in pediatric migraine. Increase in R2, R2' latency along with the increase in disease duration reveals inhibition at interneuron level of brainstem and involvement of polysynaptic pathways.

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Miscellaneous

ICNC-0860: A case of isolated unilateral oculomotor nerve palsy in the presence of ipsilateral maxillary and ethmoid sinusitis

Isolated third nerve palsy is rare in children. A variety of etiologies are reported including congenital, trauma, infection, migraine, vascular, and neoplastic origins. Whether congenital or acquired, third nerve palsy can be associated with serious underlying central nervous system pathology. A previously healthy 13-year-old boy presented to our hospital with binocular diplopia that had developed a day ago. He had no history of trauma and did not complain headache. On physical examination, his left pupil was 7 mm in size and constricted partially to light. His right pupil was 5 mm, and responded normally to light. On lighting to left eye, only right pupil constricted normally. He did not have ptosis on both eyes. He complained about binocular diplopia. On the day of admission, brain MRI and MRA were done, which revealed only left maxillary and ethmoid sinusitis. Lumbar puncture on the hospital day 6 did not reveal any pathologic findings. The patient felt discomfort in right lateral gaze on day 2, and the next day, medial movement of his left eyeball was limited. The authors presumed oculomotor nerve palsy may be due to anatomically adjacent maxillary and ethmoid sinusitis. We started combination therapy of steroid and antibiotics from day 3. On day 5, his left pupil size decreased to 6 mm, responded to light decreasing by 1~2 mm. On day 8, his eyeball movement began to improve. On day 10, he showed normal light reflex and almost full extraocular movement, and was discharged. By the 22th day from symptom onset, he was completely symptom-free. We describe a previously healthy boy who abruptly developed isolated unilateral oculomotor nerve palsy in the presence of ipsilateral maxillary and ethmoid sinusitis, which were rapidly responded and successfully treated with steroid and antibiotics. There was no other abnormality, causing oculomotor nerve palsy except sinusitis. Our case illustrated that ipsilateral ethmoid and maxillary sinusitis may be associated with oculomotor nerve palsy.

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Miscellaneous

ICNC-0861: The acute onset of fever-induced seizures and insomnia with behavioural disturbance: a case of seronegative limbic encephalitis?

Introduction: Limbic encephalitis (LE) is characterized by behavioural changes, psychiatric symptoms and seizures. Antibodies directed against the cell membrane and synaptic receptors have also been reported. Patients with LE without the characteristic antibodies still present a clinical challenge. Identification of new antibodies would lead to understanding their autoimmune etiology and to initiate of immune modulator treatment. We present a seronegative LE case. Case Description: Previously healthy 7-year-old boy had prolonged focal seizures associated with fever followed by short-term memory loss and tendency to sleep with orofacial dyskinesias. He had behavioral changes and sleep disturbances. Neurological examination revealed orientation impairment. Results of his cerebrospinal fluid (CSF) examination were normal with a negative viral PCR panel. CSF culture showed no bacterial growth. His electroencephalography revealed dysrhythmia characterized with slowing on left hemisphere, with periodic lateralized epileptic discharges on both hemispheres independently. However his first cranial magnetic resonance imaging (MRI) was normal, on his second MRI it was prominent increased signal in T2 A sequences on external capsule and bilateral edema in globus pallidum that supported limbic encephalitis. His paraneoplastic survey and limbic encephalitis antibodies were negative. Although he received intravenous immunoglobulin and pulse methylprednisolone therapies, symptoms did not improve. Any convulsions and behavioural changes had not been observed after exchange plasmaferesis. His conscious and EEG findings got better. Control cranial MR was reported normal after starting treatment 3 weeks later. Discussion: Diagnosis of seronegative limbic encephalitis is challenging in children, because of misleading presentations. Early diagnosis and appropriate treatment of this disorder may prevent sequelae.

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Miscellaneous

ICNC-0862: TRIB3 promotes endoplasmic reticulum stress-mediated cortical neuronal apoptosis in recurrent febrile seizure rats

Abstract: Febrile seizure (FS) is one of the most common types of seizures in childhood. Although it is well known that recurrent FS can result in brain injury, the underlying mechanism of brain injury during febrile seizures has not been...
clearly elucidated. Recent studies indicated that ERS can increase the expression of tribbles-related protein 3 (TRIB3), which thus binds to and inhibits the kinase activity of AKT, an important factor for cell survival. In this study, we examined whether ERS, TRIB3, and AKT signaling is involved in the cortex injury following recurrent FS. Recurrent FS was induced in Sprague-Dawley (SD) rats by using a heated water-bath. Seventy-five rats were divided into three groups: control group, hyperthermia-treated group without FS as FS control (FC group), and recurrent febrile seizure group (FS group). TdT-mediated dUTP nick-end labeling (TUNEL) assay was performed to assess cortex apoptosis, and electron microscopy was used to examine neuron ultrastructural changes in hippocampal CA1 region. Protein expression and localization of TRIB3, glucose-regulated protein 78 (GRP78), and CCAAT/enhancer-binding protein homologous protein (CHOP) as well as AKT activation level was examined by using Western blot and double immunofluorescence staining. As compared with control, apoptosis of cortex was significantly induced in FS group, not FC groups. Abundance of TRIB3, GRP78 and CHOP were remarkably elevated, while phosphor-AKT decreased significantly in cortex of rats with recurrent FS. Double co-localization staining indicated that phosphorylated AKT was not detected in cells with induction of TRIB3 in FS rats, while detected in cells without TRIB3 expression in the control and FC groups. Taken together, these results show that recurrent FS may induce injury of cortical cell by interfering with AKT activation through ERS-mediated up-regulation of TRIB3.

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Movement disorders

ICNC-0530: Spinocerebellar ataxia 27 (SCA 27): description of the clinical phenotype of two twin sisters with a deletion in the FGF14 gene

Introduction: Spinocerebellar ataxias are neurodegenerative syndromes, with spinocerebellar ataxia type 27 (SCA 27) as a rare cause of ataxia in families. The gene involved in the pathogenesis is the FGF14 gene. Case description: We present two twin sisters with episodic ataxia symptoms triggered by fever, along with a learning disorder. The Array-CGH identified a deletion of 424 kb on chromosome 13q33.1 including fibroblast stimulating factor (FGF14) gene associated with spinocerebellar ataxia (SCA) 27. This deletion was identified in both twins. Discussion: This case supports previous findings that postulate that alterations in the FGF14 gene include a phenotypic spectrum that includes symptoms of episodic ataxia and learning difficulties. Also, the clinical presentation of both patients supports the hypothesis that this gene regulates the activity in the cerebellum through Nav1.2 and 1.6 alpha subunits, whose functions appear to be susceptible to fever. The study by Array-CGH can help in the diagnosis of neurological disorders and expand the phenotypic and genotypic spectrum known syndromes, as in the case of SCA27. Deletions in FGF14 seem unusual, but perhaps other episodic cerebellar ataxia syndromes could be explained by changes in this gene or related genes.

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Movement disorders

ICNC-0809: Tick disorders in children and differential diagnosis with progressive diseases of the nervous system

Background: In the general population the prevalence of ticks is quite large and the statistics of different countries is 1 - 13% . There are two main theories of ticks: genetic determination and neurogenic stress on the background of residual-organic lesions of various structures of the extrapyramidal system. Methods: We performed a neurological, neurochemical (determination of catecholamines in the urine), neuroimaging (MRI) and psychological examination of children (5 to 15 years) with chronic tic disorder. total number 250 children were studied. Results: On the basis of complex neuropsychiatric examination, changes of catecholamines; neuroimaging and follow-up of children with chronic tic disorder evaluated the efficacy of the treatment of chronic tic disorder in children and indications for drug therapy, developed criteria for early diagnostics of ticks in the debut of hereditary degenerative diseases. Conclusion: we did set multifactorial genesis of chronic tic disorder, resulting from organic brain damage in childhood and psychological characteristics of the child's personality and its interaction with other people. At follow-up study we found that chronic tic disorder may be the initial manifestation of progressive diseases of the nervous system. The features of emotional-personal sphere of children with chronic tics and features of the interaction of the child with chronic tics within the family were identified. Thus, the primary tics can be considered typical of neuropsychiatric disorders. In MRI study any specific for chronic tic disorder changes were not found.

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Movement disorders

ICNC-0810: Hashimoto encephalitis as a rare cause of non tumoral opso-myoclonic ataxia

Background: Hashimoto encephalopathy is a rare autoimmune encephalitis. The diagnosis is arrived at by excluding other toxic, metabolic and infectious causes of encephalopathies, supportive clinical profile, elevated thyroid antibodies and optimum steroid response. Cerebellar dysfunction, behavioral abnormalities and oculomotor disturbances can be seen. Case: 16 year old male with gait disturbance admitted to our hospital. Personal history revealed Hashimoto thyroiditis(H.E). Truncal ataxia,opsomyoclonus,nystagmus was found upon neurological examination. Also obsessive compulsive symptoms developed during hospitalization. The thyroid profile revealed normal and high serum titers of anti-TPA was seen. Toxic , metabolic and infectious causes excluded. Autoimmune encephalitis autoantibodies and anti glutamic acid decarboxylate(GAD) were negative. MRI and eeg was normal. Neuroblastoma was excluded via imaging and low urinary vanilmandelic acid (VMA) excretion levels. Steroid therapy was initiated with the diagnosis of H.E. Patient’s symptoms resolved after therapy. Conclusion:In this report, we would like to present a patient with non tumoral opso-myoclonus diagnosed with Hashimoto encephalitis . Suspicion is often required in this cases for early diagnosis of H.E.

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Movement disorders

ICNC-0531: Authentic paediatric video cases: identifying criteria for optimal teaching and learning cases

Medical students and trainees often do not encounter clinical examples of key patients. Interactive analysis of authentic patient video cases (PVCs) may counteract this problem. PVCs may be particularly helpful in demonstration of movement disorders or epileptic seizures, and are widely used for demonstration in textbooks, at meetings or at conferences. As teaching programs are under increasing economic pressure there is a need to identify optimal selections of teaching and learning resources. We know little, however, about criteria for selection of optimal PVCs for teaching and learning.

Methods

We performed a literature review. We searched the databases ClinicalKey, the Cochrane library, the Education Resources Information Centre (ERIC), Embase, PsycINFO and PubMed. We identified and read relevant abstracts and full-text papers. We then assessed the evidence for each criterion identified, and labelled each of them as major or minor.

Results

We identified three major criteria for an optimal teaching and learning PVC: Key movements should be included in the PVC; 2) key movements should be subtle and/or difficult to note; and 3) the frequency of the condition should be suitable for learner in question. We identified two minor criteria: 4) the diagnosis should require clinical reasoning; and 5) it should be possible to obtain a PVC. Conclusion

We identified five criteria for selection of optimal PVCs for teaching and learning. These are useful for clinicians and teachers who wish to build libraries of PVCs for authentic and meaningful teaching and learning of pediatric neurology.

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Movement disorders

ICNC-0532: The scale for assessment and rating of Ataxia in early onset Ataxia; Always a reliable biomarker?

Introduction: Early onset ataxia (EOA) involves heterogeneous disorders regarding age-of-onset (0-25 years), pathogenesis and presentation. The Scale for Assessment and Rating of Ataxia (SARA) is uniformly interpreted in children and adults. Innovative therapeutic trials are applying SARA-scores in children and adults, using minimal quantitative cut-off points, suggesting that any smallest SARA-score difference would reflect therapeutic “ataxia” improvement. However, pediatric SARA-scores have shown to be influenced by age and muscle weakness as well. In the present EOA study, we therefore aimed to determine the influence by phenotypic heterogeneity on SARA-scores.

Methods: In 40 EOA patients [mean age 15 (range 5-34) years], we determined reliability and discriminant validity of SARA-scores (by 3 independent pediatric neurologists) in “primary” (ataxia as primary movement disorder (n =26)) and “combined” (ataxia concurring with another prevailing movement disorder (n=12)) subgroups. Results: The Interclass Correlation Coefficient revealed high, but not complete, inter-observer agreement in “primary” and “combined” EOA-subgroups (.977 and .891). In both subgroups the SARA-scores were predicted by the severity of the primary movement disorder, instead of by ataxia alone (β .83; p <.05). Discussion: In EOA, SARA-scores are not infallibly reproducible, implicating that the smallest SARA cut off may refer to the margin of error. In heterogeneous EOA-subgroups, discriminant validity between the influence by ataxia and other concurrent movement disorders is low, implicating that decreased SARA-scores in “combined” EOA patients do not necessarily reflect “ataxia improvement”. To prevent over-interpretation of SARA-scores, insight in the SARA construct is needed first.

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Movement disorders

ICNC-0533: The hallmarks of nonprogressive congenital ataxias (NPCA)

Introduction: Among patients with early onset hereditary ataxia NPCA represents a separate clinical category. The aim is to describe clinical and neuroradiological characteristics of NPCA in long-term follow-up and consider possible pathogenesis and genetic background. Materials and methods: We selected patients from the tertiary center EOA registry (n=77), after excluding patients with cerebellar malformations, later onset and/or progressive ataxias and known metabolic/genetic disease. SARA is used to examine clinical progression while repeated MRIs are used for

 movement disorders

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Methods

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Results

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We identified five criteria for selection of optimal PVCs for teaching and learning. These are useful for clinicians and teachers who wish to build libraries of PVCs for authentic and meaningful teaching and learning of pediatric neurology.

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Movement disorders

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Methods: In 40 EOA patients [mean age 15 (range 5-34) years], we determined reliability and discriminant validity of SARA-scores (by 3 independent pediatric neurologists) in “primary” (ataxia as primary movement disorder (n =26)) and “combined” (ataxia concurring with another prevailing movement disorder (n=12)) subgroups. Results: The Interclass Correlation Coefficient revealed high, but not complete, inter-observer agreement in “primary” and “combined” EOA-subgroups (.977 and .891). In both subgroups the SARA-scores were predicted by the severity of the primary movement disorder, instead of by ataxia alone (β .83; p <.05). Discussion: In EOA, SARA-scores are not infallibly reproducible, implicating that the smallest SARA cut off may refer to the margin of error. In heterogeneous EOA-subgroups, discriminant validity between the influence by ataxia and other concurrent movement disorders is low, implicating that decreased SARA-scores in “combined” EOA patients do not necessarily reflect “ataxia improvement”. To prevent over-interpretation of SARA-scores, insight in the SARA construct is needed first.

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Movement disorders

ICNC-0533: The hallmarks of nonprogressive congenital ataxias (NPCA)

Introduction: Among patients with early onset hereditary ataxia NPCA represents a separate clinical category. The aim is to describe clinical and neuroradiological characteristics of NPCA in long-term follow-up and consider possible pathogenesis and genetic background. Materials and methods: We selected patients from the tertiary center EOA registry (n=77), after excluding patients with cerebellar malformations, later onset and/or progressive ataxias and known metabolic/genetic disease. SARA is used to examine clinical progression while repeated MRIs are used for...
neuroradiological assessment. The statistical analysis was done using t test: version SPSS 15.0. Results: 17 subjects (22.1%) from 13 kindred presented with NPCA in the follow-up period 1-15yr (mean 8.1±5). 88.2% initially showed mild to severe hypotonia and global developmental delay- 82.3%; mean age of independent walking was 3.3±1.3yr and speech 2.4±0.5yr. Early cerebellar ataxia was present in all subjects, accompanied by nystagmus in 53% and other oculomotor abnormalities- 70.6%. Normal tendon reflexes were present in 82.3% and additional neurological findings in 23%. 86.6% achieved normal to low intelligence. SARA scores showed significant decrement in the follow-up (t test 0.015). Cerebellar hypoplasia/atrophy, mostly vermian, was found in 88.2% of patients on repeated MRIs. Conclusion: The hallmarks of the selected group of patients with NPCA are: variable degrees of hypotonia and developmental delay, cerebellar ataxia, ocular abnormalities, normal to low intellectual level and pure cerebellar hypoplasia, predominantly vermian. We assume that the number of genes (only confirmed in one family with ITPR1 mutation) will help delineate pathogenic mechanisms in NPCA.

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Movement disorders

ICNC-0534: Bilateral striatal necrosis following a Sydenham’s chorea: a case video-report
Introduction: Sydenham’s Chorea (SC) is considered the prototype of autoimmune diseases of central nervous system triggered by a streptococcal infection. Acute bilateral striatal necrosis has been described after viral and mycoplasma infection, in mitochondrial disorders, in hypoglycemia, and after exposure to toxins. Case Report: We describe and show the video of a 7-years-old boy, with uneventful past medical history, presenting with subacute onset of choreic movements. A diagnosis of Sydenham Chorea (SC) was made. The patient was treated with prednisone and benzathine penicillin and symptomatic therapy with haloperidol with a complete remission of symptoms in one week. The MRI performed when he was already asymptomatic demonstrated bilateral T2 hyperintensity, and mild T1 hyperintensity in the caudate nuclei and putamina, compatible with microbleeding following vasculitis in rheumatic chorea. One month after the onset, still in therapy with prednisone and haloperidol he presented involuntary movements and stiffness, mainly involving legs, initially interpreted as haloperidol adverse event. Haloperidol was gradually reduced, but neurological symptoms continued worsening; a new MRI was showing the evolution towards bilateral striatal necrosis. The following investigations were performed, resulting normal: thrombopholic, autoimmune and metabolic screening, copper, ceruloplasmin, carboxyhemoglobin, thiamin dosage, antibodies to Mycoplasma Pneumoniae, CSF anti-N-methylD-aspartate receptor (NMDAR) antibodies, CSF lactate. A cranial TC excluded cerebral calcifications. Genetic panel for genes involved in bilateral striatal necrosis is in progress. In consideration of the hypothesis of striatal necrosis associated to a post-infectious GAS autoimmune disease, the patient was treated with intravenous immunoglobulin and high dose of intravenous methylprednisolone with a considerable reduction of choreatoletic movements and dystonia. Symptomatic therapy with tetrabenazine, and oral supplementation of thiamine and biotin, was also started. At present (11 months of follow-up), the child is ongoing benzathine penicillin treatment and thiamine and biotin supplementation and has stopped prednisonsone and tetrabenazine. The neurological examination is stable since 6 months characterized by choreic hyperkinesias involving limbs, trunk and face and dystonic postures during walking and writing. No alteration of cognitive functions and behavior were noticed since the onset of symptoms. The child in now attending school regularly. Conclusions: Post-streptococcal disorders of the central nervous system remain an intriguing model of neuropsychiatric disease; we would like to underline how the spectrum is extending from “classical” Sydenham Chorea to acute bilateral striatal necrosis.

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Movement disorders

ICNC-0537: Relationship between physical activity, tic severity and quality of life in children and adolescents with tics and Tourette Syndrome
INTRODUCTION: Gilles de la Tourette’s syndrome (TS) is characterized by recurrent motor and vocal tics for at least one year. Studies have shown improvements in ADHD, anxiety and depression with physical activity; however, there is conflicting evidence in the literature as to whether physical activity improves tics. METHOD: We examined baseline data on children with TS and Persistent Tic Disorders collected from a larger randomized controlled trial (Clinicaltrials.gov identifier NCT02153463). Baseline physical activity was assessed via a pedometer which participants wore for 7 days with their daily step count recorded. Participants were assessed on tic severity via the Yale Global Tic Severity Scale (YGTSS) and on quality of life via the PEDs QL 4.0. Tic severity and quality of life was then compared between those more physically active (mean of >12,000 steps/day) and less physically active (<12,000 steps/day) via the Mann-Whitney U-Test. RESULTS: 13 children participated in this study; 4 had >12,000 steps/day and 9 had <12,000 steps/day. The active group had a significantly lower total tic severity (p=0.02), and total YGTSS score (p=0.01). Additionally, the vocal tic severity score was significantly lower in the active group (p=0.02). Motor tic severity was not significantly
different amongst the two groups. For Peds QL scores, the active group performed better in physical functioning (p=0.01), social functioning (p=0.03), school functioning (p=0.02), psychosocial functioning (p=0.03) and total Peds QL score (p=0.01).CONCLUSIONS: Our results demonstrate that more physical activity is correlated with lower vocal tic severity and improved aspects of quality of life.

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Movement disorders
ICNC-0538: Manifestations of movement disorders in anti-N-methyl-D-aspartate receptor encephalitis: a nationwide study in Taiwan
Objective: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is one of the most common autoimmune encephalitis. A wide variety of movement disorders have been reported but their incidence and manifestation remains unclear.

Materials and methods:A retrospective cohort of Anti-NMDAR antibody in 5-year period from major University hospitals in Taiwan was identified. Patients were categorized into 3 age groups: ≤10 years, 10-18 years and >18 years. Results: Total 28 patients (20 females and 8 males) with age ranging from 8 months to 38 years old were enrolled. Nearly all patients (n=27/28, 96%) presented with at least 2 types of movement disorders, including orofacial-lingual dyskinesia (13/28, 46%), tremor (n=11), bradykinesia (n=11), dystonia (n=11), choreoathetosis (n=9) and ballism (n=3). Choreaethetosis was the most common (p<0.05). The most common movement disorder in patients >10 years was catatonia (n=17/21, 81%) (p<0.05). Bradykinesia was also more common in patients >10 years (p<0.05). There were no significant difference in other presentations like orofacial-lingual dyskinesia, tremor, dystonia and ballism. All patients improved after treatment. However, compared to other movement disorders, dystonia persisted longer. Conclusions: Our study shows that movement disorders are more common but varied in anti-NMDAR encephalitis patients of different ages. Hyperkinetic movements are more prominent in younger age groups while hypokinetic movements are more common in older age group. Of all movement disorders, dystonia takes the longest time to get improved.

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Movement disorders
ICNC-0539: Diagnosis and management of drooling in children with Progressive Dystonia- a case series of patients with Megdel Syndrome
Introduction: Progressive dystonia is seen in different pediatric neurological disorders like MEGDEL syndrome. Swallowing problems are common in these patients, leading to excessive pooling of saliva, resulting in drooling affecting health and quality of life. Methods: Four MEGDEL patients, suffering anterior and posterior drooling with subsequent respiratory problems, were evaluated at the multidisciplinary saliva-control outpatient clinic. Results: One patient improved on anti-reflux medication and in one patient a medication change was necessary as she suffered from drooling (partly) as a side effect. Two other patients underwent salivary gland surgery, of whom one significantly improved and one died shortly after surgery. Conclusion/Discussion: Taking into account our experience and factors contributing to drooling we propose a practical stepwise treatment approach in patients with progressive dystonia. First, treatment of the neurological condition has to be optimized and medication inducing saliva secretion has to be replaced, if possible. Second, treatment of constipation, scoliosis and gastro-esophageal reflux disease should be improved. Third, when a risk for chronic saliva aspiration remains, more invasive treatment (anticholinergic medication, botulinum toxin injections, salivary gland surgery) follows.

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Movement disorders

**ICNC-0540: Sydenham's chorea: Clinical observations from a tertiary center in Turkey**

Introduction: Sydenham's chorea (SC) is one of the major criteria of acute rheumatic fever. Although the prevalence of SC has progressively decreased in developed countries, SC is still a major health problem in Turkey. In this study, we retrospectively reviewed the medical charts of SC patients to evaluate the demographic and clinical characteristics of these patients. Methods: The study was a retrospective study conducted in a tertiary hospital at Ankara, Turkey. The SC patients who were admitted to our pediatric outpatient neurology clinics between January 2013 and December 2014 were included. Both newly diagnosed and follow-up patients during this period were enrolled. We retrospectively reviewed the clinical charts of the 76 patients. Results: A total of 76 patients were enrolled in the study. The 65.8% (n= 50) of patients were female and 34.2% were male. The mean age of chorea onset was 10.8 ± 2.3 years (4.25-16 years). Patients were followed for a mean of 32.8 ± 24.1 months. Chorea was unilaterally observed in 38% of patients. The 92% of patients had cardiac involvement and in 66.7% of patients, brain magnetic resonance imaging (MRI) was performed. In 10 patients, non specific gliotic lesions in the white matter of the brain were observed. Recurrence of chorea was seen in 7 patients (9.2%) in 4 months-7 years. Conclusion: Sydenham's chorea is still the major cause of acquired chorea in our country. The Sydenham's chorea can be easily diagnosed with detailed history, comprehensive neurologic examination and laboratory evaluation.

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Movement disorders

**ICNC-0541: Complicated hereditary spastic paraplegia due to a novel EXOSC3 mutation**

Introduction: Mutations in the EXOSC3 gene were previously reported in pontocerebellar hypoplasia type 1 (PCH1). We describe a family with an autosomal recessive hereditary spastic paraplegia (HSP) caused by a novel mutation in the EXOSC3 gene, and suggest a broader phenotype of the EXOSC3. Methods: Two pairs of siblings from a consanguineous family manifested an autosomal recessive HSP. Clinical findings included delayed motor milestones, early-onset spastic paraplegia, variable cognitive disability, cerebellar signs, epilepsy and short stature. Brain imaging demonstrated enlarged cisterna magna and mild hypoplasia and atrophy of the lower vermis, with a normal pons. Genetic analysis using homozygosity mapping followed by whole exome sequencing identified homozygous c.571G>T; p.G191C mutation in the EXOSC3 gene. Discussion: We suggest that EXOSC3 mutations have a broader phenotypic spectrum, and may present not only as PCH1, but also as a complicated form of HSP, with cerebellar (but without pontine) hypoplasia or atrophy. This spectrum of EXOSC3 is important in the differential diagnosis of PCH, HSP, intellectual disability and even epilepsy.

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Movement disorders

**ICNC-0542: Segawa disease with action retrocollis (cervical dystonia); A case report of 23-year-old female**

Introduction: Segawa disease (SD) is characterized by levodopa-responsive dystonia with diurnal fluctuation, occurring in childhood, being proposed by Prof. Masaya Segawa. Case Description: A 23-year-old female, showing SD with involvement of the sternocleidomastoid muscle (SCM) and back neck muscle (BN). She had no family history of neurological diseases. She suffered from writer's cramp around the age of six years, and subsequently developed dystonia at the right toe. She became showing retrocollis at 15 years, and had difficulty in writing. The neurologist suspected her as dystonia. Neither levodopa nor trihexyphenidyl was effective, and botulinum toxin injection in the SCM and BN relieved her a little. Mutation in the exon 1 of GCH-1 gene (Y109H) was detected at 22 years, leading to the diagnosis of SD. Paroxysmal retrocollis was so prominent at the wakefulness that she continuously held her head with the right arm on the table. The bilateral SCM and BN showed hypertonus with fluctuation. Retrocollis with lordosis were deteriorated at stepping. Brain or spinal MRI did not demonstrate any changes. Electrooculogram revealed impairment in memory guided saccade (MGS). Somatosensory evoked potentials showed abnormal gating. On surface
Movement disorders

ICNC-0543: Impairment of sensory- motor processing in Tourette syndrome (TS) - Evaluation of pre-movement gating of somatosensory evoked potentials (SEPs)

[Objectives] Tourette syndrome (TS) is a neurobehavioral disorder characterized by motor and vocal tics. Simple tics (TS-S) are purposeless involuntary movements with spontaneous resolution before adolescence. In contrast, complex tics (TS-C) are often preceded by premonitory “urge”, which sometimes become intractable. To explore the pathophysiology of TS, we studied pre-movement attenuation (gating) of SEPs. [Subjects and methods] 34 patients (6-48 years) and 18 normal subjects were studied. Including 3 follow-up patients, 37 records were evaluated. We divided patients into two groups younger and older than 15 years. A pair of warning (auditory) and imperative electric stimuli was presented with a 1 second interstimulus interval. In the pre-movement condition, subjects responded by thumb extension with the ipsilateral hand to the electric stimulation, which also elicited SEPs before movement. In the rest condition, the subjects were instructed not to perform any movement and just listen to auditory stimuli. The amplitude of the frontal N30 (FrN30) in the pre-movement state was compared with that at rest and the pre-movement/rest ratio was evaluated. [Results] The pre-movement/rest ratio in TS-C was significantly larger than that of TS-S before (p<0.05) and after adolescence (p<0.001). No significant differences were observed in the ratio between TS-S and normal subjects. The ratio was not correlated with the comorbidity of attention deficit hyperkinetic disorder but was correlated with that of obsessive compulsive disorder (P<0.001). [Conclusion] Sensory-motor processing is preserved in TS-S, but is impaired in TS-C. Furthermore, the involvement of the non-motor striato-thalamo-cortical circuits is suggested in TS-C after adolescence.

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Movement disorders

ICNC-0419: The Burke-Fahn-Marsden Dystonia Rating Scale is Age-Dependent in Healthy Children

Background: The Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS), involving a movement scale (BFMMS) and a disability scale (BFMDS), is a universally applied instrument for quantitative assessment of dystonia in children and adults. However, immature movements by healthy young children may also reveal “dystonic characteristics” as a consequence of physiologically incomplete brain maturation. In young dystonic children, an age-related effect could theoretically confound both the BFMMS and the BFMDS. Objective: In healthy young children, we aimed to determine whether physiologically immature movements and postures can induce an age-related effect on BFMMS and BFMDS scores.

Methods: Nine assessors, specialized in movement disorders (3 adult-, 3 pediatric-neurologists and 3 MD/PhD students) independently scored BFMMS in 52 healthy children (4-16 years; 4 children/year of age; male/female=1). In another 52 healthy children (4-16 years; 4 children/year of age; male/female=1), parents scored their children’s functional motor development according to the BFMDS. By regression analysis, we determined the association between BFMMS and BFMDS outcomes and age and compared the regression coefficients using the Z-test. Results: In healthy children, assessment of physiologically immature motor performances by the BFMMS and BFMDS revealed an association with age (until 16 and 12 years of age, β=0.72 and β=0.60, respectively (both p<0.001)). The unstandardized regression coefficients between BFMMS and BFMDS revealed no significant difference (p=0.753). Conclusions: Both the quantitative BFMMS and the functional BFMDS are influenced by the age of the child in a similar pattern. For accurate interpretation of longitudinal BFMDRS scores in young dystonic children, consideration of pediatric age-relatedness appears advisory.

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Electromyogram, continuous tonic contraction was predominant at the left SCM and arms. Discussion: Cervical dystonia per se was very rare in SD. Prof. Segawa classified this kind of the complicate patients into action type. In such patients, abnormality in the MGS suggests dopaminergic dysfunction in the basal ganglia, and levodopa is usually ineffective. Deep brains stimulation may be applicable like DYT1 dystonia.

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Movement disorders

ICNC-0545: European pediatric normative values for the Scale for Assessment and Rating of Ataxia (SARA)

Introduction: The Scale for Assessment and Rating of Ataxia (SARA) is designed as a uniform and ubiquitous biomarker for quantitative ataxia assessment in children and adults. In adults, SARA is described as reliable, with outcomes that could be ascribed to the severity of ataxia, alone. In healthy children, however, we have shown that age may additionally influence the scores. For uniform longitudinal interpretation of pediatric SARA scores, we therefore aimed to obtain normative values in healthy children, first. Aim: To obtain international age-related normative SARA values in healthy European children. Methods: Twenty-two pediatric neurologists (CAG-EPNS members) independently scored 156 healthy children from nine different European countries (n=12/year; m:f=1; age range 4-16 years). We determined SARA age-dependency and international inter-observer agreement on pediatric SARA scores. Results: In healthy children, SARA scores reveal age dependency (R²=0.47). The youngest children revealed the highest scores and also obtained the most variation in scores (≤ 7 years; p<0.001). After 12 years of age, children approached adult optimum SARA values. The inter-observer agreement was substantial (Intraclass Correlation Coefficient: 0.69), revealing a positive relationship with age (p<0.01). Implications: In European healthy children, our data reveal that both total SARA scores and inter-observer agreement are age-dependent. For longitudinal pediatric trials, these data implicate that SARA outcomes and cut off points should be interpreted for the age of the child. We hope that forthcoming insight in the SARA construct will contribute to adequate data interpretation from pediatric to adult life.

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Movement disorders

ICNC-0548: Can quantitative analysis of the “Finger-to-Nose test” discern between Early Onset Ataxia and other Conditions of Coordination Impairment?

Introduction: Many pediatric conditions can affect coordination, including early onset ataxia (EOA), developmental coordination disorder (DCD) and physiologically immature coordination by age. For clinical surveillance and treatment evaluation, uniform phenotypic distinction between underlying conditions is important, but complicated. In EOA, we investigated whether quantitative analysis employing motion sensors could provide reliable and discriminative outcomes. Methods: We included 32 children with different phenotypic causes for coordination impairment, involving ataxia (n=9; 13.3 ± 3.8 y), DCD (n=7; 9.4 ± 2.1 y) and healthy age-related controls (n=16; 11.9 ± 3.3 y). All children performed the “finger-to-nose” SARA sub-test with three attached inertial measurement units, providing information on the index finger position according to a 3D upper limb model. We used quantitative movement features of the movement to classify each child as ataxic, DCD or healthy. Results: None of the children quantitatively classified as EOA were phenotyped as control; 5% classified as control were phenotyped as ataxic; 22% classified as EOA were phenotyped as DCD and 26% classified as DCD were phenotyped as ataxic. The overall agreement between quantitative classification and phenotypic assessment was 78% for ataxia, 83% for controls and 31% for DCD. Discussion: “Finger-to-Nose” test outcomes provided excellent discrimination between EOA and controls, and reasonable discrimination between EOA and DCD. As a golden standard for phenotypic DCD assessment is lacking, it remains elusive whether quantitative classification or phenotypic diagnosis was more inaccurate. In EOA, future additional quantitative gait analysis may provide a reliable and discriminative biomarker for total EOA assessment.

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Movement disorders

ICNC-0547: Bilirubin encephalopathy an underdiagnosed cause of Dyskinetic Cerebral Palsy in term and preterm infants

Aims: Bilirubin encephalopathy is still a reality in some risk groups, especially preterm infants, despite levels of hyperbilirubinemia not being sufficiently elevated to explain this condition in most cases. We sought to identify precipitating factors of bilirubin encephalopathy in these children. Methods: Single-center cohort of children with clinical diagnosis of bilirubin encephalopathy according to published criteria: 1) neonatal exposure to bilirubin 2) early generalized movement disorder and 3) Early MRI: high-intensity in subthalamic nucleus and globi pallidi on T1w; or Late
MRI: loss of volume and high-intensity in globi pallidi on T2w. Results: Eight patients (age range: 2-15y) with suspected bilirubin encephalopathy were attended in our clinic. The following risk factors were identified: prematurity (N = 5) (23-37 weeks gestational age), icteria (N = 8) (bilirubin mean: 14 mg/dL), septic shock (N = 3), G6PDH deficiency (N = 1) hypoalbuminemia (N = 1), ibuprofen treatment for the treatment for patent ductus arteriosus (N = 2). Only two patients presented with acute encephalopathy and an abnormal neonatal MRI. Seven patients were treated with phototherapy. Four patients developed deafness. In a patient with persistent indirect hyperbilirubinemia genetic analysis for Clinger-Najjar was negative. Conclusions: Most pre-term newborns who develop chronic bilirubin encephalopathy did not show a palmary picture of acute encephalopathy, hence a high index of suspicion is necessary for early identification. Surprisingly, adequate phototherapy was not sufficient to prevent kernicterus in most patients. Clinical sepsis, hypoalbuminemia and the use of ibuprofen might have contributed to this condition in half of the patients.

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Movement disorders

ICNC-0693: Hyperekplexia : report on phenotype and genotype of 17 Jordanian patients

Hyperekplexia, also known as hereditary startle disease, is a rare disorder characterized by excessive startle response to acoustic, visual, or other stimuli and hypertonia which predominates in the trunk and the lower limbs Aim: describe the clinical and genetic features of hyperekplexia in Jordanian patients . Methods: Retrospective study including all patients diagnosed with hyperekplexia and presenting to our clinic at Jordan University hospital from January 2001 till July 2015. Results: A total of 17 children from 13 families were included. The total follow up period ranged from one to eleven years. Most of the patients (82.4%) were initially misdiagnosed as epilepsy . Tonic apnic spells occurred in16/17=94.1% patients . Fifteen patients (15/17=88.2%) received clonazepam. Stopping clonazepam by three years of age failed in 12/15 (80%)due to reappearance of tonic apnic spells(8/15=53.3%) , unsteady gait ( 10/15=66.7% ) or due to both reasons (6/15=40%). Delayed motor development occurred in 5/17(29.4%) , speech delay in 4/17(29.4%) , global developmental delay in1/17(6%) , and autism spectrum disorder in 1/17 (6%) patient . The mode of inheritance is autosomal recessive in all .Mutations in GIRA1 gene was present in 9/17 (53.0%), mutations in the GLRB gene was present in 4/17(23.5%) patients and in SLC6A5 gene in 3/17 (17.6%) patients. One patient (1/17; 6.0%) has double mutation in GLRA and GLRB genes . Conclusion: Misdiagnosis of hyperekplexia is common . Many patients continue to need surveillance and follow up.

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Movement disorders

ICNC-0550: Paroxysmal dystonia due to compression injury at the cervicomedullary junction in chondrodysplasia punctata

Background: Dystonia due to spinal lesions in adult patients is characterized by the provocation and/or amelioration of the spasm by somatosensory stimulation with sensory trick. Case Report: An infant with brachytelephalangic chondrodysplasia punctata who developed flaccid tetraplegia due to cervical cord compression resulting from congenital atlantoaxial dislocation. Episodic, tonic extension of the extremities, neck, and trunk had appeared daily since 2 years of age and was often provoked by tactile stimulation. Although decompression surgery was performed at 3 years of age, progressive spinal deformity resulted in the aggravation of episodic dystonia thereafter, lasting for hours. Foot dorsiflexion and wearing a truncal brace for scoliosis showed inhibitory effects on these spasms. Intrathecal baclofen bolus injection transiently ameliorated the paroxysmal dystonia and detrusorspincter dysssynergia in the lower urinary tract. Conclusion: Paroxysmal dystonia is quite unusual in children with spinal cord lesions; however, it should be recognized for appropriate individualized clinical management

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Movement disorders

ICNC-0551: A case of a boy with ADCY5 severe dyskinesia with clinical response to caffeine

JVSF, 6 years old, male. Only child of a non-consanguineous couple. No pre or perinatal morbidity. With a normal language development but delayed acquisition of motor milestones acquiring the march 20 months. Around two years and six months began to show abnormal movement: dystonia action in four members associated with choreoathetosis and facial grimacing. He presented progressive worsening doing to leave to walk without aid. There was a dyskinetic fluctuations and was perceived by the family that there was an improvement with the intake of coffee and green teas. It was tempted therapeutic test with Levodopa-Benserazide without consistent clinical response. MRI of the brain, cerebrospinal fluid, plasma amino acid chromatography, research urinary organic acids, acyl-carnitine profile panel to neurotransmitters in cerebrospinal fluid were normal. Whole exome sequencing showed mutation in heterozygosity in ADCY5 gene variant c.2088 + 1G> T (IVS8 + 1G> T), which promotes change in RNA processing (splicing). The Family dyskinesia with Miocimia Facial is a neurogenetic disorder autosomal dominant mutation, in a gene that leads to ADCY5 disorder dystonic type of movement associated with choreoathetosis and family myokymia. It was previously described in a German family with 18 affected people (10 men and 8 women) in 5 generations. The hypothesized mechanism for clinical response to coffee would be a substance that inhibits phosphodiesterase enzyme that degrades cyclic AMP which is important in the biochemistry of the extrapyramidal system which is deficient in the disease.

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Movement disorders

ICNC-0554: Can latent class analysis be used to improve the diagnostic process in pediatric patients with chronic ataxia?

Background: Ataxia, defined as unsteady stance or impaired coordination of voluntary movement, is classified according to its presentation as acute, sub-acute, or chronic. Chronic ataxia is a relatively common symptom in children. There are numerous causes of chronic ataxia, making it difficult to derive a diagnosis in a timely manner. We hypothesized that the efficiency of the diagnostic process can be improved with systematic analysis of clinical features in pediatric patients with chronic ataxia. Methods: A cohort of 184 patients, aged 0-16 years with chronic ataxia who received medical care at Children’s Hospital during 1991-2008, was ascertained retrospectively from several hospital databases. Clinical details were extracted from hospital charts. The data were compared among the more common diseases using univariate analysis to identify pertinent clinical features that could potentially improve the efficiency of the diagnostic process. Latent class analysis was then conducted to detect unique patterns of clinical features, and to determine whether these patterns could be associated with chronic ataxia diagnoses. Results: Two models each with three classes were chosen based on statistical criteria and clinical knowledge for best fit. Each class represented a specific pattern of presenting symptoms or other clinical features. The three classes corresponded to a plausible and shorter list of possible diagnoses. Conclusions: Specific patterns of presenting symptoms or other clinical features can potentially aid in the initial assessment and diagnosis of pediatric patients with chronic ataxia. This will likely improve the efficiency of the diagnostic process.

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Movement disorders

ICNC-0555: Children with idiopathic tics reveal additional features of Hyperkinetic movement disorders

Children With Idiopathic Tics Reveal Additional Features of Hyperkinetic Movement Disorders Introduction The pathophysiology for idiopathic tic disorders is unknown, although underlying alterations within cortico-striatal-thalamo-cortical circuits appear likely. Regarding suspected inhibitory input from the basal ganglia, we aimed to phenotype other concurrent movement disorders that could contribute to the idiopathic pediatric tic spectrum. Methods In 30 children (aged 4-17 years) with idiopathic tics, we recorded standardized motor behavior according to ataxia, dystonia and chorea rating scales [Scale for Assessment and Rating of Ataxia (SARA), Burke Fahn Marsden Movement Scale (BFMMS), and Dyskinesia Impairment Scale (DIS)]. A panel of 5 (pediatric) neurologists phenotyped motor behavior. A separate panel of 3 pediatric neurologists and 3 MD/PhD researchers quantified motor behavior according to the SARA, BFMMS and DIS. Results 9 of 30 children were phenotyped with concurrent hyperkinetic movement disorders (≥2/5 assessors; chorea n=4, dystonia n=2 and myoclonus n=3). After age-correction, regression analysis showed that the choreatic phenotypic subgroup revealed significantly higher total BFMMS and DIS scores: (p=0.045, β=0.31) and (p=0.014, β=0.43), respectively. One child without any concurrent movement disorders during the analysis revealed additional chorea two months later. The two dystonic children tended to reveal higher BFMMMS and DIS scores (no statistics applicable). The ataxia-phenotype was unrelated with tics. Discussion About 30% of children with idiopathic tics can reveal other features of hyperkinetic movement disorders. Systematic phenotypic assessment of specified pediatric tic subgroups may
Movement disorders

**ICNC-0557: Beware the evolving Migraine Variant!**

We present a 9 year old girl who initially presented at 7 months of age with episodes of vomiting every 2-3 weeks, from the age of 4 weeks. There was associated left sided torticollis. Vomits would be forceful, initially clear and then bilious. Episode would last 6-8 hours at a time, followed by a long sleep. Over the course of 1-2 days she would gradually return to normal, until the next episode. She was thought to have cyclic vomiting syndrome, a migraine variant. Investigations including CT head, EEG and metabolic screen were reported as normal. Her symptoms improved slightly and she was subsequently diagnosed with Benign Paroxysmal torticollis of infancy. As she got older she was noted to be ataxic during these episodes. Development has so far been normal. Due to the emerging semiology and a family history of migraines, the possibility of episodic ataxia was considered. Following a genetic work-up, she was found to have CACNA1 gene which is implicated in Episodic Ataxia type 2. Episodic ataxia is an autosomal dominant genetic condition, resulting in various symptoms including ataxia, dysarthria, diplopia, headache, vomiting and vertigo. It is a rare condition, most commonly affecting individuals in early childhood through to adolescence. Attack frequency varies from a few times a year to several times in one week. Individual attacks may last from minutes up to days but symptoms can be successfully managed with acetazolamide. The identified genetic mutation occurs on chromosome 19p13, in the calcium gene CACNA1A. Other conditions with mutations in this gene include Familial Hemiplegic Migraine and Spinocerebellar Ataxia type 6, and symptoms can overlap between these conditions resulting in misdiagnosis. With better awareness of this condition, it may be possible to diagnose it in more individuals, particularly those who may be misdiagnosed with another migraine disorder.


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Movement disorders

**ICNC-0559: Stereotypies in Chinese patients with Rett syndrome: An analysis of 53 patients in Taiwan**

Introduction: Stereotypy is a key clinical feature of Rett syndrome (RTT). However, there were only rare studies focusing on Asian population. We aimed to analyze the stereotypies of RTT among Chinese patients in Taiwan. Methods: This is a questionnaire-based cross-sectional study. A total of 53 patients with RTT (51 females and 2 males) were recruited. Clinical features including movement disorders were collected and analyzed. Results: There were 23 (43.4%) and 30 (56.6%) cases of atypical RTT, respectively. 19 (82.6%) of typical RTT received genetic testing, and all revealed MECP2 mutation. However, 27 (90%) cases of atypical RTT received genetic testing, which 22 (81.5%) had MECP2 mutation, and 3 (11.1%) showed CDKL5 mutation. Patients with atypical RTT had more varied stereotypies (range 2-25, mean:11) compared to typical RTT (range 1-16, mean:8). The most common stereotypies were shifting weight from one leg to the other (65.2%) and bruxism (76.6%) for typical and atypical RTT, respectively. Regarding stereotypical hand movement, fingers twisting (56%) and joint hands claspimg (66.7%) were most common for typical and atypical RTT, respectively. Flapping and claspimg were significantly more common in atypical RTT. The numbers of stereotypies decreased significantly with age for both groups, with hyperkinetic movement disorders in particular. Conclusion: The stereotypical movements were varied between typical and atypical RTT in our study. However, the movement disorders in both groups tend to decrease or disappear with evolution of disease, which were comparable with previous studies.

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Movement disorders

ICNC-0560: Different clinical manifestation with a disorder of tetrahydrobiopterin (BH4) metabolism in two siblings

Disorders of tetrahydrobiopterin (BH4) metabolism may present a large spectrum of neurological symptoms. The most frequent clinical features are progressive motor and mental retardation. Hypotonia, spasticity, epilepsy, drowsiness, disturbances of posture, and some extrapyramidal movement disorders such as choreoathetosis can be detected as clinical manifestation, if we look at the literature in detail. Herein we present two siblings with one of the most common BH4 deficiencies. There is a consanguineous marriage, and both of them are females. They were presented with progressive oculogyric crisis beginning during the infancy. They have not received any regular medication until they were 17 and 19 years old. At this age, their neurological examination revealed striking oculogyric crisis more than hundred times a day, and mild-moderate parkinsonism features such as hypophonia, bradydystonia, bradykinesia, sialore, risus sardonicus in both. We detected very low level of biopterin and high neopterin in cerebrospinal fluid analysis. They are being treated by neurotransmitter precursors for three years, and most of the symptoms were markedly improved. We would like to draw attention to the importance to detect the BH4 deficiencies, because they may show various neurological phenotypes due to impaired synthesis of catecholamines and serotonin.

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Neurocutaneous disorders

ICNC-0563: Novel treatment option of Sirolimus ointment for facial angiofibromas in individuals with Tuberous Sclerosis Complex (TSC)

Introduction Facial angiofibromas afflict 80-90% of patients with TSC. They can cause recurrent bleeding, facial disfigurement and have high psychological morbidity. This is the first study to assess the efficacy and safety of Rapamycin 0.1% ointment on facial angiofibromas in TSC using a standardised and validated facial angiofibromas severity index (FASI). We also assessed quality of life. Most patients develop the rash during their childhood whilst they are cared for by paediatric neurologists. Methods In this prospective study, we recruited 14 patients from our TS clinic in Bath. The impact of Rapamycin was assessed 6 months after commencement with digital photography by blinded dermatological review using FASI. The quality of life was also assessed. Linear regression and t tests were used. Results FASI scores were improved in ten out of fourteen p= <0.001. Of the remaining four patients, three had improvement in rash but no FASI score change. One did not respond. All the children showed improvement compared with two out of six adults, P = 0.006. Response rate reduces with increasing age P=0.01. Learning difficulties or gender difference had no influence on the outcomes. Psychosocial scores have improved significantly with treatment p= 0.015. Conclusions Rapamycin is safe, well tolerated and effective in treating facial angiofibromas. It has a positive significant impact on patients’ quality of life. It is more effective in children than adults and therefore early treatment is advisable. The positive outcomes of this study could have a significant impact on the treatment of facial angiofibromas.

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Neurocutaneous disorders

ICNC-0564: Quality of life in children and adults with Tuberous Sclerosis complex

Objectives: Quality of life (QoL) in patients with TSC has not been studied before. We aimed to investigate the impact of the disease on QoL. Material and methods: We have studied the QoL of 91 TSC patients who have attended the Bath TS clinic. QoL was evaluated using the Pediatric Quality of Life Inventory (PedsQL) for children, and SF-36 for adults. The unpaired t test and linear regression were used. Results: Total self mean score was 71 out of 100, UK norm 84 (P <0.0001). Proxy mean was 48, UK norm 85 (P < 0.0001). Self-reported psychosocial score was 67, norm 82 (P <0.0001) and proxy 42, norm 82 (P <0.0001). Proxy reports were significantly worse than self-report (P = 0.001). Total proxy scores for children with asthma, diabetes, cancer and IBD are 72, 77, 71 and 73 respectively and these are significantly higher than the scores of children with TSC (P<0.0001). Pain score was 62 for adults without LD, norm 87 (P <0.0001), whilst 82 for LDs (P = 0.06). Psychosocial scores increased with increasing age (P<0.0001) r=0.44. Conclusions: QoL is significantly reduced in adults and children with TSC compared with the normal population. Psychosocial domain is most affected. Early neuropsychology intervention is necessary. Children without epilepsy also report worse QoL. Pain was reported less in adults with LD than normal intellect. Complication surveillance for SEGA and AML lesions should be assessed carefully, especially in patients with LD, as by proxy pain report may be unreliable.

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Neurocutaneous disorders

ICNC-0565: Long-term Follow-up assessing morbidity and mortality in tuberous sclerosis complex patients: An observational study

Background: Tuberous sclerosis complex (TSC) is a multisystem disorder characterized by growth of hamartomas in various organs throughout the body, including the brain, kidney, lungs, and skin. The long-term outcomes from patients with TSC are limited. Methods: All patients with TSC treated at the Kaohsiung Chang Gung Memorial Hospital (Taiwan) from January 1990 through December 2013 were recruited. The Inclusion criteria for this retrospective analysis were diagnosis of TSC according to the modified Gomez criteria (2 major or 1 major and 2 minor criteria). This study was approved by CGMH’s Institutional Review Board. Results: Of 80 patients with TSC, 67% had confirmed renal angiomyolipoma, 55 % cardiac rhabdomyomas, 28% subependymal giant cell astrocytoma (SEGA), and 18.7% lymphangioleiomyomatosis. Median follow-up was 13.5 years. Fifty patients (62.5%) had epilepsy and 48 of them were still taking anticonvulsants. Eighteen percent of the patients had low cognitive function and 17% had psychiatric diseases. Ten patients underwent operations for SEGA. A total of 13 patients had nephrectomy; 6 had 2 times. Two patients had embolization or cryotherapy. Four patients required kidney dialysis at the mean age of 32.3 years. Two deaths were recorded during the observation period (mean age 45 year) due to renal complications. Conclusions: Patients with TSC exhibit clinically significant neurological and kidney disease and early mortality because of kidney-related complications.
Neurocutaneous disorders

ICNC-0566: Polycystic Kidney Disease in patients with Tuberous Sclerosis Complex

Introduction: Tuberous sclerosis complex (TSC) is an autosomal dominant disorder affecting about 1 in 6800 individuals and characterised by the development of hamartomatous lesions in various organs. In about 1-5% of patients, large mutation affecting TSC2 and adjacent PKD1 gene is seen. In those patients, polycystic kidney disease develops. The aim of this study is to report PKD incidence in patients with TSC. Methods: We retrospectively reviewed clinical and radiographic data of 400 patients with definite TSC followed at our department between 1996 and 2014. Results: The age of patients ranged from 0 to 46 years (mean 8.4 years, SD 6.9). The prevalence of PKD in our cohort of patients with TSC has been estimated at 4.95 %. The age of ADPKD patients ranged from 1 to 19 years (mean 11.3 years, SD 5.9). Genetic analysis was performed on 10/17 patients (59%). In all cases a large deletion involving TSC2 and PKD1 had been identified. Conclusions: Screening for PKD is important in clinical workout in TSC patients.

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Neurocutaneous disorders

ICNC-0567: Neurological comorbidities in children with neurofibromatosis type 1

Aim: To investigate neurological comorbidities in children with neurofibromatosis type 1 (NF1). Method: At first, a nationwide surveillance was performed for NF1 children aged 3 to 15 years by sending questionnaire the pediatrician and pediatric neurologists. Then, the secondary questionnaire about neurological comorbidity including headache, ADHD-rating scale (RS), and social responsive scale (SRS)-2 were sent to the patients’ parents. Result: 760 NF1 patients were detected by the first surveillance, among whom 565 patients were sent the secondary questionnaire. Parental response rate was 25.1% (142; male 78, female 63, unknown 1). 44.0% (55 /125) patients had mental retardation. 33.3% (38/114, male: female, 1:1:1) of patients aged 6 to 15 were suspected to have ADHD (ADHD-RS >90 percentile). 35.0%(49/140) patients were suspected to have autism spectrum disorder (ASD) by SRS-2 score≧60, and male to female ratio was 1.72:1. 49.1% of children aged over 5 had headache and 24.2% of children had migraine (male: female, 1.9:1). The other neurological comorbidities were as follows; epilepsy 24 (16.9%), optic nerve glioma 11 (7.7%), brain tumor 5 (3.5 %), cerebrovascular disease 6 (4.2%) and hydrocephalus 2. Discussion: Genetic effects of NF1 would be large for the neurological comorbidities, such as ADHD, ASD, and migraine, because sex ratio was different from those in general population. Conclusion: ADHD, ASD and migraine were the major neurological comorbidities in NF1.

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Neurocutaneous disorders

ICNC-0568: Transcriptome profiling in Progeroid Neurocutaneous Syndrome caused by mutations in PYCR1

Introduction: Pyrroline-5-carboxylate reductase 1 (PYCR1) is a mitochondrial protein essential for the proline biosynthesis. Deficiency of PYCR1 leads to premature aging phenotype including psychomotor retardation, autism, ophthalmic degeneration, aortic root dilation, joints dislocation and progeroid cutaneous manifestations. The current studies have been interested in the genotype-phenotype correlation but the mechanisms between PYCR1 deficiencies and the connective tissue manifestation, cardiovascular disease and ophthalmologic abnormalities remain unexploited. Methods: Here we examined the effect of PYCR1 deficiency on gene expression in primary skin fibroblast. The gene expression of PYCR1 wild-type and mutant samples were compared using RNA-Seq analysis, then comparison of RNA sequencing with validated quantitative RT-PCR assays. Results: The analysis identified 81 genes with a twofold or greater difference in expression (threshold was 10 RPKM), 53 and 28 of which were more abundant in controls and patients respectively. Notably, fibroblast with PYCR1 mutations revealed a strong reduction of genes levels that coding for proteins localized in the extracellular space 27/53(51%), including many important extracellular matrix (ECM) components, which gene mutations associated with different phenotype of aging (cutis laxa, joint and dermal manifestations). Conclusion/Discussion: One of our major findings is that PYCR1 may modulate the expression of many ECM genes in skin fibroblast. These ECM genes are involved in embryonic development, tissue morphology and migration. Furthermore, we found that PYCR1 exerts its effects primarily through downstream activation of AKT signaling pathway. Our studies identify a novel role for PYCR1 in cell signaling and ECM gene regulation, which are relevant to aging progression.

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Neurocutaneous disorders

ICNC-0569: Profile of Tuberous sclerosis complex in Egyptian children in Alexandria

Introduction: tuberous sclerosis complex (TSC) is a genetic multisystem disease which its clinical expression is highly variable so that the true prevalence of the disease remains unknown though it is estimated to affect one in 10,000 births. It affects heart, kidneys, eyes, lungs and skin, also it affect the nervous system in the form of seizures, developmental delay and changes in the behavior. It may present at first year of life or may present later in life, it could misdiagnosed for years. Methods: 34 Egyptian children with TSC were presented using their prospective medical records. Initial presentation and subsequent follow up was described. Description of diagnostic methods was described. Comparison of clinical findings, course and outcomes was presented. Results: The male cases were 23 cases (68%) and the female cases were 11 cases (32%). The cases were having positive consanguine parents were 10 cases (29%). The most common type of seizure was epileptic spasms which was detected in 15 cases at early childhood (44%). The most common extra nervous system affection was the heart with 10 cases (29%). And we have no cases developed malignant malformations. Conclusions: The TSC is a disease with multisystem presentations. Successful management necessitates strict follow up and management plan with multi-disciplinary team approach. The long term follow up will depend on the complexity of system affection.

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Neurocutaneous disorders

ICNC-0571: The role of brain calcifications in cognitive functions: A prospective, longitudinal MRI study of children with Sturge-Weber-Syndrome

INTRODUCTION: Brain involvement in Sturge-Weber-Syndrome (SWS) is most commonly unilateral, and about 50% of affected children has impaired cognitive development. Magnetic resonance angiography (MRA) and head magnetic resonance imaging (MRI) are used to assess the extent of disease. The role of brain calcifications in cognitive functions is uncertain. This study aimed to evaluate the extent and progression of brain calcifications using 1.5T MRI with susceptibility weighted imaging (SWI). Methhods: Sixteen children (age: 0.7-7 years; mean: 4 years) with unilateral SWS underwent two MRI scans including susceptibility weighted imaging (SWI) and contrast images as well as T1 weighted imaging (T1WI). Clinical features, course and outcomes were correlated with MRI findings. Results: Four patients (25%) had calcifications on baseline MRI. Progression of calcifications was observed in four cases (25%). Progression was related to better cognitive outcome, whereas no progression was associated with worse cognitive outcome. Multivariate analysis showed progression of calcifications is related to better cognitive outcome (p=0.048). Conclusion: Calcifications on MRI with susceptibility weighted imaging were associated with better cognitive outcome. Further studies are needed to confirm these findings.

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Neurocutaneous disorders

ICNC-0573: mTOR inhibitors in children with Tuberous Sclerosis Complex - benefits on seizures and adenoma sebaceum?

Objective: To understand the effect of mTOR inhibitors [Sirolimus and Everolimus] on epilepsy and adenoma sebaceum in a cohort of children with tuberous sclerosis complex (TSC). Methods: All children with TSC at a tertiary paediatric centre on treatment for renal AML with mTOR inhibitors were identified. Demographic information, clinical features, seizure burden, anti-epileptic drug [AED] use were reviewed. Results: 6 children with TSC on treatment for renal AML were identified. [6 females-Age range 11-17]. All children had seizures as their first presenting symptom. 5 children had severe developmental delay, learning difficulties and challenging behaviour, 2 of whom had autism. All commenced on Sirolimus between the ages of 7-16 years. 2 children with adenoma sebaceum reported improvement in appearance. 4 children were seizure free at the start of mTOR inhibitors and maintained seizure freedom until last review. AEDs were completely withdrawn in two of these children. One child with medically refractory multifocal epilepsy showed a dramatic improvement since commencing mTOR inhibitors and started to wean AEDs. One child had improved seizure control upon starting Sirolimus but had simultaneous alteration of AEDs. All children were reported to be brighter on the
medication. Conclusion: 2 children reported improvement of adenoma sebaceum indicating its regression. There was also an observed benefit on epilepsy, with one child showing dramatic improvement in epilepsy and others showing continued seizure freedom enabling withdrawal of anticonvulsants which is unusual in children who previously had intractable epilepsy. This may indicate that mTOR inhibitors may be effective agents in controlling epilepsy.

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Neurocutaneous disorders

ICNC-0574: Alternative doses - a solution for side effects of treatment with Everolimus

Introduction: Treatment with Everolimus is available in Romania since 2014 through the National Program for Rare Diseases for the treatment of subependimal giant cell astrocytoma (SEGA) associated with Tuberous Sclerosis Complex (TSC) in children. Dose adjustment is based on drug blood levels measurements. Case Description: We present a girl patient, 16 years old, normal intellect who was diagnosed with definite TSC based on: hypomelanotic macules, facial angiofibromas, ungual fibromas, cortical tubers, subependimal nodules, SEGA>1cm, angiomylipomas. The patient was treated with Everolimus and she presented very high blood levels at normal doses associated with severe stomatitis, reversible after dose reduction. At usual Everolimus doses the patient experienced 20 times higher blood levels than the usual therapeutic concentration. Severe stomatitis was noted. The dose was decreased at one-third of the recommended dose followed by sudden drop of the blood levels under therapeutic range. The dose was adjusted again until was in normal range - an alternative treatment with Everolimus it was thought: two consecutive days the same dose (2 tablets/day) and the third day reduced the doses (1tablet/day). Results: The results in this case was: SEGA volum reduction (brain MRI was repeated 3 months after the dose has been established ) and cosmetic benefit – starting second day after treatment onset (pale angiofibromas), consolidated at one month of treatment. Conclusion: The patient has probably a particularly slow drug metabolization - regular doses leading to extremely high blood levels with severe stomatitis. It is usefull to adjust the doses according to the blood levels.

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Neurocutaneous disorders

ICNC-0575: Unusual Neurocutaneous disorders- A retrospective case series from India

Aims- To characterize the unusual neurocutaneous disorders in Pediatric Neurology practice. Method- A Retrospective study for 5 years (January 2010 to December 2014) in 0 to 18 years old Site of study -Pediatric neurology OPD at Rainbow Children’s hospital, Hyderabad, India.Results- Total number of Neurocutaneous syndromes were 117 cases (Over 5 years). In that uncommon conditions (Excluding TSC, NF1, SWS) were 27. Mean age of presentation 3.8 years (25days – 11 years). Sjogren Larssen syndrome- 7 cases All 7 cases had Icthyosis with spastic diplegia. Cockyane syndrome- 4 . PHACE syndrome( posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of the aorta, cardiac defects, and eye abnormalities)-3, one had Dandy waker syndrome. Hemangiomas responded to proponalol. Linear verrucus nevus -2, Incontinentiapigmenti-2, one with 2 episodes of stroke. Second with status epilepticus at 2 years age. Neurocutaneous melanosis -2 One with autistic features, visual impairment and epilepsy , T1 Hyperintensities in medulla and other with seizures doing well. Phylloid hypermelanosis- 1 developmental delay, Polythelia, Microcephaly presently doing well. Hypomelanosis Ito- 1 4 years old girl asymmetrical limb size with Left Hemi hypertrophy and Hypopigmented macules. Eleven years old male presented with seizures, Sebaceous naevus, CNS malformation, Aplasia cutis congenita, Limbal Dermoid (SCALP syndrome,) Haberland syndrome-1 7 years old boy with complex partial seizures, Left juvenile Ossificans mandible since 1 year of age. Pigmentary Dilution syndrome-1 Summary- This case series highlights the varied spectrum of skin manifestations in children with neurological disorder and their importance of their identification to anticipate and manage appropriately.

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Neurocutaneous disorders

**ICNC-0578: A case report of tuberous sclerosis complex caused by the new mutation in the TSC2 gene**

Introduction: clinical symptoms of mild phenotype of TSC in a child with the heterozygous mutation c.4616C>G (p.Ser1539*) in exon 36 of the TSC2 gene are presented. Case description: The boy aged 6 months presented with the onset of infantile spasms. He was born from healthy parents, uneventful pregnancy and delivery. The boy showed normal development, neurological was normal. The boy had several café-au-lait stains and 1 facial angiofibroma. EEG showed focal discharges with generalization without typical hypsarrhythmia. MRI revealed multiple tubers (up to 0.55 cm) including temporal lobe location, subependymal nodules (0.4cm). Vigabatrin was prescribed, seizures and EEG abnormalities disappeared on the dose of 55 mg/kg per day. At the age of 18 months, boy is still free of infantile spasms but rarely has febrile seizures. He is on the same dose of VGB, walks well independently, demonstrates active behavior and play, keeps eye contact, and says about 25 words. Head circumference grows according to the age. MRI shows moderate growing of subcortical tubers. Results: Screening for mutations in the TSC1 and TSC2 gene by means of PCR and DNA sequencing revealed heterozygous mutation c.4616C>G (p.Ser1539*) in exon 36 of the TSC2 gene. This mutation creates a premature stop codon. This variant was detected for the first time. Conclusion: The case report illustrates mild phenotype due to the new TSC2 mutation, although some authors suggested less severe phenotypes in patients in which no mutation were identified. This genotype –phenotype correlation may contribute to following investigations of TSC.

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Neurocutaneous disorders

**ICNC-0580: Interdependence of factors predicting cognition in children with Tuberous Sclerosis Complex**

Introduction: Patients with Tuberous Sclerosis Complex (TSC) show highly variable cognitive development. Predictors in the infant years would be valuable to counsel parents and support development. Univariable analyses have identified a number of factors that contribute to this variation. The aim of this study was to identify factors that are independently correlated with cognitive development. Methods: 102 patients treated at the ENCORE-TSC expertise center of the Erasmus MC-Sophia Children’s Hospital were included. Data from the first 24 months of life were used, including details on epilepsy, motor development and mutation status. Outcome was defined as cognitive development measured by standard neuropsychological tests. Results: In a univariable analysis, lower cognitive performance was correlated with the presence of infantile spasms, a higher number of antiepileptic drugs used, vigabatrin not used as first drug, corticosteroid treatment used, and a later age of independent walking. A higher age at seizure onset was correlated with higher cognitive performance. In a multivariable analysis, only age at seizure onset was significantly correlated with cognitive development, contributing to 28% of the variation in cognitive development. Conclusions: In our cohort, age at seizure onset was the only variable independently correlated with cognitive development. We confirm previously found univariable correlations, but show that these cannot be used as independent predictors. Considering the influence of early epilepsy on cognition, improvements in epilepsy treatment in early life may improve outcome. Prospective cohorts will be needed to answer this question.

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Neurocutaneous disorders

**ICNC-0581: Congenital hypothyroidism, hypopituitarism and precocious puberty in a patient with tuberous sclerosis: a complex case report**

Background: Tuberous sclerosis complex (TSC) is an inherited, multi-organ disorder resulting from mutations in TSC1 or TSC2. The clinical spectrum ranges from minimal signs and symptoms with no neurologic disability to epilepsy, autism and mental retardation. There is a well-established set of diagnostic criteria encompassing abnormalities in many organ systems, but endocrinological disturbances are infrequent. We report a patient with TSC who presented with drug resistant epilepsy, hypothyroidism and precocious puberty. Case Report: E.L.P., female, had congenital hypothyroidism (CH) – TSH 49.8 mcU/mL (venous sample, TSH 67.8 mcU/mL). L-thyroxine was initiated at 1 month and ultrasonography (US) showed dysgenetic thyroid. The patient presented with early refractory epilepsy and had large areas of transmantle
dysplasia and white matter heterotopía along the lateral ventricles (subependymal nodules) on MR imaging, suggestive of tuberous sclerosis. The hypothalamic and pituitary anatomy had a normal appearance. Abdominal US showed bilateral adrenal hypoechogenic nodules. Minimal skin lesions were found. At 4 years of age central hypothyroidism was diagnosed, even with appropriate dosages of levothyroxine. At 6 years of age she developed clear signs of precocious puberty (Tanner B3PH2) and pituitary function suggested central hypothyroidism (TSH 0,3mUI/L; T4 10,5 mcg/dL; T4 1,5 ng/dL), hypocortisolism (ACTH 6 and 10 pg/ml, cortisol 2.4 and 5 mcg / dl) and hypoprolactinemia (6 mcg /L). Pubertal blockade was initiated. Few cases of an association between CH and TSC have been described and suggested thyroid hamartia. Recently, a case of TSC progressing to hypopituitarism in adolescence was described. To our knowledge, the association of CH, TSC, hypopituitarism and precocious puberty has never been described. A migration defect might be the common underlying cause of these symptoms and these findings suggest a close monitoring of endocrine functions in patients with TSC.


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Neurocutaneous disorders

ICNC-0583: Sjögren-Larsson Syndrome
Introduction: Sjögren-Larsson syndrome (SLS) is a rare recessive neurocutaneous disease, with an incidence of 1: 100,000. Twenty eight patients were first described in 1957 by Sjögren and Larsson. Ichthyosis, paraplegia or quadriplegia and mental retardation were the main manifestations. The biochemical defect, enzyme fatty aldehyde dehydrogenase deficiency, caused by mutations in the ALDH3A2 gene was identified later on. Clinical case: A female patient, 14 years old, had been followed by a neuropsychiatrist since the first year of life by generalized ichthyosis and progressive pyramidal signs. Currently she presents spastic tetraparesis, mainly in the lower limbs, with clonus of both feet, with gait supported by bilateral orthoses. She was started on a physical rehabilitation program and under treatment with botulinum toxin since she was four years old. Brain MRI reveals areas of late myelination / absence of myelination spectroscopy and presence of lipid peaks in the white matter. The molecular investigation confirmed the diagnosis (ALDH3A2 gene mutation). Discussion: We describe a clinical of a rare entity, with clinical manifestations and brain imaging suggestive of SLS which was confirmed by genetic testing.

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Neurocutaneous disorders

ICNC-0584: Neurodevelopmental profiles of children with Congenital Melanocytic Naevus Syndrome
Background: Congenital melanocytic naevus Syndrome (CMN syndrome) is characterised by melanocytic naevi present at birth, and the presence of extra-cutaneous features, all due to a post-zygotic mutation in the NRAS gene. Known neurological associations are melanocytic and non-melanocytic abnormalities of the central nervous system. The subset of children with symptomatic neurodevelopmental disease on history are referred for in-depth neurodevelopmental profiling within our service. Methods: The neurodevelopmental profiles of 9 children with CMN syndrome (6 females and 3 males aged 1 to 15 years) were assessed. Results: MRI findings were: 3/9 with intraparenchymal melanosis; 1/9 with mild cauda equina enhancement; 1/9 with a midthoracic subdural lesion, 4/9 normal MRI. Four children had a history of seizures (3/4 with intraparenchymal melanosis, 1/4 normal MRI). Three children were diagnosed with Autism Spectrum Disorder; one was also diagnosed with Attention Deficit Hyperactivity Disorder. Four children (one with intraparenchymal melanosis, one with other pathology, two with normal MRI) had language difficulties. Children with intraparenchymal melanosis had cognitive abilities ranging from below average to high average. Strengths and Difficulties Questionnaire scores indicated emotional difficulties with high impact on the child’s life in 6 children (1/6 with intraparenchymal melanosis, 2/6 with other pathology, 3/6 normal MRI). Six children (2/6 with intraparenchymal melanosis, 1/6 with other pathology, 3/6 normal MRI) had difficulties in getting on with others. Conclusions: Children with CMN syndrome and neurological/ neurodevelopmental symptoms should undergo detailed profiling for associated neurodevelopmental disorders, in addition to language and emotional difficulties. Assessment and monitoring can facilitate early intervention.

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Neurocutaneous disorders
Neurocutaneous disorders

ICNC-0570: Sturge Weber Syndrome Type 3 masquerading as ‘Migraine Status’ at presentation
Introduction: To present an interesting case of SWS type 3 presenting with prolonged severe unilateral headache mimicking migraine status. Case presentation: A 9 year old boy presented with 24 hour history of vomiting and severe left temporal headache. His initial neurological examination was unremarkable. Urgent CT head with contrast showed calcification in left occipital cortical and sub-cortical lobe. He had one previous similar presentation with severe headache and prolonged seizure 3 years ago which was managed as presumed encephalitis. On day 3, he developed a dense right sided homonymous hemianopia. Urgent MRI brain with contrast showed pial angiomatosis in the occipital and parietal lobes consistent with the diagnosis of SWS. He later developed complex partial seizure and was started on anti-epileptic medication. He was started on Flunarazine as migraine prophylaxis and also Aspirin to prevent stroke like episodes. Discussion: SWS type 3 is rare and only 24 cases have been reported in literature. Type 3 has a vascular malformation in the brain with no facial naevus and no glaucoma which poses diagnostic challenge. It can only be identified through neuro-imaging with contrast therefore can be difficult to diagnose and does require high degree of suspicion. Conclusion: This case highlights the importance of high index of suspicion and low threshold for neuroimaging (with contrast) in the cases presenting with prolonged severe headaches. SWS type 3 does exist and can mimic as migraine status as the presenting feature!

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Neurocutaneous disorders

ICNC-0593: Neuro-psychosexual children with tuberous sclerosis complex
Tuberous sclerosis complex (TSC) as multisystem genetic disorder is also associated with numerous behavioural, intellectual, academic, neuropsychological, psychosocial difficulties and neurodevelopmental and psychiatric disorders. The term Tuberous sclerosis-Associated Neuropsychiatric-Disorders – TAND is generally accepted. Even so, only a small proportion of individuals with TSC were screened or receive proper help for mental health problems. We examined 13 children with TSC for associated neuro-psychological difficulties using freely available TAND check-list translated in Croatian language. Results showed that intellectual disability ranging from mild or moderate to profoundly impaired were present in 45.5% children. Specific learning disorders associated with school performance were found in 80% children with normal intellectual ability. There were 3 child (23%) with diagnosis of autistic spectrum disorder. Behavioural difficulties consists of problems with aggression (40%) and attention related behaviours such as difficulty concentrating, hyperactivity and impulsivity (49%). Symptoms of depressive mood which intensity and duration cause distress were found in approximately half of the subjects. Low self-esteem and difficulties in social relationships were present in about three-quarters of our patients. Our results are in concordance with previously known fact of high prevalence of various neuro-psychosocial difficulties in children with TSC. TAND checklist showed to be simple and useful tool in evaluating mental problems in children with TSC in everyday practice. We will proceed to encourage the regular use of TAND checklist in our country as a first step toward the holistic approach in the evaluation and treatment of children with TSC.

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Neurocutaneous disorders

ICNC-0585: Incontinentia Pigmenti in a male patient: a case report and review of literature
Introduction: The incontinentia pigmenti (IP) is an X-linked, dominant genodermatosis. In male patients, it is usually lethal, while heterozygous females survive due to functional mosaicism from X-inactivation. Male patients with skin, dental, ophthalmological and neurological defects typically of those seen in female patients with IP are rare. Case description: we describe a 2-years-old male with IP. He presented with a neonatal erythematous-vesicular rash in his left leg following Blaschko’s lines after a full-term pregnancy and eutocic delivery. Subsequently, the skin lesion progressed to a papulous form, warty hyperkeratosis, and linear hyperpigmentation. A skin biopsy confirmed marked dyskeratosis and eosinophilic infiltration consistent with IP. The karyotype analysis showed 46 XY. There was no immunodeficiency. Family history was negative. His neurological development is delayed. He is hypodontic, with conical crowns and dystrophic nails. A cerebral...
MRI at the age of 12 months showed structural brain abnormalities consistent with hypoplasia of the corpus callosum and supratentorial white matter changes. Ophthalmological examination revealed strabismus in the left eye. Discussion: IP in male patients has been reported; however, its clinical phenotype is heterogeneous and has not been well characterized. In our patient, the florid phenotype showing ectodermal, ophthalmologic, and neurologic abnormalities resembles a female phenotype. Genetic testing for NEMO mutations in blood and urine samples is ongoing. A postzygotic somatic mosaicism is the likely mechanism.

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Neurocutaneous disorders
ICNC-0586: Characteristic MR spectroscopic findings in Sjögren-Larsson Syndrome
BACKGROUND: Sjögren-Larsson Syndrome is a very rare neurocutaneous disorder, which is characterized by congenital ichthyosis, mental retardation and spasticity. Magnetic resonance (MR) spectroscopy reflects characteristic lipid accumulation in the white matter as discussed below. METHODS: A 14-month old boy of Arabic descent presented to the pediatric neurology clinic with severe motor and speech delay. He was unable to roll over, sit unsupported, or use any specific words or gestures. His examination was significant for spastic diplegia and scaly skin lesions. Later, he was diagnosed with febrile seizures. There was a history of consanguinity in parents and patient’s sister shared similar clinical findings. MR imaging and spectroscopy (Figure I) showed a characteristic pattern for Sjögren-Larsson Syndrome. Detection of homozygous deletion of exons 1 to 5 in fatty aldehyde dehydrogenase (FALDH) 3A2 gene confirmed the diagnosis. RESULTS: MRI of the brain showed symmetric hyperintense FLAIR signal in the periventricular white matter of the frontoparietal lobes. MR Spectroscopy of abnormal frontal white matter demonstrated characteristic lipid peaks with a high sharp peak at 1.3 ppm (methylene proton spins) and a small peak at 0.8 - 0.9 ppm (methyl proton spins).
CONCLUSIONS: Sjögren-Larsson Syndrome is a consequence of deficiency in the microsomal FALDH. Clinical manifestations are thought to be secondary to the tissue accumulation of fatty aldehydes and fatty alcohols. However, the exact nature of lipids responsible for MR changes is not known. Treatment strategy of leukotriene-antagonism has shown some promise in the treatment of ichthyosis.

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Neurocutaneous disorders
ICNC-0588: Sirolimus in patients with epilepsy associated with tuberous sclerosis complex
Introduction Epilepsy in tuberous sclerosis complex (TSC) is commonly drug-resistant and presents a major factor contributing to neurodevelopmental delay. Excessive mTOR activity is believed to play a pivotal role in the development of epilepsy in TSC. mTOR inhibitor, everolimus, has been recently approved for the treatment of subependymal giant-cell astrocytomas and renal angiomyolipomas in TSC patients. In this study we present the preliminary results of another mTOR inhibitor, rapamycin, treatment in children with TSC-related epilepsy. Methods Twelve children, aged 2-10 years, with TSC-related drug-resistant epilepsy were treated with rapamycin. Drug dosage (0.5-2mg/day) was established individually to blood through level and patient’s toleration. Antiepileptic effect and safety profile was assessed after 3 months of treatment. The study was approved by local Ethics Board and the informed consent from patients’ caregivers was taken prior to treatment. Results The safety profile of rapamycin in this study was comparable everolimus in TSC patients. The most frequent adverse events included upper respiratory tract infections (in 4 cases) and mild grade stomatitis (in 3 cases), not requiring rapamycin withdrawal. Eleven patients continue treatment. Subjective improvement was observed in 8 patients, with 50% seizure frequency reduction in 3 individuals. In 3 patients no improvement was seen and in 1 patient increase in seizures was reported by the parents. Conclusions This case series suggests that rapamycin is relatively safe in TSC patients, also in children <3 years, and could be a therapeutic option in drug-resistant epilepsy. Clinical efficacy, long-term safety, and drug dosage of rapamycin in TSC-related epilepsy require further large-scale studies.

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Neurocutaneous disorders

ICNC-0589: Tissue overgrowth in patients with tuberous sclerosis

Tissue overgrowth is commonly associated with genetic disorders such as Proteus syndrome, Klippel-Trenaunay syndrome and hemihypertrophy syndrome. It has been also previously reported in tuberous sclerosis (TSC) as a very rare feature. Seeing that existing literature provides strong background for the hypothesis that the PTEN gene mutation plays an important role in the control of tissue growth it may be possible that some patients carry mutations in at least two genes. In the present study we describe a series of TSC patients with concomitant tissue overgrowth. Methods: A group of eleven children diagnosed with TSC with coexisting tissue overgrowth has been identified at the Department of Neurology and Epileptology of The Children’s Memorial Health Institute in Warsaw, Poland. Patients were from different families except for 2 siblings. All patients were evaluated retrospectively and their photographs were collected. Two patients had undergone genetic testing for PTEN mutations. Results: In all patient tissue overgrowth was asymmetric. Five out of eleven patients had unilateral upper limb enlargement whereas only two presented with lower-limb enlargement. Three patients had skull bone overgrowth. One patient presented with a hemihypertrophy. In one patient a mutation in the PTEN gene has been confirmed. Conclusion: We report a rare connection of TSC and tissue overgrowth in eleven patients. The mutation in the PTEN gene in one patient expands further possible links to other genetic disorders characterized by the dysregulation of the number of cells in tissues.

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Neurocutaneous disorders

ICNC-0595: Impaired mitochondrial metabolism and turnover in neuronal models of Tuberous Sclerosis Complex

Introduction: Tuberous sclerosis complex (TSC) is a neurodevelopmental disorder caused by mutations in TSC1 or TSC2. Loss of TSC1 or TSC2 renders the mTORC1 complex constitutively active, resulting in abnormal metabolism and impaired autophagy. Whether this leads to deficits in mitochondrial function or turnover of damaged mitochondria through autophagy (mitophagy) is unknown. Methods: To study mitochondrial metabolism and turnover, we use a combination of genetic strategies, pharmacology, live imaging probes, time-lapse confocal microscopy, flow cytometry, immunocytochemistry and biochemical assays in a neuronal in vitro model of TSC and in cortical neurons differentiated from induced pluripotent stem cells (iPSC) of TSC patients and controls. Results: Knockdown of Tsc2 in neurons leads to impaired mitochondrial function and an accumulation of dysfunctional mitochondria. Similar results are obtained in human iPSC-derived cortical neurons from TSC patients. Mitochondrial accumulation is at least in part secondary to impaired mitophagic flux. Investigating local mitophagin axons, we find that axons are depleted of functional mitochondria because of impaired local degradation and subsequently increased retrograde transport of mitochondria. Mitochondrial fractions of Tsc2-deficient neurons accumulate autophagy markers but their subsequent turnover is impaired. Following induction of mitophagy, we find impaired maturation of autophagosomes and reduced autophagosome-lysosome fusion, pointing to deficits in the late stages of the autophagy pathway. Conclusions: Accumulation of damaged mitochondria in neurons in TSC due to specific deficits in axonal and global mitophagy could lead to impaired synaptic signaling and may contribute to complex disease manifestations such as epilepsy, autism-spectrum disorder or intellectual disability.

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Neurocutaneous disorders

ICNC-0590: Preliminary study for the validation of TAND checklist in Children with Tuberous Sclerosis Complex (TSC)

Introduction: This is a preliminary study that adapts TSC-Associated Neuropsychiatric Disorders (TAND) checklist and applies it to the Korean children in order to provide an understanding about neurodevelopmental and psychological comorbidities in patients with Tuberous sclerosis (TS). Methods: TAND Checklist is a survey developed in the United Kingdom that is composed of questions about the current behavioral, psychiatric, intellectual, academic, neuropsychological, and psychosocial difficulties of the patients with TS. This survey was administered to 32 patients with TS at the Department of Pediatric Neurology, Severance Children’s hospital, and the results were analyzed. Results: Of 32 patients (ages=8.4±5.4 years, 10 Males) who were diagnosed with TS, 29(94%) experienced seizure (onset age=1.4±1.7 years) and 28 were taking anticonvulsants, and eight of them (25%) had surgery and seven of them (22%) were on Ketogenic Diet treatment. From the behavioral aspect, delayed language development delay (21, 66%), social
Neurocutaneous disorders

ICNC-0591: Loss of heterozygosity for TSC1 in a fibrous hamartoma of infancy associated to tuberous sclerosis complex

Introduction. Germline TSC1 or TSC2 mutations cause tuberous sclerosis complex (TSC). Loss of heterozygosity (LOH) for TSC1 or TSC2 gene was found in human cancer specimens and it was supposed to be involved in TSC hamartoma development. Case report. A 9-year-old boy presented at birth with a soft-tissue mass on the left side of the backwall. By the age of 5 months the child was diagnosed as having TSC based on the clinical features. Molecular analysis showed a de novo mutation (c.1997+1G>A) on TSC1 gene. The back lesion had rapidly grown in one year: on magnetic resonance imaging (MRI) it was a fibro-adipose mass (grown up to 18×3 cm) which was insinuating along muscular wall. The histopathologic examination of the mass (age 13 months) revealed a fibroushamartoma (FH). The analysis of fibroblasts in the lesion showed LOH for TSC1 gene. The lesion continued to grow up to 3 years of age, then it was stable at MRI follow-up. Discussion. FH of infancy is extremely rare in TSC, reported so far in few cases. Genetic analysis of FH lesion has never been performed. In our case the analysis of FH fibroblasts showed LOH for TSC1, demonstrating a certain correlation with TSC. This argue in favour that LOH can promotes the development of FH in TSC.

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Neurocutaneous disorders

ICNC-0592: Seizures in patients with tuberous sclerosis complex

Introduction. Seizures in TSC usually occur during infancy or early childhood but may happen at any age. Epilepsy in TSC patients tends to be intractable over time. However, the description of seizures course in TSC, especially the remission is limited. The purpose the study is to display the onset, phenotype and age of seizures remission in TSC patients. Methods. Patients diagnosed with TSC were systematically evaluated from 2009 to 2015 at the Integrated Clinics for TSC, and underwent a systematic evaluation and questionnaire interview, including a medical review of epilepsy history and a neurobehavioral disorder assessment. Results. Fifty-eight patients (26 males and 36 females) were enrolled into the study. There were 81.0% (51/63) with positive seizure history and 30.0% (15/50) with history of refractory epilepsy. Age of seizures onset were recorded as 54.5% (24/44) in <1 year, 43.2% (18/44) in 1-6 years and 4.5% (2/44) in >6 years. Of 39 patients, seizures types were recorded as infantile spasm in 25.8%, generalized-tonic-clonic in 34.1%, complex partial in 78.0%, simple partial in 17.1%. When compare the groups between active (n=32) and seizure remission (n=17) patients, age, neurobehavioral disorder and RF are statistic significant (p<0.001, p=0.001 and p=0.016). Discussion. Epilepsy remains one of the major comorbidities in TSC patients, especially in infants. It develops multiple phenotypes, and seizure remission occur in adulthood, especially related minor refractory epilepsy and neurobehavioral disorders. Keywords: Tuberous sclerosis complex · Seizures Remission · Refractory epilepsy

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Neurocutaneous disorders

ICNC-0594: Effect of mTOR Inhibitor on Neuropsychiatric Symptoms in children with Tuberous Sclerosis and associated factors analysis

Objective. To evaluate the effects of mTOR inhibitor rapamycin on neuropsychiatric symptoms and prognosis in children with tuberous sclerosis complex (TSC). Methods. Clinical data of 253 children with TSC were collected from Sep. 2011 to Jan. 2015. Among them, 191 cases met inclusion criterion. Therapeutic effects were evaluated after 12 weeks and 24
weeks and 48 weeks of rapamycin treatment by epileptic seizures reduction, autism and cognitive improvement, skin lesions improvement, electroencephalogram (EEG) and imaging improvement, and the influencing factors of clinical curative effects and prognosis were analyzed. Results: There were 110 males and 81 females. The median age for rapamycin treatment was 28.5 months. 81% of children have epilepsy, 73% of children have cognitive disorder. The proportion of children with autism behavior was 52.4%. Most of patients have skin lesions. Head MRI examination often showed lesions, mostly cortical tubers and the subependymal nodules. Heart and kidney are also involved. After 12 weeks, 24weeks, and 48 weeks of rapamycin treatment, the seizures of the TSC children significantly reduced, decline percentages of seizures are statistically significant differences (p< 0.01). The kinds of antiepileptic drugs also reduced (p< 0.01). The ABC scores (to evaluate the autism) decline percentages are statistically different than before treatment (p< 0.01). Among different age groups, the decline percentages of seizures in low age groups (age< 3 years old) are significantly higher than high age group (age>6 years old) after 12 weeks and 48 weeks rapamycin treatment, (p< 0.05). In the aspects of cognitive and intellectual improvement, low age group are better than higher groups after 12 weeks of treatment (p< 0.05). Divided the TSC children with epilepsy into 3 groups, the infant spasm (IS) group, the prior IS group and the non IS group. After 12 weeks treatment, the IS group often had a more obvious improvement (p<0.05).

Conclusions: 1) Rapamycin is relatively safe and adverse reactions are less. It can obviously decrease the TSC related seizure frequency, the efficacy rate can be as high as 80%. 2) Rapamycin can obviously improve the autism behaviors of TSC children, and the cognitive and intelligence, lesions in brain, skin, heart, kidneys are also improvement in varying degrees. 3) Using rapamycin at earlier age shows more obvious improvement in reducing seizures and the cognitive and intellectual aspects. Compared to other epilepsy types, IS often had more obvious improvement.

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Neurometabolic disorders

ICNC-0633: An infantile form of Krabbe disease associated with a New GALC mutation and multiple cranial nerves involvements: case report

Krabbe disease (KD) is an autosomal recessive leukodystrophy caused by the deficiency of the galactosylceramidase (GALC) and the accumulation of a cytotoxic substrate (galactosylsphingosine). The classic presentation includes excessive irritability, muscle hypertonicity, developmental delay, failure to thrive, peripheral neuropathy, seizures, and optic nerve atrophy. The classical infantile type is the most common disease manifestation (95% of known cases). There is wide variability in the age of onset and clinical severity of KD. Typical neuroimaging findings of KD include signal abnormalities in the cerebral and cerebellar white matter and thalamus. There are unusual radiological findings in few reports that describe enlargement of the optic nerves and with nerve roots of the spinal cord. We reported a case of a enlargement of the optic nerves bilaterally associated with multiple cranial nerves enlargement (3, 5, 7 and 8) in an infantile form of KD, which has not been reported in the literature. However, we identified a new homozygous missense mutation p.G106R (c.316G>A). We presented clinical, unusual imaging finding and a new mutation of the GALC gene in a six months girl with consanguineous Turkish family.

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Neurometabolic disorders

ICNC-0634: Safety and efficacy of methylphenidate in patients with Hunter syndrome (MPS II)

Hunter syndrome (mucopolysaccharidosis type II or MPSII) is an X-linked chromosomal storage disorder due to deficiency of the lysosomal enzyme iduronate-2-sulfatase. It is clinically divided into severe or neuronopathic (2/3) and attenuated or non-neuronopathic types. Hyperactive behaviour is very common in Hunter syndrome. However, literature evidence for stimulant treatment is lacking. This study evaluates methylphenidate (MPH) safety and efficacy in boys with Hunter syndrome. Methods Seven MPS II patients (mean age 5 years, range 4 to 7 years) were put on MPH between 2010 and 2015. All the patients received weekly infusions of IV idursulfase. A retrospective chart review obtained comorbid symptoms, concomitant medication, vital signs, side effects, dosage and MPH efficacy. Results Five patients had neuronopathic involvement, all of them with IQ still above 50. Additional comorbidities included seizures (1) and supraventricular arrhythmia (1). Three patients reported MPH side effects: appetite suppression (2) anxiety / rebound (1). There were no statistically significant changes in weight, EKG or blood pressure 12 months after medication initiation. Medication efficacy was subjectively reported by parents in 6/7 patients. They remained on MPH at their most recent follow-up visit. Risperidone was also used in 1/7 patients. Conclusions This study preliminarily evaluates MPH use in a small group of Hunter syndrome patients. Stimulants were tolerated and effective in most subjects. Side effects were mostly minor. MPH may be a safe and effective intervention for Hunter syndrome children with hyperactivity disorder. Further studies with larger sample sizes are needed.

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Neurometabolic disorders

ICNC-0598: Subacute Sclerosing Panencephalitis mimicking a Metabolic disorder: Clinical, Electroencephalographic and imaging features

Subacute sclerosing panencephalitis (SSPE) is a rare, slowly progressing neurodegenerative disorder caused by a prior measles virus infection. Patients may present with atypical clinical signs, uncharacteristic electroencephalographic and imaging features which may result in delayed diagnosis and treatment. We report four patients with atypical presentation in which the subacute sclerosing panencephalitis mimicked the clinical and radiological signs of a metabolic disorder. Patient 1 presented with dystonia. She showed a very slow course without myoclonia or a periodic electroencephalogram complex. Magnetic resonance imaging (MRI) lesions were present in both periventricular temporoparietal regions, frontal lobes, and splenium of corpus callosum, mimicking a lisosomal storage disease. Patient 2 presented with syncope followed by generalized intractable seizures. EEG showed generalized epileptiform discharges. Brain MRI revealed asymetrical frontal White matter hyperintensities including corpus callosum as well as bilateral parietooccipital area which simulated a lisosomal storage disorder. Patient 3, presented with slurry speech and ataxia. EEG showed multifocal epileptiform discharges. Brain MRI showed diffuse bilateral periventricular and frontal white matter hyperintensities with a similar bilateral involvement of the superior part of the putamen, masquerading a mitochondrial disorder. Patient 4,
presented with a very slow progressive change of personality. EEG revealed diffuse slowing of background activity. MRI showed bilateral periventricular parietooccipital and frontal hyperintensities, resembling a lysosomal storage disorder. It is important for the child neurologists to be aware of the clinical heterogeneity and radiological variability of SSPE that can resemble metabolic disorders in order to avoid inappropriate diagnosis and delay in treatment.

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Neurometabolic disorders

ICNC-0635: How important is vitamin b12 for brain growth and neurodevelopment?

Objectives: To describe neurological, hematological manifestations and the outcome in patients with vitamin B12 deficiency due to maternal deficiency. Material and Methods: A retrospective review of 56 charts of children with B12 deficiency. The threshold value for vitamin B12 deficiency was determined for sex and age. Nineteen patients presented with neurologic symptoms and, 14 full filled the inclusion criteria. Inclusion criteria: Patients with neurologic manifestations with low plasma vitamin B12 levels. Only patients with mothers with low plasma vitamin B12 levels as well were included. Exclusion criteria: Patients with other concomitant diseases. Results: Age range at symptom onset: 1-9 months. In all cases folic acid levels were within normal ranges. Neurological manifestations: neurodevelopmental delay or regression 10/14, involuntary movements 9/14, irritability or apathy 8/14, acquired microcephaly 7/11, hypotonia 6/14. Hematological manifestations: anemia 11/14 (6 megaloblastic anemia), 9/14 patients also presented thrombocytopenia and/or neutropenia. Twelve patients had increased urine excretion of metilmalonic acid. All the urine tests became normal after treatment. Patients were treated with oral cianocobalamin. All patients fully recovered during the first month of treatment. 12/14 had normal development at 6 months of follow-up with head circumference catch-up. Conclusions: B12 vitamin deficiency has a clear impact on child development and directly affects cognition and brain growth. Because vitamin B12 deficiency can manifest with various neurological symptoms, such as delay or developmental regression, lethargy or irritability, in every child presenting with this findings, vitamin B12 deficiency should be checked. An early diagnosis and treatment should be established to rectify this insidious condition.

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Neurometabolic disorders

ICNC-0636: A case of juvenile Niemann-Pick Tip C disease presented with ADHD

Introduction: Niemann-Pick Tip C (NP-C), a cellular cholesterol trafficking defect, characterized by visceral, neurological, and psychiatric manifestations is a rare autosomal recessive disorder. Here, we present a case who was attended to special education for attention deficit-hyperactivity disorder (ADHD) over 2 years in a psychiatry clinic. Case: A twelve years old girl admitted to our hospital suffering from clumsiness, speech problems and ataxia for five years old. She had been attending to special education for ADHD for two years. In examination, mild cerebellar ataxia, dysmetry, dysarthry and vertical gaze palsy were determined. Plasma chitotriosidase level was 219.15 nmol/hour/ml (normal range 0-150 nmol/hour/ml). In genetic analysis, compound heterozygous mutations in the NPC1 gene were found: p.C909R and vertical gaze palsy were determined. Plasma vitamin deficiency due to maternal deficiency. Material and Methods: A retrospective review of 56 charts of children with B12 deficiency. Results: Age range at symptom onset: 1-9 months. In all cases folic acid levels were within normal ranges. Neurological manifestations: neurodevelopmental delay or regression 10/14, involuntary movements 9/14, irritability or apathy 8/14, acquired microcephaly 7/11, hypotonia 6/14. Hematological manifestations: anemia 11/14 (6 megaloblastic anemia), 9/14 patients also presented thrombocytopenia and/or neutropenia. Twelve patients had increased urine excretion of metilmalonic acid. All the urine tests became normal after treatment. Patients were treated with oral cianocobalamin. All patients fully recovered during the first month of treatment. 12/14 had normal development at 6 months of follow-up with head circumference catch-up. Conclusions: B12 vitamin deficiency has a clear impact on child development and directly affects cognition and brain growth. Because vitamin B12 deficiency can manifest with various neurological symptoms, such as delay or developmental regression, lethargy or irritability, in every child presenting with this findings, vitamin B12 deficiency should be checked. An early diagnosis and treatment should be established to rectify this insidious condition.

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Neurometabolic disorders

ICNC-0637: Histologic characterization of the progression of CNS pathology in the Mucopolysaccharidosis IIIB (MPS IIIB, Sanfilippo B) mouse model and bio-distribution and efficacy of the intracerebroventricular enzyme replacement therapy, BMN 250, a NAGLU-IGF2 fusion protein.

Mucopolysaccharidosis IIIB (MPS IIIB), is a pediatric neurodegenerative lysosomal storage disorder, caused by a deficiency of alpha-N-acetylgalcosaminidase (NAGLU) resulting in accumulation of heparan sulfate. Transgenic mice deficient in Naglu are used to preclinically model MPSIIIB but the pathologic progression and regional and cell-type distribution of storage in the central nervous system (CNS) are incompletely understood. Histologic analysis demonstrates that LAMP2, a marker of lysosomes and an indirect indicator of HS storage, is elevated in mutant mice at birth, plateaus at four weeks of age and remains stable into adulthood (24 weeks) by which time 60% of neurons exhibit abnormal LAMP2 levels. Global cortical synaptic dysfunction is histologically observed as a reduction in pre-synaptic markers and concomitant changes in distribution of post-synaptic markers. Reactive astrogliosis is observed starting at two to four weeks, but there is regional heterogeneity of the rate and pattern of increase. Interestingly, while activated
microglia increase in many CNS regions, the total number of microglia remains similar to control mice at all ages. In order to understand how different cell types were impacted by disease progression, a cell-type analysis of LAMP2 distribution was performed. 70% of total CNS LAMP2 co-localized with microglia and 20% was present in astrocytes implicating these as key cellular targets, in addition to neurons, for enzyme replacement therapy (ERT). BMN 250 is an ERT drug candidate, comprised of recombinant hNAGLU fused with insulin-like growth factor 2 (IGF2) for lysosomal targeting. When BMN 250 was administered intracerebroventricularly (ICV) to mutant mice four times over two weeks at 100 microgram doses, immunohistochemical detection of BMN 250 was observed broadly throughout the CNS and importantly in neurons, astrocytes and microglia. Marked clearance of storage and reduction of total LAMP2 was observed and effects on neuronal-specific LAMP2 and synaptic markers are currently under study.

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Neurometabolic disorders

ICNC-0638: Clinical follow up of 7 patients with Hunter Syndrome after one year of enzyme replacement therapy
Introduction: Mucopolysaccharidosis type II (MPSII) is an X-linked recessive genetic disorder, caused by deficiency of iduronate-2-sulfatase enzyme (IDS). Identification is essential to initiate early treatment. Enzyme replacement therapy (ERT) with Idursulfase (a recombinant form of human iduronate-2-sulfatase) is available for MPSII. ERT improves respiratory impairment, functional capacity and joint mobility, reduces organomegaly and coarse facial features and stabilizes cardiac manifestations. Methods: A descriptive-comparative study. We followed up 7 patients with confirmed diagnosis of MPS II in ERT (> 1 year of ERT). We compared 4 patients, pre and post state of each patient in ERT, evaluating respiratory function (PSG parameters, pulse oximetry), cardiac disease (echocardiography, EKG), liver and spleen size (clinical evaluation or abdominal echography), quality of life (survey) and cognitive function. Results: 4 patients (4 male), average age at diagnosis: 33 months. Duration of ERT: > 1 year. Patient 1 (severe phenotype): improvement in quality of life and cardiac disease. Patient 2: improvement in organomegaly. Patient 3: improvement in PSG, quality of life and organomegaly. Patient 4: improvement in PSG, quality of life and cardiac disease. In the other 3 patients the evaluation are in progress. We didn’t find improvement in cognitive capacity. Conclusions: In almost all of our patients we found some degree of improvement in cardiac disease, respiratory function, organomegaly and quality of life after one year of ERT, except in one patient who started ERT long time after diagnostic and has a severe phenotype of disease.

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Neurometabolic disorders

ICNC-0639: Clues in Oculocerebrorenal Syndrome of Lowe
Introduction: Lowe, oculocerebrorenal(OCLR) syndrome, is a rare, multisystemic X-linked recessive disorder, affecting the eye, brain and kidney, associating cataract, severe hypotonia, cognitive, behavioral abnormalities and later Fanconi renal tubulopathy. Growth failure, dysmorphism, abnormal brain imaging are also part of the complex picture of OCLR, placed at the confluence of ophthalmology, neurology and nephrology, thus important to make a diagnostic with direct therapeutic consequences. Two boys will be presented, starting from clinical similar situations, but following different diagnostic algorithms. Description of the cases: First case was diagnosed within the first months of life in a work-up for congenital cataracts and hyperaminoaciduria. A mutation in the OCLR1 gene was found. Developmental testing showed a delay with IQ of 55. He developed rickets at age of 2, for which he was treated. An MRI at age 6 showed multiple periventricular diffuse white matter lesions. Second case was admitted at 12 years for severe cognitive disability, congenital bilateral cataract, dysmorphism and epilepsy. His brother died from a progressive neurological condition before age of 2. Cerebral MRI showed extensive periventricular CSF intensity cystic lesions with confluent regions of T2 prolongation. This, the congenital cataract and high proteinuria led to the suspicion of OCLR, sustained by biological tests. Discussion: A triad of ophthalmological, neurological and renal impairments should arise early the suspicion of OCLR, a correct diagnosis allowing a prompt management plan, with direct impact on quality of life. The MRI shows some unique features, more prominent with age, making imaging a clue to the diagnostic.

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Neurometabolic disorders

ICNC-0640: Keypoints in mct8 deficiency diagnostic
Introduction: Monocarboxylate transporter 8 (MCT8) is a transporter specific for active form of thyroid hormone, T3, expressed in liver and brain. MCT8 gene mutations are responsible for an X-linked mental retardation syndrome, Allan-Herndon-Dudley, a severe neurodevelopmental disorder associating hypotonia, severe psychomotor delay, muscle hypoplasia, weakness and pathognomonic thyroid test -elevated T3. It also associates a cerebral MRI pattern suggestive for hypomyelination. 3 cases will be presented, the first one leading to the prompt diagnostic of the other two, by early recognizing of the clinical phenotype, followed by pointed laboratory investigations, saving unnecessary testing. Case descriptions: Andrei, 3rd boy of nonconsaginoues parents, with a family history of 2 brothers with similar phenotype, deceased previously, was admitted at age of 2 years for extreme hypotonia, with dyskinetic movement pattern, severe global developmental delay, muscle atrophy, slowly progressive. Extended metabolic tests were negative, but T3 level was increased and the MRI showed hypomyelination. Genetic test for MCT8 was positive in child and mother. The other 2 boys, of 1 year 7 months and 1 year 11 months presented with similar clinical features and thyroid hormones abnormalities led to the diagnostic. Conclusion: The authors want to emphasize the importance of considering MCT8 deficiency as a possible diagnostic in boys with hypotonia, developmental delay and extrapyramidal signs, and thus the using of thyroid hormones testing as a screening tool in this clinical situation, in order to adjust the management and for genetic counseling. Acknowledgements to W.E. Visser and S. Groeneweg (Erasmus University Medical Center) for genetic testing of our patients.

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Neurometabolic disorders

ICNC-0641: Hypomyelination and severe global developmental delay caused by intermediate severe Salla disease
Introduction: Free sialic acid storage disease encompasses a spectrum of clinical phenotypes resultant from mutations in SLC17A5. Different phenotypes include: (i) infantile free sialic acid storage disease, with severe global developmental delay (GDD), coarse facial features, hepatosplenomegaly and cardiomegaly; (ii) intermediate severe Salla disease, with moderate to severe GDD and hypotonia in the absence of visceromegaly; and (iii) Salla disease, with normal appearance, mild cognitive dysfunction and spasticity. Case Report: We report the case of a 3.5-year-old girl presenting with generalized dystonia, hypotonia, abnormal movements and conductive hearing loss following normal development for the first 6 months of life. Brain MRI at 19 months revealed hypomyelination and thin corpus callosum. On repeat MRI at 3 years, there was suspected iron deposition in the globus pallidus bilaterally. Urine free sialic acid was moderately elevated (218 mmol/mol creatinine; reference 7-83). Cerebrospinal fluid (CSF) free sialic acid was marginally elevated (24 micromol/L; reference 4-22). Sequencing of SLC17A5 revealed a previously described mutation (c.291G>A) and a novel deleterious mutation (c.819+1G>A), confirming the diagnosis of Salla disease. Conclusion: Despite the early-onset intermediate severe Salla disease phenotype, our patient had lower urine free sialic acid levels compared to patients reported in the literature. Our case also demonstrates that normal or marginally elevated CSF free sialic acid levels cannot exclude Salla disease. In patients with progressive GDD and hypomyelination on MRI, intermediate severe Salla disease should be included in the differential diagnosis – even with normal CSF or mild to moderately elevated urine free sialic acid levels.

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Neurometabolic disorders

ICNC-0642: Incidental finding of X-linked adrenoleukodystrophy in a male patient and gonosomal mosaicism in his mother

In a 5-year old boy, demyelination of the splenium of the corpus callosum was observed on brain MRI after prolonged headache complaints after minor head trauma. Elevated plasma VLCFA levels and adrenal insufficiency were consistent with the diagnosis of X-linked adrenoleukodystrophy (X-ALD). Sequencing analysis identified a novel intronic ABCD1 mutation (c.1866-11C>A), creating a novel splice acceptor site. Carrier testing in the mother showed a low level of heterozygocity of the mutation, suggestive of gonosomal mosaicism and was confirmed by pyrosequencing, restriction enzyme assay and subsequently sequencing of the restriction fragments. This is the second report on gonosomal mosaicism in X-ALD. Although the level of mosaicism is low (estimated 10%), it is not possible to predict the clinical outcome in the mother, as it is currently unknown to what extent X-chromosome inactivation and modifier genes play a role in the development of the AMN-like phenotype in female carriers.

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Neurometabolic disorders

ICNC-0813: Presentation long-term impact of lead poisoning on neurologic function in children and adolescents

Abstract

INTRODUCTION: Toxic lead exposure is associated with peripheral neuropathy and coordination impairment. In contrast to western countries, industrial lead pollution ceased in Peru only a decade ago. In Peruvian children, it is unknown whether previous lead pollution from 10 years ago, stillinduces neurologic impairment. We therefore investigated the neurologic effects of previous pediatric lead exposure in Peruvian subjects.

METHOD: In subjects from La Oroya, Peru, an industrial lead-polluted city (n=48; mean age 15.2y;range 8-31y); Concepción, Peru, an adjacent city of comparable socioeconomic status (n=42; meanage 14.7y; range 8-31y); and Groningen, the Netherlands, a non-polluted city of higher socioeconomicstatus (n=36; mean age 12.3y; range 8-16y), we compared vibration sensation, reflexes and Scale Assessment for Rating Ataxia (SARA) outcomes.

RESULTS: Previous blood lead levels (of 10 years ago) were available in 14 participating subjects (La Oroya n=4/48; Concepción n=10/42), revealing toxic concentrations (> 5 μg/dL) in all (n=14/14). Vibration sensation of both first metacarpals and metatarsals were decreased in 59/90 and 44/90 Peruvians, respectively (La Oroya: 29/48 and 24/48 vs Concepción: 30/42 and 20/42, respectively). Comparing Peruvian (La Oroya and Concepción) and Dutch (Groningen) age-matched subjects, revealed higher (worse) total and kinetic SARA outcomes in the Peruvian group (mean differences .26 and .29, respectively; p<0.001; mean La Oroya: .60 and .50 vs. Concepción: .61 and .53, respectively). INTERPRETATION: 10 years after toxic pediatric lead exposure, Peruvians still revealed neurologic impairment. Although socio-economic status may have contributed to these results, stratification did not substantiate this.

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Neurometabolic disorders

ICNC-0643: May Ketamine infusion be associated with Cerebral Salt Wasting Syndrome in the Treatment of Super-Refractory status Epilepticus?

INTRODUCTION: Cerebral salt-wasting is a hypovolemic and hyponatremic condition characterized by polyuria and sodium loss in urine. Although it is profoundly seen in the central nervous system disorders, it may present in other diseases, too. Early diagnosis and the definition of underlying causes are essential for treatment. This article presents an epileptic patient who developed cerebral salt-wasting during ketamine infusion and whose hyponatremia and polyuria ameliorated afterwards.

CASE REPORT: A 12-months-old infant diagnosed with mental motor retardation and epilepsy applied to our hospital. At admission the patient was in super-refractory status epilepticus and therefore monitored at the pediatric intensive care unit. Although the patient was started on phenytoin, levetiracetam and midazolam infusion, seizures persisted. Therefore, ketamine infusion was started. Seizures stopped following the ketamine infusion but on the fifth day, polyuria, hyponatremia and cerebral salt-wasting syndrome emerged. Following the stop of ketamine infusion, serum sodium levels were not normalized. The patient was administered isotonic and hypertonic saline consecutively. As the patient did not recover, fludrocortisone was given. CONCLUSION: Ketamine infusion is among treatment approaches for patients with super-refractory status epilepticus. However, it should be kept in mind that cerebral salt wasting may
Neurometabolic disorders

ICNC-0644: Aicardi syndrome in the etiology of refractory infantile epilepsy
Introduction: Aicardi Syndrome was first described by Jean Aicardi in 1965. The diagnosis is established by a triad of chorioretinal lacunae, seizures and colossal agenesis. All patients have generalized myoclonic and tonic-clonic type and sometimes even combined type seizures. Herein, we present a 2-month-old girl, who presented with refractory seizures and was diagnosed with Aicardi Syndrome. Case Report: A 2-month-old girl presented with refractory seizures. Her physical examination showed microphthalmia in the right eye with no peculiarity on other system examinations. Upon development of hiccup-type seizure, concomitant CSF and blood glycine level investigation and metabolic screening was requested. Cerebral tomography and MRI indicated corpus callosum agenesis and a smaller bulbous oculi on the right relative to the left. EEG revealed cortical and subcortical active epileptiform abnormality asymmetrical burst suppression in the right hemisphere. The patient was administered treatment with phenytoin, due to the persistence of seizures, levetiracetam, Phenobarbital, topiramate and vigabatrin were added to treatment respectively. The patient became clinically stable. Based on the clinical and imaging results, the case was considered to be Aicardi syndrome. The patient was discharged and put under follow-up at the neurology clinic.Conclusion: Aicardi syndrome is a genetic disorder of X-linked dominant inheritance, occurring in girls. There are non-specific EEG findings in this syndrome. Seizures typically have an onset in early childhood and generally are refractory to medical treatment. Aicardi Syndrome should be considered in patients with lateral microphthalmia and cerebral heterotrophy. Aicardi syndrome should also be considered in epilepsy cases.

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Neurometabolic disorders

ICNC-0645: Cerebral salt wasting in a case of relapsed medulloblastoma
Cerebral salt wasting syndrome (CSWS) is a rare clinical manifestation usually occurs due to head trauma, tumors, infections, hemorrhage and operations. Herein, we present a 7-year-old male who was diagnosed with medulloblastoma and than presented hyponatremia and was diagnosed with CSWS. Case Report: A 7-year-old male patient applied to hospital with complaints of generalised tonic clonic seizures. In physical examination his general condition was poor; the patient was unconscious, responded only to painful stimulant and was dehydrated. History of the patient revealed an operation two years ago due to a mass in the posterior fossa (medulloblastoma) and administered radiotherapy after the operation. The patient was still having chemotherapy. Routine hemogram and biochemical tests were done. Computerised tomography scan of the brain was evaluated as normal. Neither residual or recurrent mass identified in the magnetic resonance imaging of the spine and brain. Hyponatremia was detected in the laboratory results. In the spot urine, Na level was 207 mEq/L, polyuria was present (9.39 ml/kg/hour). Therefore the patient was evaluated as CSWS. Sodium deficit treatment (isotonic saline and hypertonic saline) was administered. Levetiracetam was started upon repetition of seizures. EEG results were evaluated as normal. Sodium deficit treatment was repeated on the patient whose hyponatremia continued. Fluorocortisone was started. As the serum sodium level was normal at the 13th day fluorocortisone and hypertonic saline stopped. The treatment was completed and the patient was discharged from hospital.Discussion: Cerebral salt wasting should be considered in patient with intracranial tumors in the presence of hyponatremia.

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Neurometabolic disorders

ICNC-0646: Atypical clinical case of Menkes Disease challenges usefulness of copper-histidine
Introduction. Menkes disease is a rare, X-linked, neurodegenerative disorder of copper metabolism. Typical clinical features include kinky hair, progressive neurological deterioration, drug-resistant epilepsy, with death before 3 years of life. Copper-histidine treatment is recommended in order to improve outcome. Case report. A seven month old male was hospitalised with global development delay, loss of previously obtained developmental milestones in the previous month, irritability, focal seizures and infantile spasms. On examination he had diffuse hypotonia with hyperreflexia. Microscopic
Neurometabolic disorders

**ICNC-0601: Neuronal Ceroid Lipofuscinosis-2 (CLN2) disease, a type of Batten disease caused by TPP1 enzyme deficiency: Current knowledge of the natural history from international experts**

**Background/Objectives:** The neuronal ceroid lipofuscinoses (NCLs) are the most common group of neurodegenerative disorders in children and adolescents. CLN2, a type of NCL caused by TPP1 enzyme deficiency, is characterized by seizures, rapid deterioration of language, cognition, motor skills and vision, and premature death. Our aim is to describe expert knowledge of CLN2 disease. Methods: 18 international NCL experts answered a survey on CLN2 natural history. Results: Clinical suspicion for CLN2 is low due to its rarity and non-specific presenting symptoms. A 1-4 year delay was reported between first onset of symptoms and diagnosis. Speech delay/decline, developmental delay/regression and seizure/epilepsy were identified as initial presenting symptoms. Symptom onset typically occurs between 1.5-5 years of age, but may occur later (9-12 years). Myoclonic epilepsy was the most commonly reported seizure type. Notably, seizures are refractory oftentimes requiring polytherapy. Cardiac rhythm anomalies, not previously associated with CLN2, were also identified. Conclusions: CLN2 is a severe, progressive, pediatric-onset neurodegenerative disorder. Disease awareness is low, causing delays in diagnosis. Seizures in concert with a regression of language and/or motor milestones should raise suspicion for CLN2. Knowledge of CLN2 is paramount to ensure timely diagnosis and to enable early initiation of future therapies.

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Neurometabolic disorders

**ICNC-0602: Expert opinion on the management of Intracerebroventricular (ICV) drug delivery**

**Background:** The intracerebroventricular (ICV) route of administration has been used for many decades to treat pediatric and adult patients with a broad range of central nervous system (CNS) disorders. There is no consensus in management of ICV devices and associated rates of reported complications are highly variable. A systematic literature review revealed that noninfectious complication rates per patient range from 1-33%, while infectious complication rates range from 0-27%. Objectives: 7 healthcare professionals (neurosurgeons, neuro-oncologists, pediatricians, nurse practitioners) with expertise in ICV delivery met to discuss best practices in management of ICV devices and drug administration and to provide guidance on prevention of complications. Results: Experts share common practices in the management of ICV
devices. Most are experienced in delivering drugs through a bolus injection, though one center has had clinical trial experience with an infusion. In either case, extreme care must be taken to follow strict aseptic/sterile techniques. Waiting a minimum of 5 days after device implantation before first use of device is recommended to allow proper wound healing and to reduce risk of backflow of the administered drug through the catheter tract. Experts differ in practice of hair removal over the device, on the type of skin prep solution used, and in use of gown and cap. All experts recommend use of sterile gloves and mask as well as skin disinfection with multiple separate swabs.

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Neurometabolic disorders

ICNC-0648: The iNTD registry: The clinical database of patients with inborn neurotransmitter related disorders
Background: Inherited defects of biogenic amines, tetrahydrobiopterin (BH4), folate, serine and glycine metabolism as well as vitamin B6 related disorders lead to progressive neurological symptoms in early infancy. Immediate diagnosis and treatment may result in an improved outcome. Until today there is no standardized systemic evaluation of diagnostic processes, therapeutic approaches and long term outcome of affected patients. Methods: The "International Working Group on Neurotransmitter Related Disorders" (iNTD) provides a platform for clinicians and scientists to exchange expertise and to foster international collaborations in research projects in the field of neurotransmitter related disorders. To date, it includes 27 metabolic centers from 18 countries worldwide. The webbased iNTD patient registry for inherited defects of neurotransmitter related disorders enables a standardized assessment of the epidemiology, genotype/phenotype correlation and outcome of these diseases, their impact on the quality of life of patients and current diagnostic and therapeutic strategies. The already existing registers (JAKEdb and BIODEFdb) will be unified with the iNTD registry. Based on the evaluation of the patient registry, the development of consensus care guidelines for the clinical and therapeutic management is in progress. Conclusion: The iNTD network is a growing international initiative to encourage scientific and clinical exchange on neurotransmitter related disorder. Together with the iNTD registry it aims to improve current research, basic knowledge and clinical management strategies considering the neurotransmitter related diseases.

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Neurometabolic disorders

ICNC-0603: Unusual presentations of TPP1 deficiency
Introduction: Bi-allelic mutations in TPP1 encoding tripeptidyl peptidase 1 (TPP1) cause late infantile neuronal ceroid lipofuscinosis (CLN2). Symptoms classically include visual loss, epilepsy, progressive motor/cognitive decline and premature death. TPP1 deficiency has recently been reported to also cause autosomal recessive spinocerebellar ataxia 7. Here we report two new cases of TPP1 deficiency without typical features. Case Description: Case 1: white Caucasian female, daughter of healthy non-related parents without previous medical, obstetric or family history presented at the age of 6 years with worsening balance, coordination and speech. Until the age of 13 she has made steady but slow developmental progress. On clinical examination she had spasticity with parkinsonism, mild cognitive delay and speech problems (selective mutism, stammer). She has no visual, hearing or feeding difficulties and has never had seizures and brain MRI is normal. TPP1 enzyme level was in the affected range. She is compound heterozygous for two known mutations, c.89+5G>C and c.1340G>A. Case 2: Fourth child of first cousin Pakistani parents presented at 8 months with developmental delay. He had two febrile convulsions. Although developmentally delayed he continued to make pleasing progress (mainstream school with support). At 7y he had ataxia and poor coordination. His brain MRI showed thin corpus callosum. TPP1 level was low. DNA sequencing showed a novel homozygous TPP1 mutation. Conclusion/Discussion: The presented cases broaden the clinical phenotype of CLN2. With the possibility of enzyme replacement therapy in the near future it is important to consider TPP1 deficiency in cases of developmental delay and ataxia.
ICNC-0604: PLA2G6-associated neurodegeneration (PLAN): Clinical spectrum and genetic characterization by means of a Spanish multi-centre research network

Introduction: PLAN is the second phenotype in frequency among Neurodegeneration with Brain Iron Accumulation (NBIA). Increasingly new cases are described and phenotypic spectrum is expanding. We aimed to identify and genetically characterize the Spanish population of PLAN.

Methods: Cross-sectional multi-center study of children with suspicion or confirmed diagnosis of PLAN. Patients were clinically assessed according to a video-filmed protocol. Medical notes were reviewed. PLA2G6 Sanger sequencing of the coding regions and flanking intronic regions was performed.

Results: 14 PLAN patients from 11 families (mean age 11.6 years, range 3-33; 4 males) were classified as: infantile neuroaxonal dystrophy (INAD) (n=11), atypical INAD (n=2), dystonia parkinsonism (n=1). Age at onset of the main signs and symptoms were: strabismus (1.5 years), language regression (1.5 years), gait difficulties (1.9 years), hypotonia (2 years), spasticity (4 years), epilepsy (5 years), osteo-articular deformities (7 years), hyperreflexia (7 years), bulbar dysfunction (8 years) and dystonia (11 years). Cerebellar atrophy (n=13) appeared at a mean age of 6 years, followed by iron deposition in the pallidum (n=8) at 9.6 years. Only the patient with dystonia-parkinsonism phenotype had normal MRI. This patient showed a good response to levodopa, whereas the rest of the cohort experienced progressive neurodegeneration despite multiple trials. We identified PLA2G6 gene mutations in all patients, 4 of which were novel: c.2017C>T, c.1010T>A, c.895-4T>A, c.680 C>T. Conclusion: PLA2G6-associated degeneration presents with a broad range of phenotypes, including language and motor regression, ataxia and cerebellar atrophy, with or without brain iron accumulation. Furthermore, PLA2G6 should be considered in childhood-onset dystonia parkinsonism, despite normal MRI.

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ICNC-0606: Beta-Propeller Protein Associated Neurodegeneration: Presentation a family with childhood onset

Introduction: NBIA (Neurodegeneration with Brain Iron Accumulation) is a group of genetic disorders characterized by abnormal accumulation of iron in the central nervous system especially in basal ganglia. Extrapyramidal symptoms, spasticity and progressive intellectual losses are significant. Hyperintensity due to iron accumulation is observed in globus pallidus and substantia nigra in T2-weighted sequences in Magnetic Resonance Imaging. WDR45 mutation in this group is the only type with X-linked dominant inheritance. (BPAN; beta-propeller protein associated neurodegeneration). Case: Hypointensity was observed in globus pallidus and substantia nigra in T2-weighted sequences in the brain MR images of a 9 yeras old girl, which had been referred to our Centre with significant spasticity, extrapyramidal symptoms, gait ataxia, intellectual retardation and loss of visual acuity. The patient, who was taught to have NBIA, had three siblings in her family with similar MRI findings. Loss of walking ability due to heavy extrapyramidal symptoms, spasticity, dementia and loss of visual acuity were significant for her brother and sisters in their twenties. Initially, most common subtypes PANK2 and PLA2G6 mutations were studied in the examination for this patient, but were not found positive. The patient was found to be WDR45 mutation positive with whole exome sequencing. Discussion : This case is valuable because of the emergence of extrapyramidal symptoms in the examination at an earlier age compared to other cases in the literature. Additionally, we would like to emphasize that this mutation which causes a change in WDR45 gene in the X chromosome is a rare and previously undetected mutation.

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ICNC-0650: A novel mutation of NPC1 gene responsible for Niemann Pick type c disease

Introduction: Niemann Pick type C disease is a rare genotypically and phenotypically heterogenous neurodegenerative disorder caused by mutations in the NPC1 or the NPC2 gene. An abnormal NPC1 gene is responsible for more than 90% of NP-C cases, and approximately 200 mutations have been described in NPC1 gene previously. In this report, we present a case with NP-C caused by a novel mutation in NPC1 gene. Case: A 12 year-old boy presented with slowly progressive ataxia, dysarthria, epilepsy, and neuromotor regression for six years. The perinatal and family history were unremarkable, and he was development normal until the onset of symptoms. Physical examination revealed ataxic gait, vertical supranuclear gaze palsy and mild splenomegaly. Brain magnetic resonanca imaging showed nonspecific mild periventricular hyperintensity. Electroencephalography revealed bilateral posterior sharp and spike waves. The score on NP-C suspicion index was 110. Thus we measured the plasma sphingomyelinase level which was found markedly reduced. Sequencing all exons and the intron-exon boundaries of NPC1 gene revealed novel mutations, p.N169I(c.506 A>T) in one allele and c.3742_3745delICTCA (p.L1248VfsX3) in the other, which were found to be carried by his mother and his father, respectively. Discussion: In children with symptoms suggestive of NP-C including vertical supranuclear gaze palsy, ataxia, and splenomegaly, sequencing of the NPC1 gene may lead rapid diagnosis before the traditional methods including histopathological analysis of bone marrow aspirate, liver and skin biopsies, fluorescent and electron microscopy, and cholesterol esterification assays.

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ICNC-0651: Therapeutic effects of Intravenous L-arginine administration on patients with Mitochondrial myopathy, Encephalopathy, Lactic acidosis, And Stroke-like episodes (MELAS)

Introduction: MELAS is a multisystemic disorder with a complex of biochemical and genetic mitochondrial defects and a broad range of clinical manifestations and a highly variable course. No specific treatment is available. This study was designed to retrospectively review the therapeutic effects of intravenous L-arginine administration on patients with MELAS at acute phase. Methods: Patients, whose diagnosis of MELAS was confirmed by clinical manifestations and genetic studies, were enrolled in this study. Their clinical presentations, laboratory data, and neuroimaging findings were reviewed. Enrolled parameters, including headache (present: 1, none: 0), vomiting (present: 1, none: 0), tachypnea (present: 1, none: 0), convulsion (present: 1, none: 0) and hemiparesis (present: 1, none: 0), lactate (≥20mg/dl: 1, <20mg/dl: 0), and MRS lactate peak (present:1, none:0) were scored for comparison before and after intravenous L-arginine administration. The intravenous administration of L-arginine was initiated within 24 hours of the acute phase. Results: 7 patients (male/female ratio = 4:3) were identified with trNALeu(UURU) 3243 A>G. Ages ranged from 4 years to 30 years (mean = 17.71±9.01 years). Patients with L-arginine administration (4/7; 57.14%) showed a better improvement of stroke-like episodes in comparison to patients without L-arginine therapy. Conclusion: Although there is no known treatment for MELAS, the frequency and severity of clinical symptoms of stroke-like episodes of MELAS patients significantly improved after L-arginine administration in this study, indicating that L-Arginine therapy showed promise in treating stroke-like episodes in MELAS.

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ICNC-0607: Coexistence of two rare genetic disorders: Cystic fibrosis and megalencephalic leukoencephalopathy with subcortical cysts in a child

Introduction: Cystic fibrosis (CF) is the most common autosomal recessive disease with fatal outcome in Caucasians with a frequency of 1 in 2500 live births. Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is an another rare autosomal recessive neurological disorder characterized by macrocephaly, motor and cognitive decline, ataxia, spasticity and occasional seizures. MLC gene locus has been mapped as MLC 1 gene at chromosome 22q. Case Description: A 11-year-old boy presented with progressive difficulty in walking since three years. On medical history, he had CF since his early life. On his examination, he had macrocephaly. Cranial magnetic resonance imaging was shown diffuse increased T2 signal of white matter. We analyzed a novel homozygous p.V303Gfs*76 (c.908-918delinsGCA) mutation the MLC1 gene. Conclusion: As the two gene loci are not related, it is most likely that two independent mutation events have occurred.
Neurometabolic disorders

ICNC-0652: Case report of an infant with Menkes syndrome (Occipital horn syndrome)

Background: Menkes syndrome is an X-linked, neurodegenerative disease of general copper deficiency, caused by a mutation of the Xq13.3, ATP7A gene. Classic Menkes disease includes neurological defects, growth retardation, lax skin, joints, hypothermia, hypopigmentation and peculiar "kinky" hair. Incidence ranges between 1 in 40,000 to 1 in 350,000. Occipital Horn syndrome is a milder variant of Menkes disease, also known as X-linked cutis laxa or Ehlers-Danlos type 9 (De Bie, P et al, 2007). Aim: Report of the clinical findings, radiographic, laboratory and genetic mutation analysis of Menkes disease and variants as rare conditions for earlier diagnosis and possible management. Case report: A male infant, 1 yr & 2/12 months old on presentation, the third child of a consanguinous marriage. Full term, born by Cesarean section. Presented by global developmental delay, urinary bladder diverticulae, generalized hypotonia and seizures. Clinically: Head lag, "kinky", rough and sparse hair and eye brows, wide open anterior fontanelle, pectus excavatum, faint heart sounds, mild abdominal distension, cutis laxa, arachnodactyly, hyperextensible joints, generalized hypotonia with brisk reflexes were detected. Abnormalities in laboratory tests, serum copper and ceruloplasmin levels, chest computed tomography (CT), echocardiography, contrast urinary tract radiography, CT and brain magnetic resonance imaging (MRI) were reported as well as mutation analysis being processed. Discussion/Conclusion: Diagnosis was established by the characteristic clinical picture, radiographic findings and confirmed by low levels of serum copper and ceruloplasmin. Mutation analysis result is to be confirmed. Reference: 1. P de Bie, P Muller, C Wijmenga, L W J Klomp. J Med Genet 2007;44:673-688.

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Neurometabolic disorders

ICNC-0653: Carnitine and free fatty acids levels in children with Suspected Mitochondrial Disorder

Introduction: Increased oxidative stress is a common feature of mitochondrial dysfunctions. β-oxidation of fatty acids is taking place in the mitochondria so specific defects of mitochondrial enzymes and dysregulation of carnitine transport system for the fatty acids may disturb the β-oxidation process. Increased level of fatty acids may increase oxidative stress by increasing substrates availability. Objective. To evaluate plasma acylcarnitine profile, free fatty acids levels and plasma total antioxidant capacity (TEAC) in five groups of children with different types of mitochondrial dysfunction and 50 control subjects. Methods. 81 children with suspicion of mitochondrial disease and 50 control subjects have been enrolled in the study. Six groups have been considered: group 1-with global development disorder (n=25), group 2-with epileptic encephalopathy (n=22), group 3-with cerebellar syndrome (n=10), group 4-with demyelinating disease (n=13), group 5-with cranial nerves defects (n=11) and group 6-controls (n=50). Free and total carnitine, acylcarnitine, fatty acids and TEAC levels have been measured in plasma samples. Results: All children with suspicion of mitochondrial disease have decreased TEAC and free and total carnitine values (p<0.001) when compared with controls. The levels of fatty acids were significantly increased (p<0.001) in children with suspicion of mitochondrial disease. Conclusion: Depletion of free and total carnitine and accumulation of fatty acids in children with suspected mitochondrial dysfunction may result in increased oxidative stress in these patients. Additional investigations are needed to clarify the implications of free fatty acids level perturbation on oxidative stress parameters in patients with mitochondrial dysfunction.

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Neurometabolic disorders

ICNC-0654: Mitochondrial diseases, When to suspect?

INTRODUCTION: Mitochondrial diseases have in common an alteration in the final step of oxidative metabolism, mitochondrial respiratory chain. One of the most common forms of presentation is neurological disease. METHODS: We conducted a retrospective descriptive study of patients diagnosed with mitochondrial disease between the years 2007-2015 in our hospital. RESULTS: 16 patients, 12 boys (75%) and 4 girls (25%) were included. The median age at diagnosis was 19 months (2 days - 6 years). The most frequent cause for consult were seizures in 11 patients (6 presented early
myoclonic epilepsy with suppression outbreak pattern, 2 West syndrome, 2 had minor stroke crisis, 1 myoclonus astatic epilepsy who developed a subsequent EPOCS with secondary regressive syndrome). We found delayed psychomotor development in 3 patients and strabismus in 2 patients. 68% of patients with epilepsy needed a combination therapy for seizure control. There were 11 cases that had multiple mitochondrial complexes affected and 2 with only one complex affected. We had 1 case of pyruvate dehydrogenase defect and 2 cases of Leber optic neuropathy. CONCLUSIONS: In our series most of the male patients were diagnosed in the first two years of life. 68% of patients had an affection of several complexes of the mitochondrial respiratory chain. The most common complication was epilepsy that was difficult to control in almost 60% of cases, followed by delayed psychomotor development. All that justifies performing muscle biopsy in this type of patients at early stages of the illness.

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Neurometabolic disorders

ICNC-0608: Subacute Sclerosing Panencephalitis (SSPE): Clinical, Electrophysiological and treatment evaluation

Introduction: SSPE is persistent chronic encephalitis occurring after measles infection. First described nearly a century ago, it still remains uniformly fatal disease. Methods: Children diagnosed with SSPE in a pediatric tertiary care centre in India were included. Demographics, clinical features, course, treatment approaches and response, investigations and outcomes were studied. Results: 23 patients were included (males-17, females-6). Average age at symptom onset: 7.5 ± 3.5 years and at presentation: 8.1 ± 3.5 years; average diagnostic delay: 6 months. History of measles was present in 95% patients. Most (17/23; 73%) presented in stage 2, and rest in stage 1. Major seizures types were myoclonus (73%) and drop attacks (63%). EEG showed typical pattern in majority (n=20, 86%), three patients had atypical EEGs. CSF measles antibodies were positive in 21/23. Average antivirals used were 2.5/patient and average antiepileptics used were 2.7/patient. Inosiplex was tried in all, one patient received intrathecal Interferon-α. Patients reported seizure reduction with zonisamide and levetiracetam. Eight patients (34%) tried alternative medicine- homeopathy (7/23) and ayurveda (1/23); former group reported significant symptomatic improvement. Average follow up is 24 months. 2 patients died (average 4y after onset), 2 are stable and rest show steady cognitive and motor decline. Most are bedbound and caregiver dependent. Conclusion: SSPE, virtually eradicated in developed world, is still prevalent in low resource countries, contributing to significant disability. Drugs prolong survival but do not decrease mortality. This study highlights SSPE as an important yet overlooked entity, requiring better understanding of management and complications.

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Neurometabolic disorders

ICNC-0655: Congenital disorder of glycosylation, type Iq : Diagnosis of two siblings using new generation sequencing techniques

Background: Congenital disorder of glycosylation type I (CDG1Q) is a multisystem disorder caused by a defect in glycoprotein biosynthesis and characterized by under-glycosylated serum glycoproteins. Congenital disorders of glycosylation result in a wide variety of clinical features, such as defects in the nervous system development, psychomotor retardation, dysmorphic features, hypotonia. In this report, we would like to present two siblings with CDG1Q mutation and underline the importance of genetic testing in patients with multiple abnormalities. Case report: Two siblings eight years old male and five years old female from non-consanguineus parents admitted to our hospital with motor mental retardation, microcephaly, ataxia. Prenatal, natal and postnatal history had no significant feature. The disorders began in infancy and developmental delay, hypotonia, visual loss, nystagmus, mental retardation, ataxia and facial dysmorphism was found upon physical examination. Cerebellar atrophy was found upon neuroimaging. Using new generation DNA sequencing method compound heterozygous mutation p. Trp19Ter and p. Gly166Glu found in SRD5A3 gene in both siblings. Clinical presentation was also consistent with the mutation. Isoelectric transferrin focusing was also showed type 1 pattern, consistent with the diagnosis. Conclusion: Genetic diseases are one of the most challenging situations in patients with mental motor retardation due to confounding factors and overlapping clinical findings. New generation sequencing methods are useful and cost-effective methods for such cases.

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Neurometabolic disorders

ICNC-0609: The determination of cognitive features in children with multiple Sclerosis

Aim: To determine the cognitive functions in children with multiple sclerosis. Material- Methods: 38 children with multiple sclerosis (MS), aged between 8-17, were evaluated between 2013-2014. Stroop Test (ST), Line Orientation Test (LOT), and Verbal Fluency Test (VFT) were conducted twice with a yearly interval. The effects of the variables of number of attacks, EDSS scores, and MR lesion load on the neuropsychological tests were evaluated. Results: Although the results of ST were not statistically meaningful, patients with high MR lesion load, demonstrated longer response duration, with more mistakes and corrections. The results of VFT were not statistically meaningful. Children with EDSS>1 and more attacks had lower mean scores in vocabulary generation. The LOT scores were low in children with high number of attacks and MR lesion load (p<.05). Discussion: Neuropsychological tests in MS treatment are of importance for identifying the level of cognitive destruction. The low LOT results, assessing visual-spatial perception, showed us a significant orientation and visualisation deterioration to exist in our patients that leads to a disrupted visuoconstructive performance and decrease in their life quality. Although the non-significant differences found for ST and VFT for the defined variables these could have been significant if we had more patients and if they had been followed for more than a year. Children with MS should be follow-up for cognitive evaluation with various neuropsychological tests to assess cognitive maturation and to screen for the potential late emergence of cognitive deficits.

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Neurometabolic disorders

ICNC-0656: Phenotype variability related to short-chain enoyl CoA hydratase (ECHS1 gene) in Brazilian patients

Introduction: The short-chain enoyl CoA hydratase (ECHS1 gene) involved with the final step of valine metabolism. Since 2014, different phenotypes were described and related to mutations in this gene. Here we describe 4 Brazilian patients from unrelated families presenting different clinical manifestations: epileptic encephalopathy, Leigh Like syndrome (LLS) and intermittent dystonia. Methods: clinical evaluation, metabolic exams (lactate, organic acids), muscle biopsy, brain MRI. Molecular study was performed using Whole Exome Sequencing (WES). Results: we describe 4 patients from unrelated families. Case 1: male, age of onset was 9 months presenting lactic acidosis and neurological regression during infection. He developed progressive spasticity and dystonia. Brain MRI showed bilateral striatal lesion compatible with LLS. The last clinical evaluation was at the age of 4 and he was severe handicap. The WES showed two heterozygous mutations: c.394G>A (p.Ala132Thr) and c.713C>T (p.Ala238Val). Case 2: female, age of onset 3 years and 6 months, presenting intermittent unilateral and alternating dystonia with painful cramps. Brain MRI showed bilateral putaminal hypersignal (T2 and FLAIR). The WES showed two heterozygous mutations: c.1>A (p.Met1?) and c.518C>T (p.Ala173Val). Case 3: female, age of onset 3 years presenting intermittent hemiparesis and ataxia. Brain MRI showed bilateral putaminal hypersignal (T2 and FLAIR). The WES showed two heterozygous mutations: c.518 C>T (p.Ala173Val) and c.394 C>T (p.Ala173Thr). Case 4: female, died at the age of 3 years and 10 months. She presented epileptic encephalopathy with severe neurological compromise. MRI showed brain atrophy and thin corpus callosum. The WES showed homozygous mutation: c.637T>C (p.Cys213Arg). Conclusion: The ECHS1 deficiency is related with different phenotypes including epileptic encephalopathy, LLS, intermittent ataxia and dystonia. The WES was essential for the final diagnosis. This is the first description of Brazilian patients with ECHS1 mutations. Support: Fapemig, CNPQ

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Neurometabolic disorders

ICNC-0610: Progressive Cerebellar-Cerebral Atrophy (PCCA) and Progressive encephalopathy with Edema, Hypsarrhythmia and Optic atrophy (PEHO) are allelic syndromes.

Background: Recently, a new syndrome was diagnosed in the Sephardic Jews population. It was named PCCA (Progressive Cerebellar-Cerebral Atrophy) after its classic neuroradiological findings. Known causative mutation is VPS53. PEHO (and Progressive encephalopathy with Edema, Hypsarrhythmia and Optic atrophy) is a syndrome prevalent in Finland. Known causative mutation is SEPSecs. In 2007 we diagnosed 2 siblings with PEHO based on clinical criteria. Recently, they were found to carry a mutated VPS53 gene. Methods: Whole exome sequencing was done, followed by realtime PCR. Result and Discussion: We diagnosed 2 siblings with PEHO, based on clinical criteria. They have developmental encephalopathy, limb and facial edema, infantile spasms and optic atrophy. MRI showed
cerebellar and brainstem atrophy. It’s prevalent in Finland ancestry. Known causative mutation is SEPSECS. In 2003, PCCA was discovered in Moroccan and Iraqi Jews. This syndrome Criteria includes progressive microcephaly, spasticity, profound mental retardation and generalized seizures, but no dysmorphic features. MRI demonstrate ongoing atrophy of cerebellum and cerebrum. Known causative mutation is VPSS3. Recently, the Israeli PEHO siblings were found to carry a mutated VPSS3 gene. Comparing both syndromes reveals clinical and radiological similarities. With this genetic revelation it’s plausible to conclude these syndromes are actually one syndrome, sharing similar characteristics with specific criteria each. Conclusions: Progressive Cerebello-Cerebral Atrophy (PCCA) and Progressive encephalopathy with Edema, Hypsarrhythmia and Optic atrophy (PEHO) share the same genetic and clinical spectrum and thus, are allelic syndromes.

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Neurometabolic disorders

ICNC-0657: Whole exome sequencing in identification of metabolic diseases that were missed by metabolic testing

Introduction Whole exome sequencing has emerged as a successful tool in the research of severe childhood genetic diseases and is recently employed also in routine clinical settings. Methods As a part of a collaboration study, we applied trio whole exome sequencing to a cohort of 43 undiagnosed patients with various neurological manifestations and a presumed genetic origin. Results In 16 (37%) of the 43 patients a diagnosis of a known disease was reached based on the analysis of the exome sequencing. In additional two patients a presumed diagnosis involving a novel disease causing gene was recently validated and published. Of the 16 patients with diagnosis of known diseases, 4 (25%) were diagnosed with metabolic diseases that were initially suspected clinically but later abandoned based on the results of specific metabolic tests. Among these were: Pyruvate dehydrogenase (PDH) deficiency with blood lactate/pyruvate ratio>30 and normal function of PDH complex on muscle biopsy, Glutaric aciduria type 1 with normal levels of urine glutaric acid and blood carnitine and acyl-carnitine, Peroxisomal disorder with normal levels of very long chain fatty acids (including phytanic and pristanic acids), and Neuronal ceroid lipofuscinosis with no lipofuscin accumulation on skin biopsy. Conclusion We suggest that whole exome sequencing is a valid and useful diagnostic tool that may lead to identification of known metabolic diseases in cases in which metabolic workup is negative in spite of a sound clinical suspicion.

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Neurometabolic disorders

ICNC-0658: Arrested cerebral demyelination in X-linked adrenoleukodystrophy (X-ALD): striking preliminary results

Introduction X-linked adrenoleukodystrophy (X-ALD) is a rare metabolic disorder caused by mutations in the ABCD1 gene. Core clinical features include adrenocortical insufficiency and a slowly progressive myelopathy with a highly variable age of onset. Additionally, male patients are at risk for rapidly progressive cerebral white matter abnormalities (WMA) that show rim enhancement on MRI after intravenous gadolinium administration. These WMA are considered fatal in most cases unless treated by allogeneic hematopoietic stem cell transplantation in an early stage. Because onset of cerebral disease cannot be predicted all patients undergo frequent MRI scans to detect cerebral demyelination as soon as possible. Spontaneous arrest of cerebral disease has been observed but is considered rare. The aim of our prospective longitudinal cohort study is to identify predictive factors for conversion to cerebral demyelinating disease. Methods We aim to include 50 patients with X-ALD. Patients with active cerebral demyelination at baseline, defined as WMA with gadolinium enhancement on MRI, were excluded. MRI data were evaluated. Results Preliminary imaging baseline data were available for 23 patients. Surprisingly 10/23 (43%) had WMA without gadolinium enhancement suggestive of arrested cerebral demyelination. To be confirmed. Conclusion Strikingly, preliminary imaging results suggest an unexpected high frequency (43%) of arrested cerebral demyelination in our X-ALD cohort, implying the natural history of cerebral disease is not as relentless progressive as currently assumed. It will be valuable to evaluate if these results hold when patient inclusion is completed in 2016.

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Neurometabolic disorders

ICNC-0659: Neurometabolic causes of Epileptic Encephalopathies in a tertiary care center in Saudi Arabia

Background: Epileptic encephalopathies are a group of devastating epileptic disorders that occur early in life and are characterized by pharmaco-resistant epilepsy, severe electroencephalographic abnormalities, and cognitive dysfunction. They are mostly associated with structural brain defects, hypoxic ischemic brain insult, pathogenic gene mutations, and inherited neurometabolic disorders. Aim: To identify hereditary neurometabolic disorders as a cause of epileptic encephalopathy in patients presenting to a tertiary care center in Saudi Arabia. Methods: We conducted a retrospective review of children presenting with epileptic encephalopathy to a tertiary care center in Saudi Arabia in Riyadh, Saudi Arabia from January 2012 till December 2015. The international league against epilepsy definition was used. Results: Total of 344 patients with epileptic encephalopathy were identified. 73 patients (21.2%) had neurometabolic disorders. Consanguinity was found in 61 patients (83.5%). Diagnosis was confirmed by molecular analysis in 63 patients (94%). The main neurometabolic disorders diseases identified were pyridoxine dependent epilepsy (n=13), Amino acidopathies and organic acidemias (n=11), neuronal ceroid lipofuscinosis (n=9), Mitochondrial Diseases (n=7), nonketotic hyperglycinemia (n=6), Sulfide Oxidase Deficiency/Molybdenum Cofactor Deficiency (n=6), Creatine Biosynthesis and Transport Deficiencies (n=5) and biotindase deficiency (n=4). Conclusion: Neurometabolic disorders are a common cause of epileptic encephalopathies in Saudi Arabia. Early diagnosis and treatment can have a huge impact on prognosis.

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Neurometabolic disorders

ICNC-0661: Depiction of clinical characteristics in Taiwanese Rett Syndrome

Background: Rett syndrome (RTT) is a postnatal severe and progressive neurodevelopmental disorder occurring almost exclusively in females, RTT patients show global deceleration of psychomotor development and subsequent loss of acquired cognitive function, language ability and motor skills. RTT patients also share clinical features with autistic spectrum disorder. Patients are usually misdiagnosed as cerebral palsy or infantile autism when searching for medical help. The incidence rate of RTT is 1 to 10000 in the general population that indicates there are 2500 cases in Taiwan, however, the gene-proved RTT patients accounts for 3% of estimated numbers. The wide gap between the actual and estimated numbers indicates that RTT is not well known and is underdiagnosed by pediatrician and developmental subspecialist. To help diagnosing and managing RTT, we analyzed the phenotypes of RTT patients in RTT Joint Clinic in Kaohsiung Chang Gung Memorial Hospital. Methods: RTT patients visiting RTT JOINT CLINIC in Kaohsiung Chang Gung Memorial Hospital from Feb 2015 to June 2015 were enrolled in this study. Patient information, nutrition status, diagnostic criteria, genotypes, clinical phenotypes, including motor function, language development, stereotypic hand movement, breathing patterns, sleeping problems, and gastrointestinal problems were gathered by questionnaire. The data was presented by descriptive statistics. Results: There are 20 female patients enrolled in this study, 19 of them were Mecp2 gene mutated, only one patient fit RTT diagnostic criteria without Mecp2 mutation. Their mean age was 12.5 years old. 90% of them were found “something wrong” by mother younger than 2 years old. Gross motor developmental delay (42%) was the most common firstly noticeable symptoms, and emotional instability (24.2%) was the second one. Absence of language development reached as high as 65%. Stereotypic purposeless hand movement appeared at average age of 2. After occupational therapy, 35% of patients regained their hand skill. 75% of patients had abnormal breathing patterns. Eye pointing accounts for 55% of patients. Only 25-30% of patients existed gastrointestinal problems, such as feeding difficulties and gastroesophageal reflux, however, 70% of patients had significantly lower body weight and body length compared with age-matched peers. Surprisingly only 30% of patients had been told “abnormal head circumference (HC)" younger than 6 years old. Among the patients who never knew they had abnormal HC,70% of them was found significantly smaller HC than age-match peers. 60% of our patients had delayed puberty which is rarely discussed by overviewsing references. Conclusions: We highlighted three importance issues that are easily ignored in Taiwanese RTT patients. At first, head circumference growing curve is often forgotten in examining patients with global developmental delay, though we had child health booklet. The second, delayed puberty in RTT patients is another medical problems that we pediatrician less paid attention to. Third, one-third of our patients regained their hand and language skill after occupational therapy which means early rehabilitation intervention is very important in RTT patients.

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Neurometabolic disorders

ICNC-0613: Expert recommendations for the laboratory diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2 disease): diagnostic algorithm and best practice guidelines for a timely diagnosis

Neuronal ceroid lipofuscinoses (NCLs), a heterogeneous group of lysosomal storage disorders, include the rare autosomal recessive neurodegenerative disorder CLN2 disease (CLN2). CLN2 is due to mutations in TPP1/CLN2 gene causing tripeptidyl-peptidase-1 (TPP1) enzyme deficiency. Classic late-infantile CLN2 has pediatric onset with initial symptoms of seizures and language delay followed by progressive dementia, motor and visual deterioration and early death. Variant phenotypes occur more rarely. CLN2 disease is based on laboratory testing following clinical suspicion. Early diagnosis is key to optimizing clinical care and future therapies outcomes, yet delays in diagnosis are common due to low disease awareness, non-specific initial symptoms and limited diagnostic testing access in some regions. In May 2015, international experts met to recommend best laboratory practices for early CLN2 diagnosis. When clinical signs suggest NCLs, TPP1 activity should be the first test performed (along with palmitoyl-protein-thioesterase-1 to exclude CLN1). However, since reaching initial suspicion of CLN2 and NCLs is challenging, where available, use of epilepsy gene panels to investigate unexplained seizures in childhood is endorsed. These panels should include TPP1/CLN2 besides genes for other NCLs lacking biochemical tests. Diagnostic TPP1 enzyme test in leukocytes is well established and robust and in DBS is considered diagnostic if followed by molecular testing. Future methods to measure TPP1 activity via MS/MS may improve DBS-based TPP1 testing sensitivity allowing also future newborn screening. To confirm clinical suspicion of CLN2, the recommended gold standard for laboratory diagnosis is demonstrating deficient TPP1 activity and/or detecting causative mutations in each allele of TPP1/CLN2 gene.

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Neurometabolic disorders

ICNC-0614: Metachromatic Leukodystrophy: A rare cause of neuro-regression in early childhood

We present the case of a girl who presented at 2 years of age with regression of motor milestones. She was born at term and was treated with 5 days of IV antibiotics for possible sepsis. She started walking at 1 year of age with no concerns regarding her milestones. Her family members are well. She was first brought to medical attention at the age of 2 years when she started struggling to walk, with marked discomfort in her lower limbs at nights. Her examination revealed a broad based gait, with hyperextension of knees and an exaggerated lumbar lordosis. Muscle bulk and power seemed normal but reflexes of lower limbs were difficult to elicit and plantar reflexes were up going. EMG/NCS showed absent distal sensory potentials in lower limbs and slow latencies in distal upper limbs, suggestive of possible demyelinating large fibre motor and sensory peripheral neuropathy. MRI brain showed abnormal signal in corpus callosum with a vacuolated appearance. White cell enzymes showed very low levels of Arylsulphatase A, confirming a diagnosis of Metachromatic Leukodystrophy. ARSA gene result is still awaited. Metachromatic leukodystrophy is an inherited lysosomal disorder caused by recessive mutations in ARSA encoding arylsulfatase A. Low activity of arylsulfatase A results in the accumulation of sulfatides in the central and peripheral nervous system leading to demyelination. It
manifests as a neurodegenerative disorder, with cognitive regression, pyramidal dysfunction and peripheral neuropathy. No available therapy can alter the disease course of this life-limiting late-infantile condition.

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Neurometabolic disorders

**ICNC-0662: The association between EEG abnormality and behavioral disorder: Developmental delay in Phenylketonuria**

Background One of the important clinical manifestations of phenylketonuria is brain defect leading to developmental delay. Our aim of this study was to evaluate the association between EEG abnormality and developmental delay/behavioral disorders in phenylketonuria. Patients and Methods 105 phenylketonuria patients, who were diagnosed through newborn screening tests or during follow-up evaluation, were enrolled. Patients who were seizure-free for at least six months before our study were included. The developmental score were evaluated by the ASQ questionnaire (age-stage questionnaire) and the test of child symptom inventory-4 (CSI-4), respectively Results History of seizure was reported in 55 patients 6 months before our study. Seventy had abnormal EEG (cases) and 35 had normal EEG (controls). There was no significant difference between mean phenylalanine levels in the abnormal and normal EEG groups at the time of diagnosis, after six months and at our evaluation. Distribution of DQ level in the abnormal and normal EEG groups revealed a significant difference. An abnormal EEG was associated with a higher percentage of low DQ levels. Conclusion We believe Paroxysmal epileptic discharges in PKU patients are very important. Treatment of these EEG abnormalities may affect developmental scores or may lead to correction of some behavioral disorders in these patients.

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Neurometabolic disorders

**ICNC-0663: Delayed speech, hyperactivity, and coarse facies—Does Sanfilippo Syndrome come to mind?**

Mucopolysaccharidosis-III A (MPS IIIA) or Sanfilippo-A syndrome is caused by a deficiency in lysosomal α- heparan N-sulfatase. Its clinical manifestations include progressive dementia, hyperactivity, and aggressive behavior. Unlike other mucopolysaccharide disorders, the diagnosis of MPS IIIA is challenging in both adults and children. This diagnostic challenge has been associated with the high incidence of false-negative results encountered on urinary screening tests. We herein describe Sanfilippo-A syndrome in a pediatric patient who presented with hyperactivity, delayed language and developmental delay and a negative urine screening test. These may serve as possible initial presentations of MPS IIIA. A high index of clinical suspicion of MPS IIIA is therefore warranted to avoid needless diagnostic and treatment procedures.

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Neurometabolic disorders

**ICNC-0664: A Turkish case of galactosialidosis with a new homozygous mutation in CTSA gene**

A female infant was born to consanguineous healthy (first degree cousin) Turkish parents at 35 weeks of gestation by caesarean section because of polyhydramnios. She required delivery room resuscitation for respiratory distress and she remained at the neonatal intensive care unit for 1 week. Her mother was 26 years old, he has had one previous pregnancy complicated by polyhidramnios and hydrops fetalis and that pregnancy was terminated at 20 weeks of gestation. At the time the tests for maternal infection, Rh and ABO incompatibility, and chromosome abnormalities proved negative. Family history was unremarkable for genetic diseases or neurologic disorders. At four weeks of age she was referred to our hospital for evaluation of dysmorphic facial features. Physical examination demonstrated a height and weight of 59 cm (<3th percentile) and 4.4 kg (<3 th percentile) and a head circumference of 39.5 cm (<3th th percentile) respectively. There was no corneal clouding or macular cherry red spot. The patient was edematous and noted to have dysmorphic facies including a coarse facies, prominent forehead, hypertelorism, long philtrum, micrognathia, large nose, and thin upper lip. The hair was blonde and thin. She also had a heart murmur, umbilical hernia and hepatosplenomegaly. Neurological examination revealed diffuse hypotonia. She had a weak suck and cry, and her spontaneous movements were decreased. Deep tendon reflexes were elicited. Laboratory investigations showed normal values of blood counts, chemistry, electrolytes. Urine organic acids, Tandem Mass, plasma lactate, pyruvate, thyroid function tests and karyotype were normal. A skeletal survey disclosed moderate changes of dyostosis multiplex including
beaking of vertebrae and j-shaped sella. The patient died at the age of 6 months as the result of cardiac and kidney failure. In view of the family history with previously unexplained hydrops fetalis, the clinical presentation and the presence of visceromegaly, coarse facies, we suspected a lysosomal storage disorder. Her urinalysis showed a mucopolysaccharide screen level of 106.1 mg/mM (normal for age <28) and revealed elevation of heparan sulfate on thin-layer chromatography. Enzyme analysis for galactosialidosis showed null activity of the enzyme sulphamidase activity in leucocytes (normal range 3.2-20.4 nmol/17 h), confirming the diagnosis. Mutation screening of the CTSA gene revealed a homozygous mutation (c.1284delG) that had been not reported previously.

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Neurometabolic disorders

ICNC-0667: Risk factors for death in children with Mitochondrial Disease

Introduction The aim of this study was to investigate the risk factors from clinical characteristics of the expired cases in pediatric patients with mitochondrial disease. Methods Clinical variables from medical records of 31 expired cases among 378 patients with mitochondrial disease were reviewed. Results The results of 31 children and adolescents (17 males) were analyzed. The onset age of first symptom was 1.8±2.0, the lead time to diagnosis 1.7±1.5, the duration of illness 4.3±2.7, and the duration of life 6.1±2.9 years. The most frequent first symptom was developmental delay (42%), followed by seizure (39%). Finally, most of the patients were diagnosed with epilepsy (90%), mainly with partial seizure (55%). Basal ganglia in the lesion of brain MRI (52%), mitochondrial respiratory chain complex (MRC) 1 defect in biochemical enzyme assay (68%), and Leigh disease for syndromic diagnosis (48%) seemed to be the factors most frequently involved with the expired cases. In addition, sepsis (55%) and pneumonia (42%) were identified as the major direct cause of death. All the patients suffered from CNS involvement. However, the number of organ involvement (1.4±1.39 vs. 0.56±0.38, p=0.006), as well as the diagnosis of Leigh disease (11 vs. 4, p=0.023), showed significant difference between the groups of patients who died before and after six years. Conclusion The number of organ involvement, epilepsy as a clinical manifestation, and Leigh disease as syndromic diagnosis might be the risk factors in early expired cases of children with mitochondrial disease. Examining with a larger sample was suggested for future studies.

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Neurometabolic disorders

ICNC-0669: Pyridoxine-dependent epilepsy (PDE): α-amino adipic semialdehyde levels and development during different treatment modalities

Introduction: PDE is caused by α-amino adipic semialdehyde (AASA) dehydrogenase deficiency. Pyridoxine diminishes seizures but leaves IQ decreased. The usefulness of additional treatment with dietary lysine restriction and/or arginine restriction is debated. AASA is considered the biochemical marker of control. Methods: Urinary AASA was followed using liquid-chromatography-tandem mass spectrometry in 2 PDE patients. Results are given as mmol/creatinine (reference range 0-2). Cases: Boy: onset of seizures at 3 months of age. AASA was 101.1. From 4 months he was treated with 100 mg pyridoxine/d and seizures stopped. At 3 ½ years he started lysine restriction. At 5 ½ years protein intake was increased to 20 gr and arginine was introduced (150 mg/kg/d). Girl: onset of seizures at day 1 of life. At day 3, pyridoxine 30 mg/kg/d was started and seizures stopped. AASA was 58. At day 6, lysine restriction and arginine supplementation was started. Results: Before lysine restriction, the boy his IQ was 97, speech was delayed; AASA was 20.3. On diet, mean AASA decreased to 2.4 (range 0.7-5.0). Within 2 weeks his speech ameliorated. After increasing protein intake and introduction of arginine, AASA remained comparable, mean 2.7 (range 1.6-7.0). In the girl, AASA dropped to a mean of 17.6, range 13.6-29.0). At 10 months she showed a normal development. Conclusions: Both lysine restriction and arginine supplementation lowered AASA excretion significantly and seemed to improve speech development and/or to retain normal development. Whether the combination of all 3 treatments is superior remains to be studied.

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Neurometabolic disorders

ICNC-0632: PTRH2 gene mutation causes progressive sensorineural deafness and peripheral neuropathy

Introduction: Ph2h is an evolutionarily highly conserved mitochondrial protein that belongs to a family of peptidyl-tRNA hydrolases. Recently, patients from two consanguineous families with mutant protein were reported. Global developmental delay associated with microcephaly, growth retardation, progressive ataxia, distal muscle weakness with ankle contractures, demyelinating sensorimotor neuropathy, and sensorineural deafness were common to all patients. Facial dysmorphism with hypertelorism, exotropia, thin upper lip, proximally placed thumbs, and deformities of the fingers and toes were variable. We report an additional family. Methods: Whole exome sequencing was employed and revealed a novel homozygous mutation in three siblings. The healthy parents were heterozygous carriers of this mutation. Results: We detected a novel mutation (c.254A>C; p.(Gln85Pro)) of the PTRH2 gene. The PTRH2 gene encodes the Pth2 protein which prevents the accumulation of prematurely dissociated peptidyl-tRNA that might be cytotoxic and could inhibit protein synthesis. Their clinical features somewhat resemble the previously reported cases and they also had sensorineural deafness and peripheral neuropathy. However, in contrast to the previously reported phenotype they had normal intelligence, milder microcephaly, delayed puberty, myopia and moderate insensitivity to pain. Conclusion: We assume that the clinical spectrum of this new genetic disease is wider than previously believed. This report expands our knowledge and better characterizes the full spectrum of this newly recognized disease.

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Neurometabolic disorders

ICNC-0671: Proteomic analysis of muscle mitochondria in a patient with A8296G mutation in the mitochondrial tRNALys gene

ABSTRACT Mutation in the mitochondrial tRNALys gene at position 8296 was previously found to be associated with maternally inherited diabetes mellitus and deafness, hypertrophic cardiomyopathy, myoclonic epilepsy ragged red fibers (MERRF) and mitochondrial encephalomyopathy, lactic acidosis, and stroke like episodes (MELAS). Here we present a girl with sensorineural deafness, cognitive impairment, leukodystrophy, migraine like headaches and gastrointestinal dysmotility with A8296G mutation in the mitochondrial tRNALys gene. The pathogenicity of A8296G at the MT-TK gene is unclear. To elucidate the effects of the mutation on mitochondrial proteome, we carried out global mitochondrial proteome analysis by using 2D gel electrophoresis followed by protein identification with MALDI-TOF/TOF MSMS. Total of 13 nuclear mitochondrial proteins were found to be differently expressed with respect to control. Here we discuss our patient in view of the genomic and proteomic data.

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Neurometabolic disorders

ICNC-0672: Unravelling a new mitochondrial disorder: PNPT1 mutations causing Leigh syndrome with a complex movement disorder

INTRODUCTION: Leigh syndrome comprise a complex and heterogenous presentation of mitochondrial disorders; more than 30 different genes were already described causing Leigh syndrome. Most genes are nuclear genes involved in mitochondrial metabolism (oxidative phosphorylation), as respiratory chain enzymes, nevertheless 20-25% Leigh patients are found to have mutation in mitochondrial DNA gene. Many disorders can present with neuroradiological features of Leigh syndrome, some not directly involved in mitochondrial function, so investigation of the underlying cause of Leigh syndrome as of vital importance for therapeutic management and genetic counselling of the family. OBJECTIVE: To report a new hereditary metabolic cause of Leigh syndrome in a Brazilian patient caused by enzyme deficiency of a mitochondrial polynucleotide phosphorylase (PNPase, PNPT1 gene). METHODOLOGY: Clinical neuroradiological and molecular investigation of a patient with early encephalopathy, movement disorder, developmental delay and hypotonia

RESULTS: Female patient, first child of a non-consanguineous couple, was referred for investigation of “metabolic disorder”. She presented in her first day of life with myoclonic jerk movements; hypotonia was noticed in her first months of life. Later, patient developed failure to thrive and a complex movement disorder with dystonia and upwards gaze eye movements, suggestive of oculogyric crisis. Patient started to have limbs hyperextension and severe sialorrhea. At clinical examination, patient showed convergent squint, saccadic hypokinetic conjugated eye movements, protrusion and repetitive tongue movements (orofacial dyskinesia), erratic limb movements, dystonic postures in hands and feet, decreased osteotendineous reflexes, absent cutaneous-plantar reflex and mild bilateral choleclo-palpebral reflex were
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found. mild baseline disorganization activity due to slower posterior rhythm was seen in EEG. First brain MRI was normal, but a second one performed 2 years later showed bilateral hyperintensities in putamen and caudate nuclei with minimal dilatation of supratentorial ventricular system. After extensive biochemical and targeted molecular evaluation, suspicion of a neurotransmitter disorder was suspected although the CSF findings were not diagnostic. Because of the new MRI findings, muscle biopsy was also indicated, but the family declined. In this context, whole exome analysis (Illumina HiSeq 2500) was undertaken looking for mutation in neurotransmitters genes however two deleterious heterozygous variants in PNPT1 gene were found. The first one, c.1-1del, promotes the deletion of exons 1 to 15 and the he second one, c.1.519G>T, promotes the substitution of Alanine for Serine at the position 507 (p.Ala507Ser). Patient was started on biotin, riboflavin and coenzyme Q10, showing no further evidence of deterioration.

CONCLUSIONS: Mitochondrial disorders are complex metabolic inborn errors of metabolism with a broad phenotypic range (such as Leigh syndrome, isolated sensorineural deafness). PNPT1 gene was first identified in patients with sensorineural deafness, but, later, it was reported as cause of encephalopathy in two sibs born to a consanguineous couple. Our findings reinforce the the broad clinical manifestation of mutations in such gene, to include complex movement disorder with abnormal eye movements as part of the clinical spectrum of the disease, and the “power” of whole exome sequencing in unravelling new phenotypes for already known genes. PNpase deficiency unavels another disease mechanism as cause of mitochondrial disorders: abnormal RNA import into mitochondria.

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ICNC-0673: Clinical, biochemical, and molecular studies in pyridoxine-dependent epilepsy: report of 12 cases

Purpose Pyridoxine-dependent epilepsy (PDE; OMIM 266100) is an autosomal recessive disorder that causes intractable seizures, especially in neonates and infants. Patients are typically resistant to antiepileptic drugs but respond dramatically to pyridoxine. In the majority of patients with PDE, the disorder is caused by the deficient activity of the enzyme α-aminoacidic semialdehyde dehydrogenase (antiquitin protein), which is encoded by the ALDH7A1 gene. The aim of this work was the clinical, biochemical, and genetic analysis of 12 patients, from Saudi Arabia, in an attempt to provide further valuable data regarding the wide clinical, biochemical, and genetic spectrum of the disease. Methods The diagnosis of PDE was confirmed based on the presence of picoelic acid and α-aminoacidic semialdehyde (α-AASA) in urine and by sequencing analysis of ALDH7A1 gene. Results Most of the patients had seizures in the neonatal period, 2 patients developed late-onset seizures. Seizures were intractable or partially controlled by antiepileptic drugs, but controlled after adding pyridoxin. Seizures were most of the time associated with other neurologic or systemic manifestations. All patients had elevated levels of picoelic acid and α-AASA in urine. Genetic study showed mutations (10 mutations: 5 are known, 5 new)/deletions (2 large deletions) in the ALDH7A1 gene. Outcome was favorable regarding seizures control, but 9 patients were left with mild to moderate developmental delay. Conclusion The present results broaden our knowledge of PDE, provide information regarding the clinical and genetic background of PDE in Saudi Arabia, cal, biochemical, and molecular studies in pyridoxine-dependent epilepsy: report of 12 cases

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ICNC-0674: Treatment of biotin-responsive basal ganglia disease: open comparative study between the combination of biotin plus thiamine versus thiamine alone

Summary Objective: To compare the combination of biotin plus thiamine to thiamine alone in treating patients with biotin-responsive basal ganglia disease in an open-label prospective, comparative study. Methods: twenty patients with genetically proven biotin-responsive basal ganglia disease were enrolled, and received for at least 30 months a combination of biotin plus thiamine or thiamine alone. The outcome measures included duration of the crisis, number of recurrence/admissions, the last neurological examination, the severity of dystonia using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS), and the brain MRI findings during the crisis and after 30 months of follow-up. Results: Ten children with a mean age of 6 years (5 females and 4 males) were recruited in the biotin plus thiamine group (group 1) and ten children (6 females and 4 males) with a mean age of 6 years and 2 months were recruited in the thiamine group (group 2). After 2 years of follow-up treatment, 6 of 20 children achieved complete remission, 10 had minimal sequelae in the form of mild dystonia and dysarthria (improvement of the BFMDRS, mean: 80%), and 4 had severe neurologic sequelae. All these 4 patients had delayed diagnosis and management. Regarding outcome measures, both groups have a similar outcome regarding the number of recurrences, the neurologic sequelae (mean BFMDRS score between the groups, p=0.84), and the brain MRI findings. The only difference was the duration of the acute crisis: group 1 had faster recovery (2 days),
versus 3 days in group 2 (p=0.005).

Conclusion: Our study suggests that over 30 months of treatment, the combination of biotin plus thiamine is not superior to thiamine alone in the treatment of biotin-responsive basal ganglia disease.

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Neurometabolic disorders

ICNC-0675: Glutaric Aciduria Type I - Widened clinical spectrum

Glutaric aciduria type I (GAI) is an inborn error of metabolism of lysine, hydroxylysine, and tryptophan due to deficiency of glutaryl-CoA dehydrogenase. The majority of untreated patients manifest with secondary dystonia due to striatal injury in infancy, but diverse phenotypes has been observed. Here, we report two patients with GAI. Patient 1: 3 y.o. girl with normal development till 7 months. After a minor head trauma she developed hypotonia followed by dystonia. MRI showed widened temporal and sylvian CSF spaces as well as bilateral basal ganglia injury. Urine organic acid profile revealed elevated GA level (1775 mg/g Crea). Treatment with oral carnitine, riboflavin, low protein diet and baclofen was initiated. At present she has normal head circumference, global developmental delay in all domains, dystonia with partial response to baclofen. Patient 2: 11 y.o. boy, with macrocephaly, normal physical and intellectual development. MRI - massive enlargement of CSF spaces in frontotemporal areas; basal ganglia - normal. Despite early introduction of low protein diet and carnitine supplementation urinary GA level has always been elevated, highest value being 18100 mg/g Crea. Patient has never experienced encephalopathic crises. The results of ongoing international observational studies greatly broadened the clinical spectrum of GAI to include the children with non-progressive extrapyramidal symptoms and clinically normal patients. Our clinically unaffected patient has not developed striatal injury despite high GA levels. There is little known about predisposing factors of striatal damage in GAI patients. In our second case minor head trauma likely played role in basal ganglia damage.

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Neurometabolic disorders

ICNC-0676: Buccal swab analysis reveals a high prevalence of mitochondrial respiratory chain defects in children and young adults with Autism Spectrum Disorders

Objective: Recent research has focused on mitochondrial dysfunction in Autism Spectrum Disorders (ASD). Deficiencies in biopsied skeletal muscle have been reported in isolated cases, most commonly in respiratory complex (RC) I and IV, although RC-III and RC-V defects have also been detected. Since evaluation of mitochondrial dysfunction in biopsied muscle in children is expensive and invasive, buccal swab analysis was used to sensitively assess RC-I and RC-IV activities, which has been highly correlated with similar evaluations in skeletal muscle. The aim of this study was to investigate RC defect prevalence in children and young adults with ASD. Methods: We studied 25 consecutive patients, ages 6-26 years, fulfilling DSM-5 diagnostic criteria for ASD-moderate/severe, compared to 63 age-matched controls, using combined microspectrophotometry and enzyme immunocapture techniques. Results: RC deficiencies, defined as activity values <2 SD from controls’ mean, were found in 13 of 25 (52%) ASD subjects: 8 in RC-I, 3 in RC-IV, and 2 with deficiencies in both activity levels. Moreover, increased levels of citrate synthase used as a gauge of overall mitochondrial content were detected in 7 subjects, also suggestive of significant mitochondrial dysfunction. Conclusions: Analysis of this cohort of ASD subjects, demonstrated a high prevalence of RC defects. Buccal swab RC analysis might be applied as a non-invasive instrument to evaluate mitochondrial dysfunction as a potential biomarker of ASD pathogenesis and to inform prognosis and potential therapeutic pathways. Further correlations of RC results to mitochondrial genotypes are planned.

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Neurometabolic disorders

ICNC-0618: Development of global rating instruments for pediatric patients with Ataxia Telangiectasia

Introduction: Ataxia telangiectasia (AT) is a neurodegenerative disorder with cerebellar and extrapyramidal features. Interventional and epidemiological studies in AT should rely on specific scales which encompass the specific neurological features, as well the early progressive course and the subsequent plateau. The aim of this study was to build a scale of the CGI type (Clinical Global Impression) which is disease specific, as well as to check the feasibility of the ICARS scale
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**ICNC-0677: Rett-like clinical picture due to mutations in neurotransmitter related disorders genes**

Introduction Rett syndrome (RTT) is a developmental disorder of early onset, genetic basis, X-linked dominant inheritance. RTT affects almost exclusively girls with a prevalence of 1/15000. Three genes are described causing the disease (MECP2, CDKL5 and FOXG1). However, the etiology of 30% of patients diagnosed as RTT remains unknown. Material and Methods It has been studied a cohort of Rett-like patients without genetic diagnosis by New-Generation Sequencing platforms (NGS), Gene Panel with 17 genes related to Rett like clinic (HaloPlex Target technology), Enrichment System, for Illumina Sequencing) and WES. All NGS results have been verified by Sanger sequencing and studied the origin of the mutation in the parents. Results In the patients studied were detected mutations in 4 genes that encode GABAergic pathway proteins: 1) GRIN2B: The N-methyl-D-aspartate receptor, a glutamate-activated ion channel permeable to Na+, K+, and Ca(2+), found at excitatory synapses throughout the brain. 2) GABBR2: A subunit of the G protein coupled GABAB receptor. 3) SLC6A1 or GAT1, a carrier of the brain-expressed G protein coupled GABAB receptor. 3) SLC6A1 or GAT1: Voltage-dependent GABA transporter. 4) ALDH5A1: A mitochondrial NAD(+)-dependent succinic semialdehyde dehydrogenase. We also detected mutations in STXBP1 gene who codifies the protein MUNC18-1 involved in the synaptic vesicle docking and fusion protein complex. Conclusion Clinical presentation of RTT Syndrome could be due to mutations in neurotransmitter related disorders genes: GABAergic pathway and synaptic vesicular traffic. DISEASE GENE OMIM Rett MECP2 312750 Rett CDKL5 308350 Rett FOXG1 613454 SSDH ALDH5A1 610045 GRIN2B GABBA SLC6A1 or GAT-1 Onset age 6-18 m 1-3 m Neonatal First year of life First year of life Hypotonia Yes Yes Yes +/- +/- Microcephaly Yes Yes Yes +/- +/- Epilepsy Yes Yes +/- +/- +/- Expressive language dysfunction Yes Yes Yes Yes Preserved use of hands No +/- No +/- Stereotypies Yes Yes +/- +/- +/- Autistic traits Yes +/- +/- +/- +/- Intellectual disability Yes Yes Yes Yes Respiratory dysfunction Yes (80%) Yes Yes No No MRI Normal Normal or Non specific features (cerebellum, myelination delay) Normal or Non specific features (thin cc, myelination delay Normal or high pallidum intensities, cerebellar atrophy Normal Biochemical marker found so far No No No Yes: 4-OH-butyric acid No SSDH: succinic semialdehyde dehydrogenase deficiency GRIN2B: subunit 2B of NMDA glutamatergic receptors GABBA: subunit A of gabaergic receptors SLC6A1 or GAT-1: Voltage-dependent GABA transporter M: months; DD: developmental delay

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for ataxia in this population. Methods: We recruited 63 patients with ataxia, aged 10.76±3.2 years, followed at 6 international AT centers, 49 of them (77.8%) with classical AT. All patients were evaluated for ataxia with ICARS scale. In patients with AT, two CGI scales were scored, unstructured as structured for which separate anchors were provided. Results: Mean ICARS score was 44.7±20.52, and it’s severity positively correlated with age (Spearman correlation, r=0.46, p<0.01). Mean CGI score was 2 (moderately involved). There was a high correlation between the structured and unstructured CGIs (Spearman correlation, r= 0.87, p<0.01). Both CGI scales showed positive correlation between severity and increasing age (Spearman correlation r=0.59, p<0.01 for structured CGI and r=0.61, p<0.01 for unstructured). Discussion: We succeeded to build two CGI scales: structured and unstructured, which are disease specific for AT. The unstructured scale showed better connection to disease course; the sensitivity of the unstructured scale could be improved by adding anchors related to extrapyramidal features. In addition we showed that ataxia can be reliably measured in children with AT by using ICARS.

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ICNC-0678: Serine Deficiency Disorders - Case series from a tertiary paediatric neurology centre in UK
Serine deficiency disorders are rare treatable conditions. We report 2 three-phosphoglycerate dehydrogenase deficiencies and 2 phosphoserine aminotransferase deficiencies. Cases:1A 2-year-old boy with microcephaly, irritability, generalised dystonia and developmental impairment had MRI brain demonstrating reduced white matter, abnormal myelination and atrophic posterior corpus callosum. CSF serine 10(35-80); plasma serine 44(40-280)µmol/L. He had compound heterozygous mutations in PHGDH gene. Supplementation with serine and glycine improved his dystonia. 2A year old boy with congenital microcephaly and development impairment presented with West syndrome and hypertonia. MRI brain demonstrated generalized atrophy, delayed myelination, thin corpus callosum. CSF serine 5(35-85); plasma serine 27(40-280)µmol/L. He had homozygous mutations in PHGDH gene. Treatment with L-serine normalised EEG, improved seizures and dystonia. 3A neonate presented with poor feeding and cyanotic episodes subsequently had intractable seizures, hypertonia and microcephaly. MRI brain demonstrated generalised atrophy, hypoplastic cerebellar vermis and abnormal myelination. EEG showed multifocal abnormalities. CSF serine 18(35-80); plasma serine 51(50-350)µmol/L. He had compound heterozygous mutations in PSAT1 gene. Supplementation from 11 weeks normalised levels. He deteriorated and died at 7 months. 4The younger sister of case 3 had the same mutations. At birth CSF serine 5(35-80); plasma serine 30(50-350)µmol/L. Prompt supplementation normalised values. Head growth improved. MRI brain appeared normal at 4 months. Supplementation continues at 11-years old but autistic traits, learning disability, obsessive compulsive behaviour and tics emerged. Conclusion: Serine deficiency disorders presents in infancy with microcephaly, hypertonia, and developmental impairment with or without seizures . Early diagnosis and supplementation can improve morbidity.

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ICNC-0619: Ectopic kidney and dysmorphic features: an atypical clinical phenotype of infantile neuroaxonal dystrophy
Introduction Infantile neuroaxonal dystrophy (INAD) is a rare neurodegenerative disorder characterized by onset in the first 2 years of life. Motor and cognitive regression are the most frequent presentation. We report a 5-year-old girl with INAD associated with mutation in the PLAG2G6 gene as the clinically presents with dysmorphic features and ectopic kidney. Case We describe a five-year-old patient who was born at term as the second child to consanguineous healthy parents with no significant family history. She was born at term with a birth weight of 1.8 kg (10th centile). At birth, she revealed microcephaly (33 cm -3th centile), ectopic kidney, pes equinovarus and facial dysmorphism. Genetic counseling was resulted normal 46XX karyotype and wolf hirschhorn syndrome was ruled out. Cognitive and motor functions were severely regressed after 9 month old. Neurological examination revealed optic atrophy, severe hypotonia and marked spasticity. EEG showed slowing of background activity with multifocal epileptic activity and fast spikes. Initial laboratory investigations were normal. Brain magnetic resonance imaging showed cerebellar atrophy with signal hyperintensity in cerebellar cortex and abnormal signals in periventricular white matter on T2-weighted images. Genetic analysis of the PLA2G6 mutation was performed and a homozygous c.1612C>A mutation was found. Discussion We report the first patient with INAD, presented with different clinical phenotype such as ectopic kidney, pes equinovarus and facial dysmorphism. So, we suggest that PLA2G6 should be screened in any patient exhibiting this clinical phenoype, especially when presence of neuroimaging findings.

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Neurometabolic disorders

ICNC-0679: Citrullinemia with an atypical presentation: paroxysmal hyperventilation attacks
INTRODUCTION Citrullinemia type 1 is a rare inherited urea cycle disorder resulted from the deficiency of argininosuccinate synthetase. It can cause serious hyperammonemic attacks presented with encephalopathy. We presented an infant with an atypical presentation of citrullinemia with brief-multiple hyperventilation attacks and final diagnosed as citrullinemia type 1 with a new mutation. CASE The baby boy patient was born as the second child of consanguineous marriage after an unremarkable antenatal period and delivery. In family history, his brother had an otism spectrum disorder. On 3 weeks of age, he was hospitalized due to three acute loss of tonus and siyanoic hyperventilation

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attacks lasting within 4-5 minutes. These events were prediagnosed as epileptic events with unremarkable EEG findings. On 3 months of age, he was admitted to our hospital because of going on similar previous hypoventilation/apnea episodes. The physical and neurological examination revealed within normal limits. Initial laboratory tests were found normal. Metabolic screening showed elevation of citrulline levels and increased excretion of citrulline markedly suggesting the diagnosis of citrullinemia. One new and one known mutations were identified on ASS 1 gene sequencing: a heterozygous mutation p.A94V (c.281C>T) and a heterozygous mutation p.W179R (c.535C>T) confirming the diagnosis of CTLN1. DISCUSSION Urea cycle disorders should be considered in differential diagnosis of unexplained brief apnea or hypoventilation attacks even if without long duration and hyperammonemia during infancy and childhood as our patient. To our knowledge this is the first case according to the clinical findings and a new mutation for citrullinemia type 1.

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ICNC-0680: Kidney disease in pediatric patients with mitochondrial disorders
Background Renal involvement in mitochondrial diseases has more often been reported in children than in adults, with the commonest being renal proximal tubulopathy. The overall aim of this study was to investigate the phenotypic characteristics of patients with childhood-onset mitochondrial disease who develop kidney disease. Methods Patients eligible for inclusion were those who were investigated at the Queen Silvia Children’s Hospital and diagnosed with genetically verified mitochondrial disease between 1984-2014. Of these approximately 150 patients, 10 patients developed kidney disease and were included in our study. All study related data were collected with standardized case report forms. Results Of the ten patients included in this study (3 males; 7 females), six patients -all females- had large-scale mtDNA deletion syndrome. Of the remaining four patients, one presented with Alpers syndrome and three with non-syndromic mitochondrial encephalopathy and cardiomyopathy. The median age at onset of kidney disease was seven years. All but one patients developed chronic kidney disease, most of them with both proximal and distal tubulopathy. Seven patients developed glomerulonephritis. Tubulopathy corresponded to De Toni-Debèr-Fanconi syndrome with low-molecular-weight proteinuria in two patients. Three patients had increased arterial blood pressure. Conclusion The kidneys are one of the systems affected by mitochondrial disease and should therefore be monitored closely. In the majority of our patients, the onset of kidney disease was detected on the basis of abnormal laboratory findings. Underlying mitochondrial dysfunction should be considered in the diagnostic work-up of kidney disease in childhood, especially in the presence of signs of multisystem disease.

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ICNC-0612: EXOSC3 gene mutation associated with complicated hereditary spastic paresis (HSP) - expanding spectrum
Introduction: To describe the expanding spectrum of EXOSC3 gene mutation presenting with complicated hereditary spastic paresis (HSP). Case: A 7 years old girl presented initially in the infantile period with acquired microcephaly, hypotonia and global developmental delay. She was extensively investigated in the past with detailed neurometabolic workup. Her MRI scan revealed mild cerebellar vermis hypoplasia along with mild atrophy of cerebellar hemispheres with no involvement of pons. Clinically she has marked global developmental delay but she continues to make steady developmental progress with no regression of milestones. She has pyramidal signs in lower limbs with markedly increased tone and brisk reflexes with normal tone in upper limbs, consistent with the diagnosis of HSP. Deciphering Developmental Delay (DDD) study identified homozygous mutation for c.395A>C in EXOSC3 gene which is previously been reported to be associated with Pontocerebellar hypoplasia type 1 (PCH 1B). Recently a different mutation in EXOSC3 gene has been reported to cause complicated HSP with similar clinical and radiological findings to our index case. Conclusion: Our case again highlights the expanding spectrum of EXOSC3 mutations and suggests that apart from Pontocerebellar hypoplasia type 1, EXOSC3 mutations may also present as a complicated form of hereditary spastic paraplegia without pontine hypoplasia or atrophy. Ref: Halevy A, Lerer I, Cohen R, Kornreich L, et.al. Novel EXOSC3 mutation causes complicated hereditary spastic paraplegia J Neurol. 2014 Nov;261(11):2165-9.

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ICNC-0681: A case of MELAS: Unthought diagnosis

A 10 year old male patient started with tonic seizures when he was 8 year old, and in one episode he lost bilateral vision for a week, with spontaneous resolution. He has been treated with valproic acid with partial control of seizures. Also he visited nutrition because of short stature. He was admitted to the hospital with right hemiparesis, vomiting, anomic aphasia, right amnesia and less vision on left eye, and then he had another hospitalization because of seizures, intermittent loss of vision and mutism for 4 days. His family history was unremarkable. His prenatal, perinatal birth history and early development were normal. Laboratory data included a serum lactate of 9.2 mmol/L and CSF 7.82 which is high. CT scan showed left parietal cortico subcortical hypodense with diffuse uptake of contrast. MRI brain had areas of lesion at the frontal lobes, posterior region of temporal, parietal and occipital lobes, Arachnoid cyst in the middle cranial fossa causing mild left temporal lobe adjacent compression. Genetic analysis of mitochondrial DNA of the patient was found A3243G point mutation in 30% of heteroplasy. Now he has been treated with Coenzyme Q10 and levetiracetam.

Discussion: MELAS is a mitochondrial disease. The clues for the diagnosis in this case were the characteristic findings on MRI and the protein of the symptoms. It took 2 year to presume the diagnosis and the genetic analysis confirmed the diagnosis. He is now in treatment with Coenzyme Q10 with a good evolution but we’ll need to follow him.

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Neurometabolic disorders

ICNC-0682: Clinical and genetic features of patients with Mucopolysaccharidosis type II

Introduction: Mucopolysaccharidosis type II (MPS II) is an X-linked recessive genetic disorder, caused by deficiency of iduronate-2-sulfatase enzyme (IDS), required for the degradation of glycosaminoglycan (GAG) generating progressive accumulation of substrates causing intralysosomal clinical manifestations. 80% of patients have small pathogenic variants within the gene and 20% have deletions of exons or the whole gene and rearrangements. Methods: Descriptive study. Clinical characterization and determination of genetic mutations by PCR amplification technique of 9 exons of IDS gene in 11 patients with diagnosis of MPS II (urinary GAG levels and enzymatic activity of IDS). Results: We studied 11 patients (10 male, 1 female), age at diagnosis between 15-60 months. All had a neuromopathy phenotype with intellectual disability (mild to profound). First sings were dysmorphic features (38%), followed by recurrent obstructive airway syndrome and psychomotor delay. Most of the patients had macrocephaly, scoliosis/kyphosis, hepatosplenomegaly and 50% developed heart disease. We identified 5 different mutations in 8/11 patients. Three brothers had a c.1421A>C mutation, not previously reported. Four patients present different mutations, 2 of them not previously reported in the literature. The only woman studied had a gene pseudogene recombination in heterozygous state, typically related to a later age of diagnosis. Conclusions: Our patients have classic phenotype features and systemic involvement with cognitive impairment. New and previously reported mutations have characteristic phenotype of MPS II but not specific, which makes difficult to do a genotype-phenotype correlation because of the large allelic variability present. We will continue study the three remaining patients to identify genetic mutation by other methods.

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Neurometabolic disorders

ICNC-0620: Role of routine Benzodiazepine in eliciting classical Electroencephalogram (EEG) response in suspected Sub-acute Sclerosing Panencephalitis (SSPE) cases

Background: EEG could be normal or atypical in SSPE in spite of clinically suggestive and CSF measles antibody positive status but typical pattern could be obtained after intravenous benzodiazepine (BDZ) during routine EEG. Objectives: The purpose was to find out the necessity of routine benzodiazepine during EEG recording of SSPE cases and to compare efficacy of diazepam and midazolam in eliciting EEG pattern. Methodology: This double blind, randomized clinical trial was conducted over 2 yrs among measles antibody positive SSPE cases who received either diazepam or midazolam IV alternately during EEG recording with due precaution. The bilaterally symmetrical, synchronous, high voltage bursts of polyphasic, stereotyped delta waves were designated as “typical periodic slow wave complex (PSWC)” and non-symmetrical, asynchronous high voltage delta waves were designated an atypical PSWC. All atypical PSWC, normal EEGs and other EEG abnormalities were included in “non-typical PSWC” group during analysis. Result: Total 26 cases having mean age was 10.54±1.503 yrs with a male: female of 1.6:1.0 were analyzed. The typical PSWC was found in 8/26 (30.8%) before BDZ. The remaining 18/26 (69.2%) had non- typical PSWC- 10 (38.5%) normal EEG, 3 (11.5%) atypical PSWC and 5 (19.2%) other EEGs. After BDZ, 15 more typical PSWCs elicited
Neurometabolic disorders

ICNC-0683: Clinical phenotypes of GLUT1 Deficiency Syndrome
Glucose transporter deficiency syndrome (GLUT1DS) is a genetic metabolic disorder which results from impaired glucose transport into the brain. GLUT1DS has a broad clinical spectrum with variable combinations of intellectual impairment, acquired microcephaly, epilepsy and movement disorders. Clinical phenotypes of this syndrome can be classified in three groups: 1) classical phenotype (epilepsy + intellectual impairment ± movement disorder); 2) non-classic phenotype A (intellectual impairment + movement disorder, except exercise induced dyskinesia); 3) non-classic phenotype B (exercise induced dyskinesia ± absence epilepsy or minimal phenotype). Here, we present four GLUT1DS female patients, including two classic phenotype (12 months and 9.5 years), one nonclassic A phenotype (17 years) and one nonclassic B phenotype (5 years). Patients with classic phenotype have microcephaly, but non-classic patients have normal head circumference. CSF glucose and CSF/blood glucose ratio were low in patients with classic phenotype and nonclassic phenotype A, but normal with non-classic phenotype B (early-onset absence epilepsy). We detected two different de novo mutations of the SLC2A1 gene in two patients with the classic phenotype (c.170-171insA and c.680-1G>T). We also found two mutations previously identified for GLUT1DS, in patients with nonclassic A and nonclassic B phenotypes (respectively c.542del ve c.940G>A). SLC2A1 gene analysis were normal in all parents and siblings. Ketogenic diet was well tolerated for all patients, but compliance was poor for patient with nonclassic A phenotype. The GLUT1DS patients were generally diagnosed late as in our group, but early diagnosis is crucial for an effective etiological therapy, and compliance to ketogenic diet is much better when it begins in the early childhood.

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Neurometabolic disorders

ICNC-0684: Pyruvate dehydrogenase-E1 α deficiency presenting as acute upper and lower extremities proximal muscle weakness in a 8-year-old boy
The mitochondrial pyruvate dehydrogenase enzyme complex (PDHC) plays an important role in aerobic energy metabolism and acid-base equilibrium. PDHC contains of 5 enzymes, 3 catalytic (E1, E2, E3) and 2 regulatory, in addition three cofactors and an additional protein (E3-binding protein) encoded by nuclear genes. The clinical presentation of PDHC deficiency ranges from fatal neonatal lactic acidosis to chronic neurologic dysfunction without lactic acidosis. Paroxysmal neurologic problems also can rarely be seen such as intermittent ataxia, episodic weakness, exercise induced dystonia and recurrent demyelination. Here, we present a 8-year-old boy complaining acute upper and lower extremities proximal muscle weakness with normal mental status. He had a history of Guillain-Barre like syndrome at the ages of 2 years. Electrophysiologic studies showedsensorial polyneuropathy findings in the first attack and sensori-motor polyneuropathy findings in the last attack. The genetic analysis revealed a previously reported hemizygote mutation of the PDHA1 gene (p.A353T/c.1057G>A) which encodes E1α subunit of PDHC. Thiamine was ordered (15 mg/kg/day), dietary carbohydrates were restricted and clinical findings improved in a few weeks. We aimed to discuss this rare phenotype of PDHC deficiency.

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Neurometabolic disorders

ICNC-0685: Molybdenum cofactor deficiency Mimicking Hypoxic-Ischemic Encephalopathy

Molybdenum cofactor deficiency (MoCD) is a rare neurometabolic disorder characterized by neonatal onset seizures, severe psychomotor retardation, dysmorphic features and dislocated lenses. It is often mistaken for hypoxic ischemic encephalopathy secondary to perinatal asphyxia. Here, we present a 2-month old boy who presented with seizures, microcephaly, psycho-motor retardation, hypertonia and other pyramidal tract signs. The patient was diagnosed as hypoxic-ischemic encephalopathy, phenobarbital was ordered to control seizures, and reported to our clinic. The weight and height of the patient were in normal ranges. He had no eye contact and head control. Cranial magnetic resonance showed diffused subcortical cystic encephalomalacia, enlarged extraaxial cerebrospinal fluid spaces and mild ventriculomegaly. Perinatal history was not compatible with asphyxia. Biochemical analysis showed low serum uric acid levels (<0.5 mg/dl) at different examinations. Urine sulfates were negative, but urine sulfites could not be examined. The routine screening tests for inborn errors of metabolism disorders were normal. The patient was diagnosed as MoCD and definite diagnosis by genetic analysis was planned. MoCD may be confused with hypoxic-ischemic encephalopathy according to clinical and cranial magnetic resonance imaging findings. Low serum uric acid levels and elevated urinary sulfites are simple but very helpful diagnostic tests to diagnose MoCD. It is important ro recognize MoCD to provide appropriate genetic counseling and prenatal diagnosis.

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Neurometabolic disorders

ICNC-0630: Menkes disease and response to copper histidine: an Indian case series

IntroductionMenkes disease (MD) is an X-linked recessive disorder caused by mutations in ATP7A. Depending on residual ATP7A activity, manifestation could be classical MD, occipital horn syndrome or distal motor neuropathy. Neurological sparing is expected in female carriers. However, they can manifest with classical clinical phenotype in skewed X chromosome inactivation, X chromosome to autosomal translocation and XO genotype. MethodsHere we describe the clinical profile, laboratory and radiological findings of 4 patients with MD and their response to copper histidine therapy. This series also include a girl with X chromosome to chromosome 13 translocation manifesting neurological symptoms.ResultsAll the 4 children had developmental delay, recurrent respiratory tract infection, hair and skeletal changes, axial hypotonia, tortuous vessels on imaging, low serum copper and elevated lactate. Foetal hypokinesia and foetal growth retardation were present in 2 cases. Failure to thrive was present in 3 children and only one child had epilepsy. The range of serum copper varied from 8-24mg/dL and ceruloplasmin was 45-133mg/dL. The average time lapse in treatment was 20.3 months and average duration of follow-up was 14.3 months. Subcutaneous copper histidine was administered to all children.ConclusionWe conclude that copper histidine therapy is beneficial in reversing the skin and hair changes, improving appendicular tone, socio-cognitive milestones, improved weight gain and immunity. Early diagnosis and management of MD are essential to have a better clinical outcome. More research is needed to explore and devise new strategies in the management of patients with MD.Key words: Menkes disease; copper histidine; ATP7A; X-linked recessive

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Neurometabolic disorders

ICNC-0621: A familial case of spino cerebellar ataxia type 29

Spinocerebellar ataxia type29 (SCA29) is a rare autosomal dominant neurologic disorder characterized by early gross motor delay, nonprogressive cerebellar ataxia, mild cognitive delay, and cerebellar atrophy shown by brain magnetic resonance imaging (MRI). Recently, mutations of the inositol 1,4,5-triphosphate receptor type1 (ITPR1) gene have been identified in two pedigrees families with SCA29. In addition to these pedigrees, sporadic Japanese cases of nonprogressive spino cerebellar ataxia patients have been associated with missense mutation of ITPR1 gene. We herein report the first Japanese familial case of SCA29, caused by a de novo missense mutation of ITPR1 gene. Patient-1 is a 4-year-old girl who has been seen at our hospital since 17 months of age. She presented with gross motor delay, hypotonia and language delay at her first visit, and gradually developed ataxia. Her brain MRI showed cerebellar atrophy from her first visit. She has started independent gait at 3 years of age, and her ataxic symptoms have been non-progressive. Patient-2 is her father who has had gross motor delay and hypotonia but no cognitive dysfunction since his early infancy, and his brain MRI showed cerebellar atrophy. His ataxic symptoms have been non-progressive. We performed sequencing of ITP1 gene, and identified a novel c.A1702G missense mutation of ITP1 gene in both patients. SCA29 must be included in differential diagnoses of non-progressive spino cerebellar ataxia, especially for familial cases.
Neurometabolic disorders

**ICNC-0853: Cognitive follow up of a pediatric patient with GLUT-1 deficiency treated with Acetazolamide**
Introduction: The clinical features of GLUT-1 deficiency syndrome include cognitive impairment, acquired microcephaly, epilepsy, and/or movement disorder caused by mutations in the SLC2A1 gene. Initially, mental retardation was considered as being inseparable from classic glucose transporter protein type 1 deficiency. Ketogenic diet was the main treatment used to control symptoms and prevent further neurologic deterioration. Acetazolamide was reported to be beneficial for paroxysmal dyskinesias. Case report: Our patient presented at 14 months of age, with recurrent attacks of abnormal eye movements, later adding intermittent cerebellar ataxia and weakness; monthly episodes, lasting from minutes to one hour. Mild hypoglycorrachia (39 mg/dl; 0.49 CSF-to-blood glucose ratio) and missense heterozygote mutation C. 119G>A in the SLC2A1 gene was found. Oral acetazolamide was started, resulting in immediate and complete disappearance of the attacks, being currently symptom free for 3 years. Results: Testing of intellectual functioning performed when acetazolamide was started showed average general intellectual ability, with better performance in verbal than performance domains. Follow up testing revealed a stable profile, with marked improvement in sensory motor integration tasks but a low performance in visual constructive tasks. Normal attention profile. Conclusion: Acetazolamide could be an alternative therapy for patients with mild forms of Glut 1 deficiency syndrome with movements disorders. Even though earlier studies stated that medications do not correct inadequate nourishment necessary for brain growth and development, we report a patient with normal and stable cognitive profile after three years of treatment with acetazolamide during early development.

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Neurometabolic disorders

**ICNC-0854: Clinical experience of neonatal hypoglycaemic brain injury(NHBI) patients from semi urban area in western India**
• Introduction: Perinatal injuries are still most common cause of neurodevelopmental disabilities in India. The objective is to assess the particular sequel associated to isolated hypoglycemia, to know events surrounding hypoglycemia and thereby to learn steps to avoid this preventable condition with morbid outcome. • Methods: Infants and children with abnormal brain MRI scans after symptomatic neonatal hypoglycaemia without evidence of hypoxic-ischemic encephalopathy were considered for this study. No specific definition of hypoglycemia was used in this study and mention of hypoglycemia in neonatal discharge summary was considered appropriate. Retrospective chart review of all patients with hypoglycemic brain injury over 5 month (February to June 2015) at outpatient clinic was done. Perinatal data and neurodevelopmental outcome were assessed in this group • Results: one in every forty patients is with NHBI. Mental retardation, epilepsy, vision problems and autism are main presentations either alone or in different combinations and hypertonia is rare. Almost 50% patients had refractory epilepsy. Isolated symptomatic hypoglycaemia with poor neurodevelopment outcome more in full term neonates and appropriate for gestational age babies. seizure was the most common manifestation of symptomatic hypoglycaemia and mostly happened after 24-48 hr of normal post natal period. Only 20% parents were explained BF in detail and only one third patients were on exclusive BF in spite of all hospital delivery. • Conclusion: NHBI is quite common with morbid outcome. It is a common etiology of refractory epilepsy. Feeding counseling needs resuscitation as most patients are without biological risk factors.

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Neurometabolic disorders

**ICNC-0623: Efficiency of electrostimulation at treatment of post-traumatic Neyropathy in children**
Introduction. Neuropathy – is a condition, which occurs due to impact of various factors and follows by dystrophic or degenerative changes of nerves. As nerve tissue possesses the least expressed regenerative properties, neuropathy differs with a chronic progress and can lead to the patient's disability. Objective: to study efficiency of application of electrostimulation for children with post-traumatic neuropathy of peroneal and tibial nerves. Methods. 32 children with post-traumatic neuropathy were examined. In 20 of them, a peroneal nerve was damaged, in 7 of them – a tibial nerve and in 5 patients a combined damage of both nerves was detected. Besides clinical and neurological examination, all patients underwent the electro stimulation of nerves with the help of electromyography (EMG). Results. After 7-12 days of electro stimulation of damaged nerves the regeneration of axons was detected in 92% of patients, while only 50% of patients had the clinical improvement. After 35-44 days of treatment it was managed to register the reinnervation of myofibrils. After the treatment the sensitivity of the innervation area of damaged nerve was recovered, and the muscular
activity was increased up to 3-5 points. Conclusions. The electro stimulations of damaged nerves at neuropathies could be considered as effective method of treatment of posttraumatic neuropathy in children.

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Neurometabolic disorders

ICNC-0625: Phenotypic profiles in a cohort of patients affected with variant Late Infantile Ceroid-lipofuscinosis 5 (CLN5)

Introduction: CLN5 is a rare form of neuronal ceroid-lipofuscinosis (NCL). CLN5 codes for a soluble lysosomal protein of still undetermined function. Late Infantile onset is most common; Juvenile and Adult cases have also been described. Methods: Records of 15 children belonging to different ethnic groups were obtained from the datasets of the DEM-CHILD International NCL Registry and in collaboration with international clinical experts. Mutation analysis of CLN5 was performed by Sanger sequencing. All patients underwent EM investigations of peripheral tissues. pCLN5 was characterized in vitro in 5 cases. Results: Disease onset was at 2-7 years of age: behavioural disturbances and language delays were the most common early symptoms; impaired early cognitive development occurred in children with later onset. Seizures were the initial symptom in one child only; however they were present in all patients from 5 months to 5 years after disease onset. The course was relatively slow, and the eldest patient of the cohort is now 24 years old (onset at 5). 10 mutations were detected of 22 alleles, including 6 mutations predicting a truncated protein. Mixed cytosomes were observed by EM. WB of cultured fibroblasts revealed either fully expressed protein or absence of signal in the patient carrying the most severe, homozygous mutation. Conclusions: Clinical features of this cohort of CLN5 patients confirm that behaviour and cognitive difficulties are early markers of this condition. Progressive loss of motor and visual skills with severe epilepsy occur later. No clear evidence of genotype-phenotype correlations was shown

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Neurometabolic disorders

ICNC-0687: Vitamin B12 deficiency in an adolescent woman masquerading as encephalomyelitis

INTRODUCTION: Vitamin B12 deficiency is classically encountered in adult Caucasian population in developed countries and manifests as subacute combined degeneration. However, it is extremely rare in children and pernicious anemia is an even rarer etiology. Therefore, the presentation in children is not as easily recognizable or well characterized and may result in missed or delayed diagnosis. CASE REPORT: We report the case of a previously healthy adolescent female who presented with ten days of progressively worsening emotional lability and difficulty walking. Physical examination showed scattered ulcerations on her soft palate and posterior pharynx with hyperpigmentation in her palmar creases and interphalangeal joints. Neurological examination demonstrated impaired speech, recall and orientation, and hyperreflexia with sustained ankle clonus. Her gait was wide-based with impaired proprioception. Initial differential diagnosis included viral encephalomyelitis given palatal ulcers, as well as autoimmune encephalitis with predominant psychiatric symptoms. Laboratory investigations revealed macrocytic anemia and MRI showed T2 prolongation with associated enhancement along the posterior columns of the cervical and thoracic spinal cord and spotty T2 prolongation within subcortical white matter of the right frontal and parietal lobe, consistent with subacute combined degeneration. Further investigations revealed B12 deficiency secondary to pernicious anemia. Treatment was initiated with intramuscular cyanocobalamin with gradual improvement in symptoms. CONCLUSION: Though uncommon in pediatrics, this case illustrates the necessity of maintaining a high degree of suspicion for B12 deficiency as an etiology of neurological symptoms in children since early recognition and treatment is key to preventing long term neurodevelopmental sequelae.

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Neurometabolic disorders

ICNC-0690: Glut1 transporter deficiency syndrome: The Greek experience
Introduction: Glut1 DSI Sisarare neurometabolic disorder that results in impaired glucose transport in the brain. It causes a variety of clinical phenotypes, including neurodevelopmental delays, seizures, and a neurological phenotype including ADHD. Carnitine therapy not only reverses the myopathy and cardiomyopathy of OCTN2 deficiency, but may improve the exercise intolerance and behavioural problems. Studies and Results: L-3[3H]-carnitine uptake studies in his cultured skin fibroblasts confirmed OCTN2 deficiency. Molecular analysis of SLC22A5 gene in genomic DNA from the proband and his parents by PCR and Sanger sequencing revealed heterozygosity for a premature stop codon (p.R282X) (paternal inheritance) and a novel in-frame deletion (p.T440-Y449) (maternal inheritance) and a novel in-frame deletion (p.T440-Y449) (maternal inheritance) in a highly conserved putative caveolin-1 binding site. Immunoblot of fibroblasts with anti-mOCTn2 antibody revealed a reduced truncated protein. Conclusion: L-carnitine therapy not only reverses the myopathy and cardiomyopathy of OCTN2 deficiency, but may improve the neurological phenotype including ADHD.

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Neurometabolic disorders

ICNC-0691: Congenital neuro-malformation due to inborn errors of metabolism: an expanding area of lecture
Both brain malformations and inherited metabolic diseases are common, mainly in highly consanguineous population. Causes of malformations include genetic abnormalities, environmental factors such as maternal diseases, infections, and teratogens, and other causes. It has been asserted that the metabolic malformation syndromes such as Smith-Lemli-Opitz represent the exceptions rather than the rule. In a strict sense, this may be the case. However, metabolic pathways and developmental pathways do not sit in exclusively different compartments, and interactions between the two are not only possible but likely. The number of inborn error of metabolism associated with congenital neuro-malformation is growing, such as mitochondrial disease, non-ketotic hyperglycinemia, serine metabolism or Smith-Lemli-Opitz syndrome. The careful assessment of patients with malformation of the central nervous system/structural brain defects and the recognition of possible underlying inborn error of metabolism is important in order to provide a possible treatment, an accurate prognosis and genetic counseling. The most recent literature regarding mechanisms of brain development and malformation in the context of inborn error of metabolism, approach and future paths of research are discussed.

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Neurometabolic disorders

ICNC-0666: Attention deficit-hyperactivity disorder as a dominant clinical presentation in a boy with OCTN2 Deficiency
We report a novel OCTN2 mutation (novel in-frame deletion (p.T440-Y449) in a patient with ADHD. Case report: This boy presented with ADHD at 3 years and at 8½ years was notably hyperactive in the absence of hypoglycemic hypoketotic coma and had myopathy, cardiomyopathy, and very low serum carnitine. Formal psychological evaluation with the standardized Attention-Deficit/Hyperactivity Disorder Test (ADHD), gave a score consistent with severe ADHD. He had elevated aminotransferases. His sister died of sudden infant death. On clinical suspicion of OCTN2 deficiency, he was treated with high dose oral L-carnitine (100 mg/kg/day) which led to significant improvements in his cardiomyopathy, exercise intolerance and behavioural problems. Studies and Results: L-[3H]-L-carnitine uptake studies in his cultured skin fibroblasts confirmed OCTN2 deficiency. Molecular analysis of SLC22A5 gene in genomic DNA from the proband and his parents by PCR and Sanger sequencing revealed heterozygosity for a premature stop codon (p.R282X) (paternal inheritance) and a novel in-frame deletion (p.T440-Y449) (maternal inheritance) in a highly conserved putative caveolin-1 binding site. Immunoblot of fibroblasts with anti-mOCTn2 antibody revealed a reduced truncated protein. Conclusion: L-carnitine therapy not only reverses the myopathy and cardiomyopathy of OCTN2 deficiency, but may improve the neurological phenotype including ADHD.

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Neurometabolic disorders

ICNC-0655: Mental retardation, microcephaly, and developmental delay: a novel TCTP (tissue transglutaminase) mutation associated with a severe phenotype
We report a novel TCTP (tissue transglutaminase) mutation (c.2137+1G>A) in a patient with mental retardation and dysmorphic features. We performed molecular analyses of this patient and his parents, and the results revealed heterozygosity for a splicing defect in TCTP gene. The results of our study suggest that TCTP gene mutations may be involved in mental retardation and dysmorphic features.

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Neurometabolic disorders

ICNC-0626: Congenital Parry-Romberg Syndrome with central nervous system involvement
Introduction: Epilepsy of infancy with migrating focal seizures (EIMFS) is a severe pharmaco resistant epilepsy syndrome. Mutations in a number of causative genes, including KCNT1, have been previously reported, and it is clear that EIMFS is genetically heterogeneous. Here we present the first report of mutations in SLC12A5, encoding the potassium chloride co-transporter KCC2, as a recessive cause of EIMFS. Methods: Two families (each with 2 affected children) were studied using autozygosity mapping and whole exome sequencing strategies. To determine the effects of mutant protein, structural homology modelling, immunoblotting, confocal microscopy and voltage-clamp recording were undertaken. TALEN-mediated genome editing was utilised to generate a double KCC2a-KCC2b knockout zebrafish model. Results: Genetic investigations revealed compound heterozygous SLC12A5 missense variants in Family 1 (c.1277T>C, L426P; c.1652G>A, G551D) and a homozygous missense variant in Family 2 (c.932T>A, L311H). Protein homology modelling predicted detrimental effects on protein structure and substrate binding. Mutant KCC2 exhibits a depolarised chloride reversal potential and delayed recovery from chloride load. Reduced total and cell surface expression of mutant KCC2 was evident with impaired protein glycosylation. The knockout zebrafish demonstrated abnormal jerky movements on tactile response testing at 2 days post-fertilisation. Conclusions: We report loss-of-function SLC12A5 mutations in EIMFS. KCC2 plays a fundamental role in fast synaptic inhibition. We show that these EIMFS mutations result in reduced KCC2-mediated chloride extrusion, thereby impairing normal synaptic inhibition and promoting neuronal excitability. Elucidation of novel disease mechanisms is vital to the future development of targeted therapies for these early onset epilepsies.

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Neurometabolic disorders

ICNC-0695: A case of hyperphosphatasia with mental retardation syndrome (HPMRS4, PGAP3 deficiency) with normal peripheral blood GPI-anchor protein expression.
[Background] Hyperphosphatasia with mental retardation syndrome (HPMRS) is a rare congenital disorder characterized by hyperphosphatasia, dysmorphic features, mental retardation, and various neurologic abnormalities. Recent studies have revealed that several genes involved in glycosylphosphatidylinositol (GPI) biosynthesis are responsible for HPMRS. GPI attaches to the C-terminus of precursor proteins of GPI-anchored proteins (GPI-APs) during posttranslational modification. The defect in GPI synthesis causes reduction of the number of cell-surface GPI-APs. Therefore, flow cytometric assay (FACS) of peripheral blood cells for GPI-APs is regarded as a good method to screen inherited GPI-anchor deficiencies (IGDs). [Methods] A boy with characteristic facial features, cleft palate, bilateral sensorineural hearing loss, severe psychomotor retardation, and hyperphosphatasia (1,848〜5,275 IU/L) underwent FACS for GPI-APs and genetic analysis for known IGDs. Functional assays were conducted afterwards. [Results] Genetic analysis revealed compound heterozygous mutations c.511T>C (p.C171R)/c.842T>C (p.L281P) of the PGAP3 gene. Although both mutations were novel missense mutations, functional assays revealed their pathogenicity. Surface expression of GPI-APs on peripheral blood cells showed no apparent abnormality. [Discussion] We present a case of genetically and biochemically proven PGAP3 deficiency without reduction of cell-surface GPI-APs. The lack of PGAP3 yields GPI-APs with abnormal unsaturated fatty acids, not allowing them to localize in lipid rafts. Further studies are required to reveal the pathomechanism of PGAP3 deficiency; however, the defect in localization of GPI-APs, not the reduction, may be responsible for its pathomechanism. Clinicians should be aware that patients with PGAP3 deficiency might not exhibit reduction of cell surface GPI-APs on peripheral blood cells.

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Neurometabolic disorders

ICNC-0627: A population screening of Niemann-Pick Type C disease in Turkey: an innovative approach and key findings
[Background] Niemann-Pick disease type C (NP-C) is a rare lysosomal storage disease caused by mutations in either the NPC1 gene or the NPC2 gene. Here we report allele frequency analysis of pathological mutations in 510 individuals from four Turkish families, each with at least one homozygous index case diagnosed. Methods: We performed...
direct sequencing of exon 8 of the NPC1 gene, exon 4 and exon 5 of the NPC2 gene. Results: Novel homozygous mutations in the NPC1 (p.T375P; c.1123A>G) and NPC2 (p.V145E; c.434T>A) genes were identified. Furthermore, a homozygous mutation in NPC2 (p.E118X; c.352G>T) was observed in two families living in different regions. The observed heterozygous frequency of NP-C was 22.7%. Finally, two new patients were diagnosed with NP-C during the study.

Conclusions: Identification of mutations in patients with NP-C disease is important for genetic counseling and prenatal diagnosis of relatives to allow earlier diagnosis and treatment. We have shown that population-based screening studies can be used to detect new patients in targeted families with high consanguinity rates. Additionally, p.E118X in NPC2 might be a founder effect in this population.

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Neurometabolic disorders

ICNC-0628: A new culture model of myelination: morphological findings and attempts to reproduce CMT pathology.

Charcot–Marie-Tooth disease type (CMT) is a most common hereditary neuropathy characterized by progressive weakness, atrophy and sensory loss of the distal muscles of the limbs. However, there is no current consensus on treatment for CMT. In order to development of therapeutic approaches for these intractable diseases, we developed an experimental system to reproduce peripheral nerve system (PNS). In previous reports, co-cultures systems making use of dissociated rat dorsal root ganglia (DRG)/Schwann cells are widely used to essentially study myelination in vitro. On the other hand, our model of PNS myelination in vitro is the “explant culture” of rat DRG. Schwann cells migrated along the neuritis after culture started. Mature segments of myelin immunostained with anti-MBP antibody were observed in compact myelin on 2-3 days after induction of myelination. The number of MBP positive Schwann cells increased day by day until 14 days after induction of myelination. The ultrastructural analysis confirmed that many axons were surrounded by a dense myelin sheath. These findings morphologically resemble peripheral nerve structures in vivo. This model may be more relevant and convenient model to observe the developmental process of PNS than the previous methods. Therefore, this approach may be also useful to perform the drug screening for the therapy of CMT.

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Neurometabolic disorders

ICNC-0696: A case of SURF1 deficiency with unusual radiologic findings

Leigh Syndrome is a common presentation of paediatric mitochondrial disease and is characterised by severe neurodevelopmental delay, a subacute necrotising encephalopathy, basal ganglia involvement on MRI and marked biochemical and genetic heterogeneity. We describe the clinical and laboratory findings in a 5 month of old female patient who presented with resistant convulsions. Only areflexia was detected in initial physical examination. Laboratory tests including serum lactate and first step metabolic investigatement was normal. Brain MR imaging showed hydrocephalia; there was no abnormality on basal ganglia or brain stem. MR Spectroscopy was normal. A diagnostic muscle biopsy revealed a diffuse, global loss of cytochrome c oxidase (COX) activity prompting molecular genetic studies which revealed a well-characterised, homozygous missense mutation (c.769G>A; p.Gly257Arg), in the SURF1 gene. Mutations in SURF1 are a recognised cause of COX-deficient Leigh syndrome, although missense variants are relatively uncommon. Of particular interest, our patient’s radiologic and biochemical findings did not show many clues to a diagnosis of mitochondrial disease, although neurological findings of her clinical presentation did prompt further investigation, aiding a genetic diagnosis.

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Neurometabolic disorders

ICNC-0960: Non-motor symptoms in Tyrosine Hydroxylase Deficiency: Consequences of a late diagnosis

Introduction Tyrosine Hydroxylase Deficiency (THD) is a rare, autosomal recessive neurometabolic disorder that leads to a deficiency of dopamine, norepinephrine and epinephrine. It can present as a progressive extrapyramidal movement disorder (hypokinetic-rigid syndrome with dystonia) with onset in infancy or childhood, or as a complex encephalopathy with onset in the neonatal period or early infancy. The first subtype responds good to levodopa. Consequences of late diagnosis and non-motor symptoms of THD have not been delineated well. Case Report This patient showed dystonic posturing of limbs from age 4 months. She became able to sit and walk with support, but progressively lost all motor skills. Cognitive abilities were normal. At age 30 years, she was profoundly hypokinetic with generalized dystonia. From age 4, she developed severe psychiatric complaints with mood disorder, obsessions and compulsions, and hallucinations. At age 31 years, the diagnosis of THD was proven and levodopa was started, leading to a modest improvement in motor status. Now aged 35 years, her psychiatric complaints remain severe despite treatment.

Discussion So far, little attention has been given to non-motor consequences of congenital neurotransmitter disorders. Although in dopa responsive dystonia caused by GCH1 mutations an increased incidence of neuropsychiatric complaints is reported, this is not confirmed by others. We are planning a follow-up study of THD patients in the Netherlands, with attention to neuropsychiatric and neuropsychological features to better understand the complete spectrum of the disease.


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Neurometabolic disorders

ICNC-0605: The CATNAP study: Children Ataxia Telangiectasia Neuro Assessment Project

Introduction: Ataxia Telangiectasia (A-T) is a rare genetic disorder with symptoms including ataxia and involuntary movements, telangiectasia, and higher risk of infections and cancer [1]. Although symptoms can be managed, there is currently no treatment for A-T related neurodegeneration[2]. We present the rationale, protocol and current status of the on-going Children Ataxia Telangiectasia Neuro Assessment Project (CATNAP) which aims to find quantitative magnetic resonance (MR) neuroimaging biomarkers that correlate with the severity of A-T. Methods: CATNAP will recruit 30 children with A-T and 20 healthy children. Neurological severity is assessed using the A-T Neurological Examination Scale Toolkit (A-T NEST). All children undergo MR imaging using a 3T GE MR750 and 32-channel head coil, including 3D 1mm isotropic T1 volume, MEGA-PRESS MR spectroscopy to measure glutathione [3], pcASL perfusion imaging, resting state fMRI and 32-direction diffusion tensor imaging. During the scan children watch videos using an MR compatible TV screen and headphones (turned off for resting state fMRI). Head movement is minimised using inflatable foam pads.


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ICNC-0599: Use of Ketogenic diet for epilepsy in Batten Disease

Abstract - The Ketogenic diet (KD) is a high-fat, low-carbohydrate diet that is used primarily to treat drug-resistant epilepsy. Neuronal Ceroid Lipofuscinoses (NCLs) are rare genetic neurodegenerative disorders usually presenting in childhood, in which epilepsy is prominent. We are a specialist centre supporting patients with NCL and we share our experience of KD in the NCL cohort seen here. A retrospective case-note review of all children with NCL who were treated with KD was undertaken. 8 children were identified, 6 had CLN2 disease (classic late infantile), and 2 had a variant late infantile phenotype (CLN7 and CLN8). Diet was initiated between 3.7 years and 7 years in 4 different centres. 6 were established on a classical KD, one on a restricted modular diet and 2 on MCT diet, one of who was later changed to a classical diet. In a condition where seizure control is not generally achieved, 6/8 had improved seizure control and 2 had no response to dietary therapy. 2/8 also was documented to have improved general alertness. 4 children have died (1 remained on KD until death). KD is being used in 2 children. KD was well tolerated. One child developed hypercholesterolemia and 1 became severely hypokalaemic, which was suspected to be secondary to a modular gluten and dairy free KD. KD is generally well tolerated in NCL and maybe as effective as additional drug treatment for epilepsy. We believe KD should be considered even in children with severe degenerative conditions, but should be monitored closely.

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Neurometabolic disorders

ICNC-0624: Expert opinion on the management of CLN2 disease

Objectives: CLN2 disease, an inherited, rare, pediatric-onset, rapidly progressive neurodegenerative lysosomal storage disorder caused by TPP1 enzyme deficiency, is characterized by language delay, seizures, movement disorder, motor deterioration, dementia, blindness and early death. No management guidelines exist for this condition. Our aim is to gain insight into current management strategies. Methods: 24 disease experts (healthcare professionals and patient advocates) completed an online survey with a smaller group participating in a discussion of management practices. Results: Experts share common goals in the management of patients and their families. Goals and interventions evolve as the disease progresses, with a shift in focus from maintenance of function early in the disease to maintenance of quality of life (QoL). The goal of antiepileptic medication is to achieve sufficient seizure control to support function balancing the side effects. Antiepileptic medications may have unique response in patients with CLN2. Carbamazepine and phenytoin should be used with caution. School and home environments should be adapted to accommodate physical and cognitive/behavioral impairments for ongoing benefit of maintaining social interactions. Physical, occupational and speech therapies should be initiated early and assessed frequently, including use of adaptive devices to support function and independence. Palliative care team engagement is essential soon after diagnosis is made. Conclusions: CLN2 management practices are consistent among experts worldwide. A multidisciplinary approach is critical for optimizing care and QoL of patients and families throughout the disease course. This effort to identify common management practices represents an initial step towards development of consensus-based management recommendations.

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Neurometabolic disorders

ICNC-0699: Late-Onset biotinidase deficiency mimicking neuromyelitis optica
Biotinidase deficiency usually presents during the first year of life with hypotonia, seizures, ataxia, dermatitis and alopecia. It can rarely occur later in life in previously asymptomatic cases. A 14-years-old boy was referred with progressive vision loss and weakness at upper extremities. Muscle strength at upper limbs was 3/5. His visual acuity was 20/400 on the right and 20/200 on the left side. Visual evoked potential revealed bilateral partial conduction delay. Exaggerated startle reflex, decline at school performance and obsesive-compulsive behavior for one-year was noted. The craniospinal MRI revealed bilateral, symmetric increased signal intensity from mesencephalic tectal region and medulla oblangata to C6 cervical vertebra with symmetric linear contrast enhancement. Increased signal intensity and contrast enhancement at optic chiasm was noted. He was initially diagnosed as neuromyelitis optica and pulse steroid therapy was initiated. The oligoclonal band and aquaporin-4 antibody was negative. After steroid therapy the muscle strength at upper extremities increased to 4/5 and a slight visual improvement was noted. Control cranio cervical imaging demonstrated no improvement in the brainstem and cervical lesions while contrast enhancement at the optic chiasm dissapearee. The biotinidase level was found 0.58 nmol/min/ml (N: 4.4-12) and the activity was 8%. The genetic analysis revealed heterozygous c.98-104delinsTCC and p.V437M mutations. Biotin therapy was started and his control cranio cervical at the third month was completely normal. His asymptomatic mother and 6 years-old brother also had very low biotin levels and were started treatment. Differential diagnosis of juvenile-onset vision loss should include biotinidase deficiency.

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Neurometabolic disorders

ICNC-0700: Familial hypermanganesemia among five Egyptian families: further delineation and management
Familial hypermanganesemia is a rare metabolic error caused by recessive mutations in SLC30A10 gene responsible for manganese transporter. Manganese accumulates in the liver, muscle, bloodstream, and basal ganglia resulting in extrapyramidal manifestations, polycythemia and liver cirrhosis. We describe 9 patients from 5 unrelated consanguineous Egyptian families with cardinal manifestations of manganism. They were 7 males and 2 females with aged ranged from 1 4/12y to 18 years old. Six patients (F1 and 2) presented with insidious regressive walking around the age of 2 9/12 and one patient (F3) had sudden acute dystonia of lower limbs with inability to walk at the age of 1 4/12 year. Interestingly, 2 patients (F4,5) manifested with early onset progressive dystonia and obvious signs of hepatic fibrosis around the age of 2 in contrary to all reports represented late liver involvement. All affected had hemoglobin concentration of 17 -21 g/dl and blood manganese level was above 2000 nmol/L. Brain MRI showed the typical picture of manganese deposition in basal ganglia classically on T1-weighted images, with no corresponding abnormality on T2-weighted scans. Molecular analysis for these 5 families revealed novel mutations in SLC30A10 gene in 4 of them. We designated oral treatment with 2,3 dimercaptosuccinic acid (DMSA), iron supplementation and levodopa that showed satisfactory preliminary results in chelating manganese with improvement of biochemical markers, alleviation of clinical symptoms in mild stabilization for those with hepatic involvement. In this report we further delineate the clinical spectrum of familial hypermanganesemia. It emphasizes the importance of considering early diagnosis of this treatable metabolic error in order to eliminate hepatic involvement.

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Neuromuscular disorders

ICNC-0701: Spectrum of clinical manifestations in two young Turkish patients with Congenital Generalized Lipodystrophy type 4

Congenital generalized lipodystrophy (CGL) type 4 is an extremely rare autosomal recessive disorder. We report our clinical experience on two Turkish families with CGL type 4. A novel homozygous PTRF mutation, c.259C>T (p.Gln87*), was identified in a 13-year-old girl. She presented with generalized lipodystrophy and myopathy. Further tests revealed ventricular and supraventricular arrhythmias, gastrointestinal dysmotility, atlantoaxial instability, lumbosacral scoliosis, and metabolic abnormalities associated with insulin resistance. A 16-year-old girl with CGL type 4 caused by homozygous PTRF c.481-482insGTGA (p.Lys161Serfs*41) mutation was previously reported. Here, we report on her long term clinical follow-up. She received several course of anti-arrhythmic treatments for catecholaminergic polymorphic ventricular tachycardia (CPVT) and rapid atrial fibrillation. An implantable cardioverter defibrillator (ICD) was also placed. Our data indicate that patients with CGL type 4 should be meticulously evaluated for cardiac, neuromuscular, gastrointestinal and skeletal diseases, as well as metabolic abnormalities associated with insulin resistance.

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Neuromuscular disorders

ICNC-0702: Postural orthostatic tachycardia syndrome (POTS): treatable but overlooked cause of recurrent neuropathic pain in childhood

Postural orthostatic tachycardia syndrome (POTS) is defined as a sustained heart rate increase of >30 bpm within the first 10 min of orthostasis associated with symptoms of orthostatic intolerance and without significant orthostatic hypotension. We describe 2 pediatric patients with POTS who have been referred to our Child Neurology Dpt. because of recurrent “unexplained” crisis of severe pain in limbs. Case 1: 16 y.o. girl who suffered from severe paroxysmal pain in arms and legs associated to sudden changes in distal skin colour and short bursts of tachycardia since 6 months before consultation. She also had chronic headaches and nephrolithiasis. Case 2: 15 y.o. boy referred because of paroxysmal pain and cyanosis in both feet and hands associated with dyspnea and fatigue after postural changes. Both patients underwent brain MRI, routine lab, reumathology and endocrinology panels, Nerve conduction studies, metabolic workup including heavy metals, alpha-galactosidase activity (Fabry) and porphiria tests, EKG and echocardiogram. All studies were normal. In both cases QST showed abnormal threshold for cold and warm stimulus (small fiber neuropathy) and Head-Up Tilt test triggered orthostatic tachycardia without hypotension. Patient 1 was treated with beta-blockers, pregabalin and valproic acid. Patient 2 was initially treated with midodrine and because lack of response was switched to diosmine with better outcome. Conclusions: POTS is a condition characterized by an abnormal persistent orthostatic tachycardia but also may include neurological symptoms as small fiber neuropathic pain. It is important that this disorder is recognized as some useful treatment options exist.

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Neuromuscular disorder

**ICNC-0703: X-linked polyneuropathy with transient cerebral white matter lesions associated with a novel connexin 32 mutation in Argentinean patient**

Background: X-linked hereditary CMT (Charcot Marie Tooth) disease is quite common and accounts for approximately 10 to 20 % of all hereditary demyelinating neuropathies. Connexine 32 is a GAP junction protein expressed in Schwann cells, oligodendrocytes and astrocytes. Transient demyelinating episodes have been described in central nervous system (CNS). We described a 13 year old boy with reversible central white matter lesions (WML) associated with demyelinating polyneuropathy. Case report: A 13-year-old boy was hospitalized because of two episodes of dysarthria and hemiparesia that lasted few hours each. They resolved spontaneously. MRI showed bilateral parietal WML with diffusion restriction. At physical examination symmetrical mild weakness in distal upper and lower limbs, hypotrophy in distal limbs and pes cavus were found. Reflexes were absent in lower limbs. He had familial story of distal weakness in mother and maternal grandmother. EMG was performed and sensory motor demyelinating polyneuropathy was confirmed. Metabolic analysis were negative (lactic acid in CSF, plasmatic aminoacids, urinary organic acids, VLCFA, aethylA and betagalactocerebrosidase). Molecular analysis confirmed mutation c.491G>A in exon2 of the GJB1 gene confirming connexine 32 associated polyneuropathy. Control MRI, six months later, showed spontaneous improvement of WML.

Conclusion: Acute CNS white matter lesions may be the presentation of a peripheral nervous system disease. Detailed physical examination could be the clue for diagnosis. Given the frequency of this disease we consider that connexine 32 molecular study should be requested in all males with CNS demyelinating polyneuropathy.

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Neuromuscular disorder

**ICNC-0704: Increased heterogeneity in T2-Relaxation times in the dystrophic soleus muscle**

Introduction: Quantitative MRI is gaining momentum as a possible outcome measure in clinical trials for neuromuscular diseases. Both inflammation and increased fat content result in a longer T2 relaxation time and different approaches of extracting the underlying disease activity have been proposed. Here we measure T2 in the soleus (SOL) and tibialis anterior (TA) muscles, using a tri-exponential fitting and analyze its relation with age.

Methods: Multiecho axial MR imaging (17 echoes, no fat suppression, 5 slices) of the right lower leg was performed at a 3T in 26 boys with DMD (mean age 10.1±2.8 years) and 12 age- and sex-matched controls (10.3±2.7 years). The muscle T2 was calculated voxelwise with a tri-exponential fit. Mean T2 and T2 heterogeneity (coefficient of variation) were calculated per muscle. In 5 patients MR-spectroscopy was added to the protocol.

Results: The mean T2 was higher in patients (SOL: 37.0±4.0ms vs. 35.3±1.2ms, TA 37.0±2.2ms vs. 35.4±1.2ms, no statistical significance). The T2 heterogeneity was significantly higher for the SOL of patients (7.5±4.3% vs. 4.3±1.1%, p=0.014) correlating positively with age (r^2=0.609, p<0.001). The T2 of the SOL measured using spectroscopy showed a correlation trend with the T2 from imaging.


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Neuromuscular disorder

**ICNC-0706: Clinical findings and long-term course in Selenoprotein N1-related myopathies (SEPN1-RM)**

Introduction: SEPN1-RM consists of patients who share key myopathic features including early axial hypotonia with dropped head, spine rigidity, and life-threatening respiratory failure. Methods: We reviewed clinical findings and long-term course of 14 patients (7 boys, 7 girls), retrospectively. Results: Fourteen patients from 12 families, aged 4-22 years, were evaluated over a mean follow-up period of 3.4 y (6 mo-9 y). The mean age at first symptoms, and referral to our clinic were 3.5 y (6mo-13y), and 8 y (2-14 y), respectively. Twelve patients had parental consanguinity. The most frequent presenting symptoms were failure to thrive (n=9), cervical weakness with head lag (n=6), motor developmental delay (n=5), scoliosis (n=4), and respiratory failure (n=3). The phenotype was compatible with rigid spine muscular dystrophy (RSMED) in 10 patients (70%) and, myopathy in the remaining. Body mass index was below 20kg/m2 in 12/14 patients. Muscle biopsy findings of 8 patients revealed myopathic changes with cores (n=4), nonspecific myopathic (n=3), and mild dystrophic changes (n=1). Ten patients required noninvasive ventilation (NIV), and 4 needed tracheostomy during follow-up. The mean age of NIV requirement was 9.8y (5-15y). Two of ten patients who developed scoliosis underwent spinal surgery. Two patients aged 12 and 18 years died from respiratory failure. Mutation analysis confirmed the diagnosis in all of the patients. Conclusions: Failure to thrive, asthenic phenotype, head lag, rigid spine deformity accompanying scoliosis...
are initial clues for SEPN1-RM. Early respiratory failure not proportional to degree of muscle weakness is a warning sign.

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Neuromuscular disorder

ICNC-0708: Neuropysiological evaluation of children with beta-Thalassemia Major
Introduction: Neural pathway involvement is considered to be a neurological complication in β-Thalassemia major (BTM). Objectives: This study is aimed to detect possible involvement of central and peripheral neural pathways in a group of neurologically asymptomatic patients with beta-thalassemia major. Subjects and Methods: It was carried out on 30 patients diagnosed as having BTM (group I). They were 14 males (46.7%) and 16 females (53.3%), and another 10 healthy children with a matched age and sex as a control group (group II). Serum ferritin and iron, glucose tolerance test, Intelligence Quotient test and Electroencephalogram (EEG) were assessed in BTM patients. Electrophysiological study was assessed in both patients and control. The mean age of the patients was 10.45±2.88 years. Results: The results of the present study showed that 66.7% of patients had subclinical sensory peripheral neuropathy. 20% of patients had abnormal Somatosensory evoked potentials. 63.3% of the studied patients had either low average or slow learner total IQ score. This is not correlating with age, disease duration, serum iron, and ferritin. 23 patients had mature EEG background activity, while 7 patients had immature background activity. One patient showed epileptiform discharge in the form of paroxysmal generalized slow waves. The EEG background maturity had significant correlation with age, duration of deferoxamine therapy and serum iron. There was no correlation between serum ferritin level with EEG and electrophysiological findings. Conclusions: Regular early electrophysiological monitoring and intellectual evaluation is recommended in order to detect relevant abnormalities and apply appropriate management.

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Neuromuscular disorder

ICNC-0709: Analysis of large deletions and duplications in dystrophin-gen in a south-america country
Backround: Duchenne muscular dystrophy (DMD), X-linked, is a progressive neuromuscular disease caused by mutation in the dystrophin-gen. International reports sign that 70-80% are large detions and duplications. No reports in south-america. The analyse of the type and frequency of mutations is a tool for diagnostics, scientific research, trial planning and treatment. AIM: to describe the type and frequency of mutations in the quantitative PCR-based technique of multiplex ligation-dependt probe amplification (MLPA) in dystrophin-gen in a south-america country. Patients and Method: male patients with mutations in MLPA of dystrophin-gen from 2010-2015. The genetic labotatory is the only taht process the test in the country. Results: 84 male patiendes with mutation in MLPA. 17 cases with large duplication (76% in Hotspot exon 2-20), most frecuent duplication are 4 case in Exon 2, 49 cases with large deletion(70% Hotspot 45-50 and 25% Hotspot 2-20). The most frecuenct deletions are Exon 48-50, 49-50 and 5-7 (6% from deletion respectively), different frequency to other reports. No deletion in Exon 45, the most frecuently in other report. The possible therapy with exon-skipping is applicable in Exon 51 (21% deletion), Exon 53 (13.4%) and Exon 45 and 44 (7.4 and 7.4% respectcibtely), similar to international reports. Conclusion: We find different frequency from in the most frecuent mutation in compare with another report. No report deletion in Exon 45, the most frecuent. We have the same frequency of patients who would benefit from exon-skipping therapy.

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Neuromuscular disorders

ICNC-0711: Safety and tolerability of Ataluren in a phase 3 study of patients with Nonsense Mutation Duchenne Muscular Dystrophy
Background: A randomized, double-blind, placebo-controlled Phase 2b study of ataluren in nonsense mutation Duchenne muscular dystrophy (nmDMD) reported that ataluren was generally well tolerated. Methods: In this Phase 3, Ataluren Confirmatory Trial in Duchenne Muscular Dystrophy (ACT DMD), multicenter study, males aged 7–16 years with nmDMD, baseline six-minute walk distance (6MWD) ≥150m and ≤80% of predicted, and steroid use ≥6 months were randomized 1:1 to ataluren, 10, 10, 20 mg/kg or placebo orally 3 times daily for 48 weeks. Results: 230 patients were randomized (ataluren, n=115; placebo, n=115). Demographics were well balanced across treatment arms. 96.1% of
patients completed the 48-week trial, and 97% of those continued in the extension study. 103 (89.6%) receiving ataluren and 100 (87.0%) receiving placebo experienced treatment-emergent adverse events (TEAEs). The most common TEAEs in the ataluren and placebo arms, respectively, were vomiting (22.6% and 18.3%), nasopharyngitis (20.9% and 19.1%), fall (19.1% and 17.4%), headache (18.3% for both), and cough (16.5% and 11.3%). Four patients in each arm had ≥1 serious adverse event (SAE): SAEs for ataluren were pneumonia/bronchiolitis (1 patient), pneumonia/post-traumatic pain (1 patient), tendon disorder (1 patient), and adenoidal/nasal turbinate hypertrophy (1 patient); none were considered ataluren-related by the investigator. One patient in each arm discontinued treatment due to TEAEs: 1 due to Grade 2 constipation considered possibly related to treatment (ataluren), and 1 due to loss of ambulation (placebo). Conclusions: Ataluren was generally well-tolerated by patients with nmDMD, and the spectrum and severity of adverse events was consistent with previous studies.

Study Supported By: PTC Therapeutics Inc.

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Neuromuscular disorder

ICNC-0714: Prominent skeletal muscle lipid storage in a child with a novel thymidine kinase 2 gene mutation
Prominent skeletal muscle lipid storage in a child with a novel thymidine kinase 2 (TK2) has been reported to cause a myopathic form of Mitochondrial DNA depletion syndrome (MDS), which is recessively inherited and manifests by severe skeletal myopathy in infancy. Histopathological findings on skeletal muscle include prominent fiber size variance resembling dystrophic features, ragged red fibers and cytochrome c oxidase (COX)-negative fibers are present, whereas electron microscopy shows abnormal mitochondria. Here we describe the clinical, pathologic and genetic findings in a child with isolated fatal skeletal myopathy. The one-year-old boy suffered from rapidly progress, acute onset muscular weakness, mildly elevated creatine kinase (701 IU/L, norm :25-195 IU/L) and lactate levels 4.13 mmol/L (Norm 0.5-2mmol/L, and he died of respiratory failure and bronchopneumonia at age 2 years old. The muscle biopsy showed prominent lipid storage without ragged red fibers, whereas electron microscopy confirmed the lipid storage with abnormal mitochondria. Sequence analysis of the TK2 gene revealed two heterozygous variants: one previously reported pathogenic mutation: 923A>G and one novel missense mutation: 673C>T, which transformed a stop codon to Trp (p.Ter208Trp), misleading the synthesis of a functional protein. This report extends the phenotype and genotype of TK2 defects.

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Neuromuscular disorder

ICNC-0715: Urinary Metabolomic Profiling of Acylcarnitine and Amino Acid Metabolism in Spinal Muscular Atrophy Types I, II and III
Background: Dysregulation of fatty acid oxidation and amino acid (AA) metabolism have been noticed in spinal muscular atrophy (SMA). This study evaluated the metabolomic profiling of acylcarnitines (ACNs) and AAs in SMA Methods: A total of 62 SMA patients, 4 type I, 24 type II, and 34 type III were examined. Thirty-five normal subjects were controls. And 37 ACN species and 12 AAs were analyzed from urine by tandem mass spectrometry. Results: Urinary levels of very long-chain ACNs (C16 to C18:1) were similar among the four groups. Long-chain to short-chain ACNs (except C8) were significantly lower in SMA types I and II, whereas only C4, C4-DC, C5, and C5:1 were also lower in SMA type III when compared to controls. AAs concentrations of valine, phenylalanine, methionine, and tyrosine were lower in SMA types I and II; arginine, citrulline and ornithine were lower in all SMA patients. We proposed impaired mitochondria beta oxidation and reduced AA catabolism in SMA patients. Importantly, we found that C4 could predict the SMA severity and its odds ratio (OR) was six-fold higher than others [OR=6.166, 95% CI (1.338-28.417), p<0.01]. Conclusions: Our study demonstrated impaired mitochondria beta oxidation and reduced AA catabolism in SMA type I, II and III patients. The urinary concentrations of C4 may serve as a novel biomarker for SMA.

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Neuromuscular disorder

**ICNCE0692: Bone Health In Steroid Treated Duchenne Muscular Dystrophy: A Regional Case Series**

Introduction Duchenne Muscular Dystrophy (DMD), the commonest form of muscular dystrophy, progresses to loss of ambulation and premature death. Since treatment with corticosteroids has become the 'standard of care' there have been increasing reports of an increase in often painful and debilitating long-bone and vertebral fractures, thought to be associated with steroid-induced osteoporosis. This project aims to describe the screening and management of bone health in a cohort of steroid treated DMD patients. Methods The data of fifty-four patients undergoing treatment for DMD over a 10 year period (2004-2015) in the South-West region of England were analysed and recorded. Results 68% of boys, with a mean age of 7 years, initiated a steroid regime before the study period. All had measurements of their bone biochemistry. 54% of boys have received a DEXA scan to date, with a mean BMD Total Body Less Head z score of -2.33. 13 boys have sustained a fracture. All received a prescription of vitamin D and calcium supplementation. 7 boys have received bisphosphonate therapy, with 4 self-reporting a reduction in bone pain. Conclusions This cohort is consistent with recent findings of a low BMD and high fracture rate in steroid-treated DMD patients. Proactive management of bone health is imperative to optimize quality of life in these patients. A central database would facilitate the production of evidence based guidelines for the optimal timing of DEXA screening and response to bisphosphonate treatment.

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Neuromuscular disorder

**ICNCE0718: The neuromuscular phenotype of shoulder deformities in CHARGE-Syndrome**

Introduction CHARGE syndrome is a rare congenital disorder (6 per 100,000 newborns), caused by mutations in the CHD7 (chromodomain helicase DNA binding protein 7) gene. CHD7 is a transcription regulator which interacts with homeobox genes during embryologic patterning of body segments and influences neural crest migration. CHARGE syndrome patients may thus present with neurodevelopmental crest, cerebellar, otologic and cranial nerve defects. Sparse reports have also described shoulder deformities, for which etiology and prevalence are unknown. We aimed to assess the neuromuscular phenotype of shoulder deformities in one of the largest CHARGE-patient cohorts. Materials and methods: In 37 CHARGE-patients (mean age 11.9 years; range 2.0-17.9), we neurologically evaluated shoulder anteverision, sloping, and scapular winging. In 14 CHARGE-patients and age-matched controls, we determined and compared muscle ultrasound density (MUD) of biceps (C5-6), quadriceps (L2-4) and tibial anterior (L4-S1) muscles. Results: 87% (32/37) of CHARGE-patients showed shoulder deformities, including: ante-version (n=32/32), sloping (n=21/32), winging (n=10/32) and abduction impairment (n=8/32). Interpretation of neurologic parameters reflected segmental involvement of shoulder and/or upper arm myotomes (mostly including C5). Comparing MUD-outcomes of biceps muscles (C5) revealed significantly higher outcomes in CHARGE patients than controls (p=0.007). All other investigated muscles revealed no significant differences. Conclusions: Shoulder deformities are common in CHARGE-syndrome, although rarely reported. Present findings appear suggestive for chronic segmental impairment of shoulder and upper arm myotomes. Considering the interaction of CHD7 with homeobox genes it is tempting to speculate that abnormal embryonic patterning may be the underlying pathogenetic mechanism.

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Neuromuscular disorder

**ICCNCE0719: A clinical point of view distinguishing juvenile immune-mediated necrotizing myopathies and Muscular dystrophy**

Abstract Immune-mediated necrotizing myopathies (IMNM)s are a subgroup of idiopathic inflammatory myopathies, and poorly recognized because its category had been established rather recently. Juvenile IMNMs sometimes mimic muscular dystrophy in clinical presentation. The most reliable diagnosis is muscle biopsy however it is sometimes difficult to distinguish IMNMs from muscular dystrophy. Therefore we performed retrospective analysis in 5 individuals who had been initially misdiagnosed as muscular dystrophy but determined later to have IMNMs after further evaluation, and
investigated manifestations in clinical features and diagnostic tests for suspect juvenile IMNMs. Illness onset speed were slow (3-6 months) or insidious (>6 month). All 5 patients had muscle weakness dominantly in proximal, high levels of serum creatine kinase (2000-13,000 U/L), fibrillation potentials and positive sharp waves in needle electromyography. Skeletal muscle MRI imaging of lower legs on STIR exhibited muscle edema and myofascitis. On muscle biopsy, consistent findings were necrotic and regenerating changes with minimum to mild inflammatory cellular infiltrations, and then we could not confirm the diagnosis of IMNMs only in their biopsy findings. Autoantibodies tests finally revealed their definite diagnosis, 2 patients had positive anti-SRP antibody and 3 patients had positive anti-HMGCT antibody. Our observation demonstrates that the comprehensive and detailed analysis of both clinical and laboratory findings could lead to the diagnosis of IMNMs. The findings of striking myofascitis based on MRI are helpful to distinguish juvenile IMNMs from muscular dystrophy. Since IMNMs are treatable disease, early and prompt diagnosis is highly recommended.

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Neuromuscular disorder

ICNC-0720: Gene mutation in DYNC1H1 responsible in one family for different phenotype; HMSN as well distal Spinal Muscular Atrophy with lower extremity predominance (SMA-LED)

Introduction: since 2010 the clinical phenotype of SMA-LED and DYNC1H1-gene mutations is described in the literature. The spectrum of the DYNC1H1 mutations is broadening and gives a possible explanation for the different phenotypes found in families carrying this mutation. Case: The indexpatient was born in 1993 and seen 3 months postnatal because of areflexia. Her cognitive and fine motor skill development were typical. At age 1 she was a shuffler. At age 4 she had atrophic calves and areflexia, walked without support, broadbased with pes valgus. Clinical diagnosis was SMA type 3. After Grice arthrodesis at age 8 an unsupported waddling gait rested. Since age 14 she was wheelchair bound, with predominantly paresis of the legs. Nowadays she is a wheelchair bound young adult with normal cognitive development, managing transfers 5-10 meter. Family history showed SMA and Hereditary Motor and Sensory Neuropathy (HMSN) as changing clinical diagnosis of her mother and grandfather. They were wheelchair bound due to paresis of hands and legs. Diagnostics: SMN gene and HMSN-1 gene showed no deletion. EMG showed neurogenic abnormalities at age 3 and at age 10 repeated EMG showed normal motor velocity, absent H-reflex and myography with broadened high voltaged motor Unit Potentials (MUP’s). Muscle biopsy was not conclusive. In 2014 Next Generation Sequencing (NGS) with HMSN panel was done in the mother. The mutation found in the DYNC1H1 gene c:1792C>T(p.Arg598Cys, Ref. NM_001376.4) was also found in our index case. Discussion: DYNC1H1-gene variants are discussed in relation to motor neuron diseases.

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Neuromuscular disorders

ICNC-0721: Chemotherapy induced peripheral neuropathy among survivors of childhood acute lymphoblastic leukemia

Introduction: Chemotherapy induced peripheral neuropathy (CIPN) is one of the most common neurological complication in cancer treatment. The aims of this study were to determine the prevalence of CIPN in survivors of childhood acute lymphoblastic leukemia (ALL) who were on the MASPORE-ALL 2003 protocol and its long term impact on motor function status and quality of life (QoL). Method: 174 ALL survivors on regular follow up in our tertiary centre from the MASPORE-ALL 2003 registry were identified and the chemotherapy data were collected. Of these, 101 survivors aged 4-18 who had at least 2 years post-completion of chemotherapy were recruited. CIPN evaluation was performed via the modified Total Peripheral Neuropathy Score (mTNS) and nerve conduction studies (NCS). Motor functional impact and QoL were assessed using the Bruininks-Oseretsky test of Motor Proficiency (BOT-2) and PedsQL4.0. Results: The prevalence of mTNS and NCS defined CIPN were 26.7% and 65.3% respectively. 12.9% of the survivors had BOT-2 performance below average for age. All survivors with mTNS defined CIPN had mild neurological symptoms and no significant correlation in motor function status and QoL. NCS defined CIPD was significantly associated with the higher risk protocols as compared to the standard risk MASPORE-ALL 2003 protocol (OR 3.4; 95% CI: 1.4-8.2). However CIPN among ALL survivors had no significant impact on either motor function or QoL. Conclusion: CIPN is prevalent among MASPORE-ALL 2003 survivors with the risk of CIPN increased in survivors who had received the higher risk protocol. The motor function status and QoL were not affected by the presence of CIPN among the survivors. This reassuring long-term results is invaluable when counselling of potential CIPN side-effects when treating patients with ALL.
Neuromuscular disorders

Neuromuscular disorder

**ICN0723: A case of primary Hypokalemic Paralysis in a male child**

Introduction: Primary Hypokalemic paralysis is a form of metabolic myopathy, which represents a heterogeneous group of disorder characterized by hypokalemia, acute flaccid paralysis. It can be a primary disorder, which may be familial with autosomal-dominant inheritance or sporadic, or may be secondary with causes like renal tubular acidosis, thyrotoxic periodic paralysis, primary hyperaldosteronism, Gitelman syndrome, barium poisoning, and diarrhea. Case: A 12-year-old male child presented with loose motion for 1 day, and acute, non-progressive weakness of both upper and lower limb since last four hours. Both the upper and lower limb was affected. He had no history of similar illness in the past. There was no history of poliuria, recurrent UTI or similar complaints in the family. The patient reported that eating meals high in carbohydrates a day before. Motor system showed normal bulk of the muscles, reduced tone in all four limbs, power 1/5 in all limbs, normal superficial reflexes, absent deep tendon reflexes. Laboratory investigations showed low potassium 1.8 meq/l. Secondary causes such as renal tubular acidosis, thyrotoxic periodic paralysis, primary hyperaldosteronism, drug abuse or intoxication, and diarrhea were excluded. The child was treated with intravenous potassium.

Primary Hypokalemic paralysis was diagnosed based on clinical and biochemical parameters.

Conclusion: Primary Hypokalemic paralysis is a rare medical emergency. It should be included in the differential diagnosis of acute-onset muscle weakness in all ages.

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Neuromuscular disorder

**ICN0724: ACT DMD: Effect of ataluren on timed function tests in nonsense Mutation Duchenne Muscular Dystrophy**

Background: Ataluren is the first drug to treat the underlying cause of nonsense mutation Duchenne muscular dystrophy (nmDMD) by promoting readthrough of a premature stop codon to produce full-length functional dystrophin. Methods: ACT DMD (Ataluren Confirmatory Trial in Duchenne Muscular Dystrophy) is a Phase 3, randomized, double-blind study. Males 7–16 years with nmDMD and a screening six-minute walk distance (6MWD) ≥150m and <80%-predicted were randomized to ataluren 40 mg/kg/day or placebo for 48 weeks. A pre-specified subgroup included patients with baseline 6MWD 300–400m. Secondary endpoints included 10-meter walk/run, 4-stair climb, 4-stair descend. A meta-analysis of the overall ACT DMD population and the ‘ambulatory decline phase’ subgroup of the Phase 2b study (those patients meeting ACT DMD entry criteria) was pre-specified in the ACT DMD statistical plan. Results: In the overall ACT DMD population (N=228), changes in TFTs favored ataluren over placebo: 10-meter walk/run, -1.2s (p=0.117); 4-stair climb, -1.8s (p=0.058); 4-stair descend, -1.8s (p=0.012). In the pre-specified subgroup (n=99), these differences increased to -2.1s, -3.6s, and -4.3s, respectively, and were statistically significant for 4-stair climb (p=0.003) and 4-stair descend (p=0.001), and approached significance for 10-meter walk/run (p=0.066). Results are supported by the meta-analysis (N=291), which demonstrated significant differences in TFTs: 10-meter walk/run, -1.4s (p=0.025); 4-stair climb, -1.6s (p=0.018); 4-stair descend, -2.0s (p=0.004). Conclusions: TFT results showed a benefit for ataluren in ACT DMD, and a larger treatment effect in the pre-specified baseline 6MWD 300–400m subgroup as well as the pre-specified meta-analysis of ACT DMD and the Phase 2b study decline subgroup. Study Supported By: PTC Therapeutics Inc.

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Neuromuscular disorders

ICNC-0726: Clinical profile of Hereditary Sensory Autonomic Neuropathy Type IV (HSAN)

Introduction: Hereditary sensory autonomic neuropathies are a rare group of genetic disorders characterized by congenital insensitivity to pain, temperature changes and autonomic nerve formation disorders. HSAN IV is inherited as autosomal recessive trait characterized by lack of temperature and pain sensation. Methods: This is a retrospective chart review of all HSAN cases managed at tertiary care pediatric teaching hospital. A detailed history, examination and relevant instigations were carried out. Results: A total of 8 children analyzed all of who were girls with mean age of presentation 3 years. History of Consanguineous marriages was seen in 4/8 (50%). Presenting symptoms were developmental delay, difficulty in walking, self mutilation, absent of sweating, temper tantrums and high body temperature in all children. Breath holding spells in 4/8 (50%) and teeth amputation in 3/8 (37.5%) are noted. Examination shows pallor, bald tongue and non healing ulcers in all children. Other features seen were osteomyelitis and epilepsy in one case each. Discussion and conclusion: Very few conditions mimic HSAN type IV in the form of loss of pain and self mutilation. They are Lesch-Nyhan syndrome, Tourette syndrome, De Lange syndrome. A classical history of high body temperature on exposure to sunlight, behavioral problems, lack of pain, non healing ulcers on foot and Anhidrosis should prompt the diagnosis and avoids extensive investigations.

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Neuromuscular disorders

ICNC-0727: Cohort of Neurometabolic Disorders at a tertiary care children hospital from South India

Introduction: Neurometabolic disorders are a group of disorders that mainly present in newborn and infants. Neurological symptoms/ signs predominate in this group. Objective of our study is to find out pattern of Neurometabolic disorders in South India. Methods: This is a retrospective chart review in the department of pediatric neurology at a tertiary care hospital between September 2012 and August 2015. Results: A total of 16109 children were included over a study period of 4 years. Age group included 1 day to 16 year old. A total 5540 (34.39%) cases were suspected as IEM based on history and examination. On investigations a total of 683 (4.23%) patients had Neurometabolic disorders. Out of 683 patients, complex molecular disorders in 348 (50.95%), small molecule disorders in 216 (31.62%), mitochondrial disorders 69 (10.10%) and miscellaneous 50 (7.32%). In the complex molecular disorders, lysosomal disorders in 96.5% and peroxisomal disorders in 3.5% were noted. In the lysosomal disorders, mucopolysacharidosis (35.3%), GM1 Gangliosidosis and Taysach’s disease each 17.5% each, Niemann-Pick disease 8.9%, metachromatic leukodystrophy 10.4% and others. In the Peroxisomal disorders adrenoleukodystrophy in 83.3% and Zellweger in 16.6%. Among small molecular disorders, aminoacidopaties 86 (39.81%), organic acidurias 80 (37%), urea cycle disorders 22 (10.1%) and disorders of energy molecules 28 (12.9%). In aminoacidopathies most common are phenylketonuria 55, maple syrup urine disease 20, homocysteinurias- 8 and others 3. In organic acidurias, glutaric aciduria 31, biotinidase deficiency 25, methyl melonic and ethyl melonic acidemias 17 and others 7. In urea cycle disorder most common is arginase deficiency. In disorders of energy metabolism common disorders observed were glycogen storage disorders-17 and fatty acid oxidation defects-11. In mitochondrial disorder common diseases were Leigh’s disease 50 (72.4%) followed by MELAS-7. Discussion and conclusion: There is a lack of data about different types of Neurometabolic disorders seen in Indian subcontinent. Our study tries to describe these heterogeneous groups of disorders. These are not very rare as our study shows 4.23% of neurology patients had Neurometabolic disorders.

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Neuromuscular disorder

ICNC-0728: Next generation sequencing (NGS) and Muscle MRI: a powerful tools for studying Rigid spine patients and multiminicore myopathy

Introduction: The selenoprotein N gene (SEPN1) is related to different forms of myopathies including dystrophy with rigid spine (MDRS) multiminicore myopathy, myopathy with fiber type disproportion, myopathy associated with desmin accumulation and myopathy with inclusions type Mallory body. Here we evaluate the presence of mutations in the SEPN1 gene and other neuromuscular genes, in brazilian patients with these phenotypes, using Sangers’ and next generation sequencing (NGS). Methodology: Patients with myopathy related to SEPN1 were submitted to clinical evaluation, CPK, ENMG, muscle biopsy with histochemistry and muscle MRI analyses. DNA study was performed through SANGER sequencing for the SEPN1 gene and using a next generation sequencing customized panel for 88 genes involved in neuromuscular disorders (Illumina). Results: We evaluated twelve patients from ten unrelated families: 8 were classified with MDRS, 3 patients with myopathy multiminicore and one patient with congenital fiber disproportion.
The molecular analysis revealed pathogenic SEPN1 mutations in 4 families (c.T1384G, c.713-14insA, c.1406G>A, c.1397G>A and novel c. G1010T ). In the patient 1 who was heterozygous compound for c. T1384G and the novel c. G1010T S mutations the muscle MRI showed changes compatible with the pattern of SEPN1. One patient with rigid spine phenotype showed a known mutation in the COL6A1 gene and muscle MRI compatible with COL6 pattern. A second one withmultiminicore myopathy was a compound heterozygous for 2 novel germlins mutations in the COL6A3 gene. In three siblings we found two compound heterozygous mutations in LAMA2 (one novel mutation p.P418frs) and muscle MRI compatible with this gene pattern. Conclusion: Myopathies related to selenoprotein N have a broad clinical phenotype and histology and the rigid spine phenotype and multiminicore myopathy can be related to different genes. The use of NGS panel could confirm mutations in SEPN1 (4 patients) and also is helpful for identifying mutations in others neuromuscular genes. Supported by CNPQ and FAFEMIG.

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Neuromuscular disorder

ICNC-0729: Pompe’s Disease initially diagnosed as central core Myopathy based on muscle biopsy

INTRODUCTION: We present a case of Pompe's Disease which was initially diagnosed as Central Core Myopathy. Due to a clinical course inconsistent with this diagnosis, a muscle biopsy was repeated, revealing the diagnosis of Pompe's Disease. CASE DESCRIPTION: A 17-year-old female was referred for diffuse myaligias and creatine kinase levels up to 2,000 U/L. Her symptoms consisted of diffuse progressive pain with functional decline. She had a normal developmental history and neuromuscular exam. RESULTS: Magnetic resonance imaging of the thighs showed evidence of myositis. Evaluation for systemic and autoimmune disease was unremarkable. Muscle biopsy showed type 1 fiber predominance and central core formation consistent with central core myopathy. Mild focal myofiber glycogen was noted on electron microscopy but no increase in glycogen content was seen with staining. Genetic testing revealed a variant of unclear significance in the RYR1 gene. Due to the inconsistency in her course with this diagnosis, a second muscle biopsy was performed with results consistent with Pompe's disease; diagnosis was confirmed by showing reduced acid alpha-glucosidase activity. CONCLUSION: This is a case of Pompe's disease misdiagnosed based on biopsy features suggestive of central core disease. While both diagnoses may co-occur, treatment with enzyme replacement infusions was delayed due to acceptance of the initial diagnosis. Although histopathology is often confirmatory for the diagnosis of muscular disease, inconsistent clinical features should alert the physician to conduct further investigations to ensure that timely treatment is provided.

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Neuromuscular disorder

ICNC-0730: Guillain–Barré syndrome with hyperreflexia and bilateral papillitis in a child

Introduction: Guillain–Barré syndrome (GBS) is an acute inflammatory polyneuropathy characterized by rapidly progressive, symmetric weakness, and areflexia. Areflexia is necessary for the diagnosis of GBS. However, recently there have been rarely studies of hyperreflexia with axonal neuropathy form of GBS. Case Description: A 14-year-old male patient was admitted to our hospital with sudden onset loss of vision, numbness, and weakness of the legs and the arms. On examination, he had bilateral papillitis, his muscle strength was graded as 4/5 in the bilaterally distal muscles including the arms and legs symmetrically. Deep tendon reflexes were brisk in all extremities without spasticity. Conclusion: Hyperactive deep tendon reflexes are rare in GBS does not exclude the diagnosis. Therefore, the nerve conduction studies should be performed for evaluation to confirm the diagnosis of GBS.

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Neuromuscular disorder

ICNC-0733: Co-occurrence of Familial Exudative Vitreoretinopathy and Spinal Muscular Atrophy

Introduction: Spinal muscular atrophy (SMA) is characterized by degeneration of the anterior motor neuron in the spinal cord and the motor nuclei of the brain stem. The incidence of SMA is about 4 to 10 per 100,000 live births. SMA is caused by mutation or deletion on survival of motor neuron 1 (SMN1) gene. Those patients usually present with generalized muscle weakness and atrophy. However, ophthalmological presentation of SMA is rarely reported. Familial
Neuromuscular disorders

exudative vitreoretinopathy (FEVR) is a rare hereditary disorder characterized by the failure of peripheral retinal vascularization. Case Report: This 3-year-old boy had no perinatal insult, respiratory distress or muscle weakness at birth. Smaller size of right eye was found and FEVR was diagnosed by eye ground examination at 8 months old. Genetic analysis also confirmed frizzled class receptor 4 (FZD4) gene mutation. Vitrectomy was performed due to tractional retinal detachment over his right eye. His mother and elder brother were also diagnosed FEVR but they were both asymptomatic. Besides, the patient had motor delay since early infancy and prominent muscle weakness developed since about 18 months old. SMA was diagnosed by genetic study (SMN1:SMN2 = 0:3) at 2 years old. Conclusion: SMA and FEVR are both rare disease and the co-occurrence of these two diseases is extremely rare. Only one similar case report is published before (Eur J Ophthalmol 2015;25:e116). Further molecular pathemechanism analysis may be helpful to elucidate the relationship between SMA and FEVR.

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Neuromuscular disorder
ICNC-0734: Chronic inflammatory demyelinating polyradiculoneuropathy in children: Treatment and outcome with literature review
Background: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a clinically heterogeneous group of sensory and motor peripheral neuropathy, presumed to occur due to immune related reactions. Because childhood CIDP is very rare, there are very few published studies to help clinicians in treating refractory cases. Aim of this study is to investigate the clinical features and treatment outcome. Methods: 10 pediatric patients who were diagnosed as either probable or definite CIDP according to EFNS/PNS criteria with sufficiently documented clinical data with follow up period of at least 12 months were enrolled. We reviewed the clinical features and treatment response of 10 patients retrospectively. The functional status of the patient was evaluated from the clinical report according to the modified Rankin scale. Results: The most common chief complaint was weakness in the lower extremities. The disease course was monophasic in 2 patients, relapsing-remitting in 6 patients and progressive in 2 patients. IVIG (intravenous immunoglobulin) treatment was used in all patients and steroid was given in 8, plasmapheresis in 9 patients. Five patients, who were considered refractory to conventional therapy, received additional immunosuppressant therapy with cyclosporine or azathioprine. Monophasic CIDP patients responded well to any of the first line treatment. Progressive CIDP patients responded well to plasmapheresis compared to IVIG. Adding cyclosporine in refractory cases of relapsing-remitting type CIDP increased relapse free period significantly. None had serious adverse effects caused by cyclosporine therapy. Conclusion: We conclude that treatment response may differ depending on clinical course of CIDP and cyclosporine is a relatively safe and effective therapeutic option in refractory cases of relapsing-remitting type of CIDP.

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Neuromuscular disorder
ICNC-0735: Hirayama Disease (monomelic amyotrophy); case report
INTRODUCTION: “Hirayama Disease” was first defined by Hirayama and friends in 1959. The disease is characterized by slowly progressing muscle weakness and atrophy in hands and underarm. No sensory disorder is seen or it remains in the background compared to motor symptoms or signs. This paper presents a case of a 16-year-old patient who is monitored in the paediatric neurology clinic with Hirayama Disease diagnosis. CASE REPORT: The 16-years-old male patient applied to hospital with complaints of weakness and wasting of the right hand. There was no preceding illness, trauma, exposure to toxins or family history. Clinical examination revealed moderate to severe atrophy of tenar muscles of the right hand. Remaining system examinations were normal. No specialities were reported in the laboratory examinations. EMG showed low right median nerve motor amplitude whereas sensory examinations were normal. The patient was diagnosed with Hirayama Disease and is followed up with ambulatory treatment at the paediatric neurology polyclinic. CONCLUSIONS: Hirayama Disease is defined ischemic deformations, caused by spinal anterior horn deformation, especially resulting from spinal strengthening during excessive anterior displacement of the dural sac during neck flexion. In the treatment, spinal decompression methods have been identified to hinder progression. Exercises and activities demanding excessive arm and neck movements as well as giving neck protectors restricting movement is seen sufficient for most of the patients. Although the patients have tenar muscle atrophy, no sensory or function loss occurs. Tenar atrophy limits itself within 2-5 years. There is no definite treatment method.

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Neuromuscular disorder

ICNC-0737: Collagen VI related muscle disorder – previously unreported mutation
We report a case of a 3 year old girl who presented with gait difficulties, frequent falling and delayed motor milestones. Clinically she had proximal muscle weakness without facial weakness, difficulties in climbing stairs, Gower’s maneuver, distal hyperlaxity, pronounced lumbar lordosis, no contractures and no respiratory involvement. She also had discrete skin changes in terms of follicular hyperkeratosis. Symptoms were present from birth but overlooked as hypotonia with mild motor developmental delay. There was no previous neurological evaluation.Neuro muscular disease was suspected and diagnostic work-up showed slightly elevated creatine kinase level, myopathic electromyoneurography with normal nerve conduction study.Clinical presentation suggested collagen VI related muscle disorder and COL6A1 sequencing was performed. Previously unreported heterozygous pathogenic variant in exon 8 of the gene, c.769G>T (p.Gly257*) was found. It creates a premature stop codon. Family history is negative and parental carrier testing is planned to establish whether this pathogenic variant is de novo or inherited. To date, this mutation variant was not described in the Exome Sequencing Project or the 1000 Genomes Browser.

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Neuromuscular disorder

ICNC-0738: Fetal acetylcholine receptor inactivation syndrome: case report
Introduction: The term “fetal acetylcholine receptor (AChRs) inactivation syndrome” was proposed by M.Oskouli (2008) for the description of a typical phenotype of the child, who was born from mother suffering from autoimmune myasthenia with high levels of antibodies to fetal AChRs. This phenotype includes facial diplegia, highly arched palate, velopharyngeal incompetence and conductive hearing loss. Case report: A 38-year-old woman has suffered from generalized myasthenia for the last 14 years. The level of AChR Ab is more than 5.0 nmol/l (normal<0.4). She had four pregnancies and she was treated with pyridostigmine alone. The first child was born healthy. The second one (our patient) had hypotonia, poor suck, inability to swallow and respiratory failure requiring mechanical ventilation for 6 days after birth. The facial weakness and highly arched palate was observed since the first days of her life. By the age of 4 the girl has no progressive facial diplegia with inability to close her mouth or eyes completely, hypernasal poorly intelligible speech. Brain MRI, serum CK, AChR Ab and repetitive median and accessory nerve stimulation at 3 Hz are normal. The third pregnancy was unsuccessful (miscarriage at 7-8 weeks). The child from the fourth pregnancy was born with severe hypotonia and died of a respiratory failure on the 18th day. Conclusion. In our case, we could not determine the antibodies to fetal AChRs in the mother. However a typical phenotype, signs of transient neonatal myasthenia in two children, a spontaneous miscarriage may indirectly point at a high level of these antibodies.

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Neuromuscular disorder

ICNC-0739: Ataluren: An overview of clinical trial results in Nonsense Mutation Duchenne Muscular Dystrophy (nmDMD)
Background: Ataluren is the first drug to treat the underlying cause of nmDMD. It enables ribosomal readthrough of a premature stop codon to produce full-length functional dystrophin, without affecting normal stop codons. Methods: Phase 2 and 3 studies of ataluren in nmDMD were reviewed, with efficacy and safety/tolerability findings summarized. Results: Ataluren nmDMD trials include: a Phase 2a proof-of-concept study (N=38)whose primary endpoint was dystrophin expression following 28 days of treatment; a Phase 2b randomized controlled trial (RCT) (N=174); an ongoing US-based open-label safety extension study (N=108); an ongoing non-US-based open-label safety/efficacy extension study (N=94); and a Phase 3 RCT, ACT DMD (N=228), whose primary endpoint was change in 6MWD over 48 weeks. The proof-of-concept study demonstrated increased dystrophin production in post-treatment muscle biopsies from ataluren-treated patients with nmDMD. The Phase 2b results demonstrated an ataluren treatment effect in 6MWD, timed function tests, and other measures of physical functioning, with larger treatment effects in patients at higher risk of ambulatory decline. This study was the basis for ataluren’s approval in the European Union. The Phase 3 ACT DMD results demonstrated an ataluren treatment effect in patients with nmDMD in both primary and secondary endpoints, particularly in those with a baseline 6MWD of 300–400m. Ataluren was consistently well-tolerated in all three trials, as well as in the ongoing extension studies. Trial findings will be presented in detail. Conclusions: The totality of the results demonstrates that ataluren enables nonsense mutation readthrough in the dystrophin mRNA, producing functional dystrophin and slowing disease progression. Study Supported By: PTC Therapeutics Inc.
Neuromuscular disorders

ICNC-0740: Use of the six-minute walk distance (6MWD) across Duchenne Muscular Dystrophy (DMD) studies

Background: 6MWD is a validated endpoint for ambulatory DMD studies, used in trials of ataluren, drisapersen, tadafil, and eteplirsen. Decline in 6MWD is predictive of disease progression, time to loss-of-ambulation, and subsequent disease milestones. 6MWT Inclusion criteria have been tightened, thereby excluding patients with near-normal or severely affected walking abilities. Methods: Recent studies were reviewed to determine how the 6MWT has evolved as a sensitive clinical endpoint. Results: 6MWT inclusion criteria for DMD studies have evolved from the original criteria of 75m with no ceiling value for the first two trials initiated in 2008. These baseline 6MWT criteria have narrowed to a floor value as high as 300m for the eteplirsen open-label phase III study (Sarepta 4658-301 initiated 2015) and ceiling values as low as 400m in the tadafil phase III trial (Eli Lilly H6D-MC-LVJJ initiated 2013). The Phase 3 ataluren study (ACT DMD; initiated 2013) included patients with a baseline ≥150m and <80% predicted, with a pre-specified subgroup of 300-400m baseline. In the ACT DMD study, the benefit of ataluren over placebo observed in the overall population (48-week difference=15m; p=0.213) was enhanced in the pre-specified 300-400m subgroup (47m; p=0.007). Sensitivity analyses confirmed an ataluren effect with 6MWD ≥250 to <400m (29.5m; p=0.035); ≥200 to <400m (26.6m; p=0.0501); and ≥300 to <450m (24.4m; p=0.0501). Conclusions: When evaluating drugs expected to slow disease progression, narrower 6MWD ranges are used as inclusion criteria. For ataluren, a pre-specified range of 300–400m demonstrated the greatest treatment effect. Meaningful effects were seen with 6MWD from 200-450m. Study Supported By: PTC Therapeutics Inc.

ICNC-0741: Genetically unconfirmed diagnosis of spinal muscular atrophy, type 1. Clinical case

Background: The frequency of SMA is 1 in 6000-10 000 newborns. Over 95% of patients with I–III variants of SMA have the deletion of the 7th and/or 8th exon of the telomeric copy of the SMN gene in the homozygous state. Methods: A clinical case of SMA type 1 is given on the example of one patient. Clinical, neurological, genetic and instrumental studies were conducted. Results: boy, 6 months, with complaints about the absence of sucking, swallowing, movements in extremities. The child was born at 33 weeks of pregnancy. In 2 months, decrease in motor activity in the lower extremities. In 2.5 months, weakness of the lower limbs, loss of acquired skills, the disappearance of the head fixation. In 3.5 months the reduction of the sucking reflex, which completely disappeared in 4 months, and atrophic changes of the lower extremities. Neurological status: Total areflexia, atonia, atrophy. Blood tests for the main spectrum of SMA, mutations associated with X-linked variant of the SMA, mutation in the gene responsible for the formation of SMA with diaphragm paralysis type 1: mutations have not been identified. A blood test for Pompe disease: negative. A blood test for TSM: no pathology. Echocardiography: signs of hypertrophic cardiomyopathy. Brain and spinal cord MRI: without pathology. EMG: signs of a lesion of the peripheral motor neuron. Muscle biopsy: typical for SMA type 1. Conclusions: the Clinical picture typical for SMA type 1. The case has not been confirmed genetically, that requires further examination and differential diagnosis.

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Neuromuscular disorder

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ICNC-0742: Malignant course of myasthenia gravis at early age child. Clinical case
Background: Myasthenia gravis in childhood occurs in 4 clinical forms: neonatal myasthenia gravis (transient), congenital (CMG), early children and juvenile (JMG). The frequency of JMG is 1 in 10,000 and CMG is 1 in 500,000. Methods: Clinical case of myasthenia gravis at early age child. Clinical, neurological, laboratory and instrumental studies were conducted. Results: a little girl, 1 year 10 months, admitted with complaints about drooping of both eyelids (ptosis), double vision (diplopia), weakness, fatigue. Perinatal anamnesis: IUP 30 wks, intrauterine hypoxic damage, cesarean section. Weight at birth 970 g, growth 36 cm. NICU care: 2 mo. Ventilation care – 1 day. O2 therapy – 1 mno. 1 month of life; prenatal pneumonia, severe form; retinopathy of premature 1-2 degree. 4 month: aspiration pneumonia, severe form. 7 month: myasthenia, generalized form; bulbar syndrome. 9 month: myasthenia, myasthenic crisis. 12 month: myasthenia, myasthenic crisis; ICU care with ventilation, intubation - 11 days. Neurological status: Bilateral ptosis, ophthalmoplegia. No facial dysmorphism. Muscle hypotonia. Muscle strength 4-4.5 points. Tendon reflexes are caused, symmetric. Coordination and balance - normal. EMG: signs of violation of neuromuscular transmission type decrement (myasthenic type). Neostigmine test: weakly positive. CT scan of the chest: thymomegally 1-2 degree. Antibodies to ACR: positively 6,566 nmol/L (N 0-0,500). Brain MRI: hyperintense signal in the periventricular frontal and occipital white matter areas. Conclusions: The case requires a differential diagnosis between juvenile myasthenia gravis, congenital myasthenia gravis and myasthenic syndromes. Generalized or ocular form? Genetic studies planned to clarify the diagnosis.

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Neuromuscular disorders

ICNC-0746: A novel homozygous mutation in PRDM12 gene causing Hereditary Sensory Autonomic Neuropathy type VIII
Introduction: Hereditary sensory and autonomic neuropathy (HSAN) type VIII is a recently described rare recessively inherited disorder caused due to homozygous mutations in PRDM 12 gene located on chromosome 9q34.12. (1) We describe a novel homozygous mutation in PRDM12 gene causing HSAN-VIII. Case Description: A 20-month-old boy, born to consanguineous muslim parents presented to us with global delay, and insensitivity to pain and temperature noticed since early infancy. He never experienced any pain and perceived any difference in temperature. There was no history of episodes of hyperthermia, anhidrosis, flushing of any part of body, absence of tears or behavior abnormalities. Examination, he had a normal head circumference, dolicocephalic head, subtle dysmorphism – frontal bossing and deep set eyes. A cleft was seen in lower lip and anterior portion of tongue, with preserved fungiform papillae. (Figure A) Neurological examination revealed distal hypotonia with absent superficial and deep tendon reflexes, generalized absence of response to pain and temperature. Clinical possibility of HSAN was considered. His hematological and biochemical profile were normal, serum uric acid was 5.2 mg/dL (range 4-8 mg/dL). Electrophysiological studies revealed absent sensory nerve action potentials. Motor nerve conduction study and concentric needle EMG were normal. MRI Brain was unremarkable. Parents refused for skin biopsy and nerve biopsy. Result: Next-generation-sequencing of pain related genes (ATL1, ATL3, DNMT1, RAB7A, SPTLC1, SPTLC2 (HSAN 1); WNK1/HSN2, FAM134B, KIF1A (HSAN2); IKBKAP (HSAN3); NTRK1, NGF (HSAN4/5); DST (HSAN6); PRDM12 (HSAN8), SCN9A and SCN11A) revealed a homozygous canonical splice-site mutation in PRDM12 (OMIM #616488, Transcript NM_021619), c.224-2A>G (hg19: Chr:9:133,541,993). Both the parents were heterozygous carriers of the splice-site mutation. Based on the clinical and genetic analysis a diagnosis of HSAN type-VIII was made. Pre-natal diagnosis for prevention of recurrence in subsequent pregnancies has been recommended to the parents. Conclusion: Our case highlights a novel PRDM12 mutation causing HSAN type-VIII, presenting as early-onset, autosomal-recessive sensory polyneuropathy, congenital insensitivity to pain, touch and temperature, global delay and early loss of muscle stretch reflexes. Such presentations should be kept in mind while evaluating children with pain-insensitivity and self-mutilation behavior. Acknowledgments: Martin Voigt from the Institute of Human Genetics, Jena University Hospital, 07743 Jena, Germany for helping Dr Ingo Kurth with the genetic analysis of the patient. References: 1. Chen Y C., Auer-Grumbach M, Matsukawa S et al. Transcriptional regulator PRDM12 is essential for human pain perception. Nature Genet. 47: 803-808, 2015.

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Neuromuscular disorder

ICNC-0747: Severe congenital multiple arthrogryposis due to mutation in MYH7 gene

MNR, 3 years old female. Second child of a non-consanguineous couple. It was detected a prenatal diagnosis of arthrogryposis by morphological ultrasound. Mother advises that noticed little fetal movement. At birth it was noted multiple arthrogryposis of shoulders, elbows, wrists, hips, knees and ankles. She had normal intellectual development but with delay of motor milestones, sitting alone with about 1 years but crawling with difficulty and unable to stand up. It presents muscular weakness in the 4 members, areflexia and overall muscle atrophy. Electromyography showed myopathic pattern and the doppler echocardiogram was normal. Whole exome sequencing showed a heterozygous mutation in the gene MYH7 (myosin, heavy chain 7, cardiac muscle, beta) that promotes the substitution of arginine for histidine at position 108 (p.Arg108His) and is absent from about 61 thousand brazilian and foreign subjects. It has never been previously reported in the literature. Sanger sequencing was performed and the presence of the variant in p.Arg108His patient was confirmed and the same mutations were absent in their progenitors, suggesting that de novo mutation. Pathogenic variants in the gene in heterozygous MYH7 have been associated with myopathy, cardiomyopathy and hypertrophic dilated cardiomyopathy. The occurrence of arthrogryposis has been reported with deleterious variants in other genes family myosin (MYH3 and MYH8) but not in MYH7.

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Neuromuscular disorder

ICNC-0748: Hereditary neuropathies

Introduction: Hereditary neuropathies are common neuromuscular diseases (about 30 / 100,000); clinical manifestations usually start in the first decade of life and are underdiagnosed in pediatric age (only 7%). The demyelinating diseases are more prevalent than the axonal neuropathies. The most common genetic finding is the duplication of the PMP22 gene. Methods: Retrospective analysis of clinical aspects and genetic investigations of pediatric patients followed in Hospital Santo Antônio, Porto, during the last 20 years. Results: 420 patients were observed during this period and 28 have a hereditary neuropathy. The age of onset varied between 1 and 13 years. Age at diagnosis ranged from 2 to 16 years. Fifteen patients were males and 13 females. Twenty-one patients had a demyelinating neuropathy; 11 had PMP22 gene duplication (CMT1A), two had a mutation in the MPZ gene (CMT1B) and one a mutation in the connexin gene (CMTX1). One patient had an axonal neuropathy with a mutation in the MFN2 (CMT2A2) gene. Three patients with a demyelinating neuropathy, two of them brothers with an autosomal dominant history, but without duplication or point mutations in the PMP22, MPZ or LITAF genes were identified. In all cases, the symptoms were predominantly distal and in the lower limbs. Six patients did not have an autonomous march and one of them was under noninvasive ventilation. Conclusion: Genetic heterogeneity was identified in our group of patients although CMT1A mutations were the most frequent molecular finding. In a group of patients it was not possible to identify the genetic defect.

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Neuromuscular disorder

ICNC-0750: Severe childhood Guillain-Barré Syndrome associated with a Mycoplasma Pneumoniae Infection: a case series

Guillain-Barré syndrome (GBS) is one of the most severe extrapulmonary complications of infections with the respiratory pathogen Mycoplasma pneumoniae. However, GBS in children associated with M. pneumoniae infection is a rare entity, whose clinical phenotype and pathomechanism are not yet described. We report a case series of 7 children with recent M. pneumoniae infection and severe GBS that presented to two European medical centers from 2012. The case definition for severe GBS included respiratory failure, central nervous system (CNS) involvement, or death. Of these 7 patients, 5 patients had GBS, 1 Bickerstaff brain stem encephalitis (BBS), and 1 acute-onset chronic inflammatory demyelinating polyneuropathy (A-CIDP). Five patients were mechanically ventilated and 4 patients had CNS involvement (2 patients were comatose). Most patients had nonspecific clinical symptoms at onset and at admission. Patients showed a rapidly progressive disease course. Antibodies against M. pneumoniae were detected in all patients and were found to be intrathecally synthesized in 2 cases (GBS and BBE), which proves CNS infection. One patient died and only two patients had complete recovery. This case series shows that M. pneumoniae infection in children can be followed by severe and complicated forms of GBS, including cases with respiratory failure, CNS involvement, and progression to A-CIDP. Nonspecific clinical features of GBS in such patients may predispose a potentially life-threatening delay in diagnosis. These cases illustrate that GBS following M. pneumoniae infection may present as a continuous spectrum of severe post-inflammatory disorders of both the peripheral and central nervous system.

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Neuromuscular disorders

ICNC-0751: Pediatric ocular myasthenia gravis: Treatment regimen and outcome

AIM: to determine treatment needs and clinical outcomes in pediatric ocular myasthenia. MATERIAL AND METHOD: retrospective study of 11 patients, 16 years or less (female 1.2 :1), in a neurological center, between January 2009 and December 2015. Mean age of onset 8.1 year (range 3-15), follow-up 3.81 year (range 2.8-6) RESULTS: 1) Initial signs: ptosis 100%, strabismus 64%, amblyopia 18%. 2) Outcome: complete stable remission 9%, pharmacologic remission 18%, minimal manifestation 54%, improvement 18%. 3) Current treatment: without drugs 2/10 (20%), steroid 2/10 (20%), azathioprine 3/10 (30%), pyridostigmine 5/10 (50%). 4) Treatment required in some point: no medication 2/11 (18%) pyridostigmine 9/11 (82%) steroids 7/11 (64%), azathioprine 4/11 (36%), thymectomy 0/11 (0%) 5) Exacerbation: during steroid withdrawal 4/7 (57%) or azathioprine decrease 1/3 (33%) CONCLUSION: All patient could control (82%) or improve (18%) with medications but more than half needed with immunosupresion. We observed high rate exacerbation on steroid withdrawal. Stable remissions were rare. There were no after-treatment ambylopias in our cases.

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Neuromuscular disorder

ICNC-0752: Duchenne Muscular Dystrophy: Phenotype of our patients

Introduction: Duchenne muscular dystrophy (DMD) is common X-linked genetic myopathies. We described the clinical features of 4 patients with DMD diagnosed regarding clinical, pathological, and genetic studies at our hospital in the last 7 years. Methods: A retrospective study was conducted of medical records from January 2008 to January 2020. Results: The mean age at diagnosis was 2.75 years (Current average age is 5.7 y). The main complaint was elevation serum CK levels in routine blood test in half of them (2). Two have started corticosteroids. No patient is wheelchair bound. Patient 1, at the age of 15months, was incidentally found to have hypertransaminemia and elevated serum creatine kinase (CK) in study failure to thrive. DPM engine retardation level and calf pseudohypertrophy. Genetic study showed deletion of exon 45. At the age of 5y 4m corticosteroid treatment was started and Enalapril (at 7y 6m) due to a electrocardiogram changes. Currently continues on corticosteroid and Enalapril and psycho-pedagogical support. Patient 2, history of progressive weakening muscles and pseudohypertrophy of calves at 2 years and 3 months. Serum CK with elevation higher than 10 times the normal value.EMG: myopathic pattern. Heart examination: ECG with signs of ischemia in the inferior wall. Deletion heterozygous exons 45 to 52, inclusive. Corticoids treatment was initiated at 4y and 6m and he received physical therapy and psychological support. Patient 3 diagnosed with Sotos syndrome (material loss of NSD1 and FGFR4), presented an elevation of CK in blood test control. Mild weakness shoulder girdle. EMG: myopathic pattern. Normal Heart examination. Genetic study with 297.14 kb deletion interval X p.21.1 Cr. Currently 5 years and 9 months, treatment with a speech therapist, physical therapy and cognitive stimulation. Patient 4 showed at 3 y and 3m elevated CPK levels and hypertransaminemia in analytical control by fever. Pseudohypertrophy twin. 2 maternal uncles died from Duchenne disease. EMG: myopathic pattern .He is pending genetic study. Conclusion: In a child with a significant increase (x10), twin hypertrophy and psychomotor retardation, the first diagnostic possibility is a muscular dystrophy. The multidisciplinary disease management is essential. Glucocorticoids should start administered when the driving function is in phase stability, being the only known drugs that slow the rate of deterioration in motor function and muscle strength.

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Neuromuscular disorders

**ICNC-0753: Guillaine Barre Syndrome in north Indian children: clinical and serial electrophysiological features**

**Purpose:** This study aimed to study the clinical and electrophysiological profile of Guillain-Barre syndrome (GBS) in North Indian children. We also evaluated whether serial electrophysiological studies were helpful in classification of GBS subtypes. Methods: This prospective study enrolled consecutive children aged 2 to 18 years with Guillaine-Barre syndrome presenting within 4-weeks of onset of weakness diagnosed on the basis of clinical and/or electrophysiological grounds. They underwent detailed clinical-assessment followed by nerve-conduction-studies. They were managed as per standard guidelines. Repeat nerve-conduction-studies were done after 2-weeks of the first study to look for change in electrophysiological-subtype. Functional ability of the patients was tested by using GBS Disability score and severity of motor weakness by MRC-Sum-score. The patients were followed for 3 months. Erasmus GBS Outcome Score (EGOS) was also computed to determine the risk of non-ambulation. Results: Thirty six children were studied. The mean age at presentation was 5.1 years (SD-2.1). The Mean MRC-sum-score at admission was 24.1 (SD-10.4). Thirty-three children (91%) had loss of ambulation, 24 (66%) had cranial-nerve involvement and 6 (16.6%) required ventilation. At presentation, 20 had Acute-motor-axonal-neuropathy (AMAN), 13 had Acute-inflammatory-demyelinating-polynerveuropathy (AIDP), 2 had in-excitable nerves and 1 had normal-study. Four children, initially diagnosed as AIDP, had AMAN with reversible-conduction-failure on the repeat study. The final-classification was AMAN in 25 (69.4%; 95% CI, 51.9% to 83.7%) and AIDP in 9 children (25%; 95% CI, 12.1% to 42.2%). Only one patient was non-ambulatory at 3-months follow-up (n=32). The Erasmus-GBS-outcome-score was 2 in 2(5.6%), 3 in 5 (13.9%), 4 in 26 (72.2%) and in 3 (8.3%) patients. Conclusion: Serial electrophysiological-studies were helpful in achieving the final correct diagnosis. Majority of the patients had favourable outcome at 3-months irrespective of the electrophysiological-subtype or the Erasmus-GBS-outcome-score.

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**Neuromuscular disorder**

**ICNC-0755: Electrophysiological pattern in Guillain-Barré syndrome: A comparison between pediatric and adult patients**

**Introduction:** Guillain-Barré syndrome (GBS) is a disorder causing muscle weakness and sometimes paralysis. It is the foremost cause of acute, generalized, peripheral neuropathic weakness. Nerve conduction studies are a diagnostic aid being an extension of clinical neurological examination. We aimed to compare the pediatric and adult GBS cases referred to our laboratory. Methods: Demographic profiles, electrophysiological pattern and diagnoses of fifteen pediatric GBS and thirty five adult GBS patients were compared. Descriptive statistics was employed to analyze electrophysiological data. Results: Age of the pediatric patients ranged from 4 to 15 years and adult from 17 to 88 years. Most common age group in adults was 20-30 years (43%) followed by 31-40 years (26%). Male represented two-third of the pediatric cases whereas adults were comparable gender wise. Pediatric patients presented mainly with both upper and lower limbs weakness; however, the maximal adults with only lower limbs weakness. Maximum pediatric cases were electrophysiologically diagnosed as axonal type neuropathy (73.3%), followed by mixed (n=2) and demyelinating (n=1). Adult cases showed similar pattern. Sixty percent of pediatric cases had both motor and sensory nerve involvement. In adults, both motor and sensory nerves (65.71%) were most commonly involved followed by motor (n=74, 24.18%). 6.66% and 23% of cases showed normal electrophysiological picture in pediatric and adults respectively. Conclusion: Electrophysiological pattern in pediatric and adults were maximally comparable. The electrophysiological diagnoses were not consistent with clinical diagnoses in significant number of adult cases. Keywords: Guillain-Barré syndrome, nerve conduction study, neuropathy

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**Neuromuscular disorder**

**ICNC-0712: The effectiveness of steroid therapy in idiopathic facial nerve palsy in childhood**

**Introduction** Idiopathic facial nerve palsy is mostly a benign condition. This study was conducted to show the efficacy of polenical steroid therapy. Methods: Files of patients diagnosed with idiopathic facial nerve palsy in our pediatric neurology department between January 2013 - August 2015 were retrospectively reviewed. Patients were divided into 3 groups. First group consisted of patients receiving 10 days of oral steroid; the second group received a single dose of intravenous pulse steroid and the third group did not receive steroid therapy. Results: The study was performed on 69 children (53.6%, n=37 female) with a mean age of 10.09±4.48 years. The time interval from beginning of the symptoms to treatment ranged from 6 to 46 hours with average of 24±9.45 hours. 25 patients received oral methylprednisolone therapy for 10 days, 27 patients received a single dose methylprednisolone and 17 patients were followed without medication. At the end of six-months all patients recovered fully except two patients, who had only mild sequelae.
Average full-recovery time was 20 days for oral steroid group and 15 days for the other two groups. We found out that single dose treatment quickens recovery time however at the end of six-month period there is no difference with regard to full-recovery. Conclusion: Full recovery was achieved in all patients independent of treatment modality. We therefore conclude that prognosis of idiopathic facial nerve palsy in children is benign and steroid treatment, which has wide spectrum of side effects, has no marked effect on recovery.

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Neuromuscular disorder
ICNC-0756: The frequency of late-onset Pompe disease in pediatric patients with unclassified limb-girdle myopathy and nonspecific hyperCKemia: a multicenter study
Introduction: Pompe disease, also known as glycogen storage disease type II is a lysosomal storage disorder characterized by an absence or deficiency of acid a-glucosidase. Unlike the classical form, late-onset Pompe disease, presents with slowly progressive axial and limb girdle muscle weakness and respiratory distress. Since the disease is rare and may mimic other neuromuscular disorders, the diagnosis of the late-onset form is challenging. We aimed to screen for Pompe disease in pediatric patients with unclassified limb-girdle muscular dystrophy or nonspecific hyperCKemia using dried blood spot assays. Methods: A retrospective, multicenter study was conducted. We looked for the patients with unclassified limb-girdle muscular dystrophy or nonspecific hyperCKemia in the databases of four pediatric neurology centers. All the patients were called by telephone and were invited to the hospital for screening. Results: Of the 98 patients called 72 agreed in screening. A total of 37 unclassified limb-girdle muscular dystrophy and 35 nonspecific hyperCKemia patients were enrolled in the study. The test was positive in 6 patients and Pompe disease was confirmed in 3 by genetic analysis. Conclusion: Pompe disease should be considered in the differential diagnosis of pediatric patients with unexplained limb-girdle muscular weakness and nonspecific hyperCKemia. We think dried blood spot sampling is an easy and quick way of screening Pompe disease. The results should further be confirmed by biochemical and/or molecular genetic analysis.

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Neuromuscular disorder
ICNC-0758: Evaluation of cardiac follow up for patients with Duchenne muscular dystrophy in a tertiary centre: are we following the standards of care?
Introduction: Duchenne muscular dystrophy is the commonest muscular dystrophy with prevalence of 6 in 100,000. About 10% deaths is due to cardiac complications. Comprehensive multidisciplinary follow up is vital for better survival and quality of life. Standard of care published in 2010 has been endorsed by clinicians and is accredited by NICE UK. Recommendations for cardiac follow up is echo at diagnosis or by 6 years then every 2 years till the age of 10 and annually thereafter. We look at cardiac follow up of DMD patients in our regional neuromuscular clinic. Method: Retrospective case note analysis of cardiac follow up at diagnosis and over the last two years. Results: Cardiac follow up of 70 patients with DMD was evaluated. 71% had first echo done the same year of diagnosis and 83% diagnosed before 6 years of age had it done by 6 years. 31/36 patients up to 10 years had echo in the last two years and 25/34 patients more than 10 years had echo in the last year. Mean time of onset since diagnosis of cardiac complication was 8.6 years. 17 patients are on medication for cardiomyopathy and Enalapril was the most common agent used. Conclusion: Though majority of children with DMD had cardiac follow up as per recommendations, we found a few cases that slipped through the routine review. A more robust system of identification of children with missed appointments is recommended to achieve the set standards.

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Neuromuscular disorder
ICNC-0859: Muscle Ultrasound Density from Pre- to Postnatal life in Healthy Fetuses and infants
Introduction: Muscle ultrasound can non-invasively reveal myopathy by enhanced reflection of the ultrasound beam, causing increased muscle ultrasound density (MUD). In healthy fetuses and infants, we reasoned that physiological muscle maturation could also increase MUD (by alterations in muscle peptide and water content). If so, pediatric-MUD parameters should be interpreted against physiological reference values. We therefore aimed to determine MUD-
outcomes in healthy children, from the first trimester of pregnancy until the first year of postnatal life. Methods: In 21 healthy control fetuses and infants, we determined cross-sectional MUD values of biceps, quadriceps, tibial anterior and calf muscles at the 1st, 2nd and 3rd trimester of pregnancy and at the 0th, 6th and 12th month postnatal age. Results: In healthy fetuses and infants, MUD of all muscles increased from the first trimester of pregnancy until the sixth month after birth [median MUD increase: 33% (range 15-49%)], and stabilized thereafter. Comparing fetal-MUD revealed relatively lower MUD-outcomes in hamstrings and gluteal muscles than in biceps, quadriceps, tibial anterior and calf muscles (p<.05). Postnatally, MUD of the hamstrings remained relatively lower than the other muscles (p<.05). Conclusions: In healthy control fetuses and infants, MUD increases continuously from pre- to postnatal life. In addition to an identical developmental MUD increment in all muscles, we also observed intrinsically different MUD outcomes between individual muscles (potentially due to differential structural organisation and muscle fibre content). These control data can provide a reference frame for myopathic MUD assessment in fetuses and infants during the first year of life.

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Neuromuscular disorder

ICNC-0957: Presentation use of steroid in childhood ocular myasthenia gravis in Hong Kong
Objective: To review the use of oral prednisolone in the treatment of childhood ocular myasthenia gravis in a tertiary hospital in Hong Kong and review the current literature on treatment recommendation. Methods: Medical records of patients diagnosed with ocular myasthenia gravis during January 2000 to December 2014 were reviewed. Their demographic data, presentation signs and symptoms, treatment effect and outcome were reviewed. Results: 11 patients were studied with seven female and four male patients. The median age of onset was 6.7 years old (range 1.5 -17 years). The median mean follow up time was 6 years (range 6 months to 24 years). The most frequent clinical presentation was ptosis (82%), followed by diplopia (73%). All patients demonstrated typical fatigability on physical examination. Only one received thymectomy with good response. All patients received acetylcholinesterase inhibitor (Pyridostigmine), five patients (45%) had poor response and required oral steroids and three patients received additional azathioprine Steroids were well tolerated in all patients. Relapses are common among steroid users. Majority (82%) of patients were symptom free or near-symptom free at latest follow up. Only one boy had developed generalized myasthenia. Conclusion: Use of oral prednisolone was quite common among children with ocular myasthenia gravis and they were in general well tolerated. The rate of generalization was low in our cohort of patients.

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Stroke and vascular disorders

ICNC-0880: Intracranial internal carotid artery dissection following waterslide use: the first case report

Dissection of carotid artery after blunt head or neck trauma has been reported in adults, but is unusual and difficult to diagnose in the pediatric population because of the possible delay in neurologic symptoms, and the absence of ischemic abnormalities on initial computed tomographic scans. We present, the first pediatric case of a previously well girl who developed intracranial internal carotid artery dissection following a waterslide use. CASE REPORT A previously healthy 5 year old girl presented to the emergency department after suddenly developing right facial drop, weakness of her right arm and leg with associated slurring of speech. Her history was unremarkable for trauma or any other diseases. On further questioning her mother mentioned waterslide use while on vacation with her parents. Immediately after waterslide use, she had headache and her mother noticed slurring speech and right facial drop. At admission, she was semiconscious with a right hemiparesis, 1/5 upper limb and 4/5 lower limb with associated gait unsteadiness and a complete right-side peripheral facial palsy. Magnetic resonance imaging and angiography (MRI/MRA) of the brain and carotid vessels performed in a few hours following admission revealed evidence of acute ischemic stroke at left hemisphere of brain with dissection of the left internal carotid artery (Figure 1). Cerebral catheter angiography performed revealed no aneurysm and no subarachnoid hemorrhage was present on MRI.

DISCUSSION Our knowledge, the case described here is the first reported case of intracranial internal carotid artery dissection secondary to “water slide use.”

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Stroke and vascular disorders

ICNC-0881: Outcome of Childhood Stroke: Prospective Cohort Study

Aim: To study sensorimotor outcome of childhood stroke. Methods: 74 patients were investigated. Diagnosis of stroke was confirmed by CT/MRI/MRA scan. Follow-up assessment was done with Pediatric Stroke Outcome Measure (PSOM) and IPSS Stroke Recovery and Recurrence Questionnaire (RRQ) at discharge and after 2-5 years from discharge. Inclusion: Children with the diagnosis of stroke aged 1 month to 16 years of age admitted at M. Iashvili Children’s Central Hospital after January 2010. Exclusion: Perinatal cerebral infarction and Transient ischemic attack (TIA). Results and conclusions: 41 of these patients were males and 33 were females. Arterial ischemic stroke (AIS) was reported in 39 patients, hemorrhagic stroke - in 28 and cerebral sinovenous thrombosis (CSVT) in 7 patients. The most – 32 of childhood stroke cases were obtained in patients aged 0-24 months, 10 patients were in the age group of 2-5 years, 15 were aged 5-10 years and 17 - above 10 years of age. Focal signs occurred in all cases of AIS, - in 11 of hemorrhagic stroke and in 6 of CSVT. Seizures were presenting symptom in 30 patients. Risk factors were identified in 43 cases - in 16 of AIS, in 3 of CSVT and in 24 of Hemorrhagic stroke: 3 patients were diagnosed as having Cardiac disease, 8 - having Leukemia, 3 - having Factor VIII deficiency, Arteriovenous Malformation (AVM) was a risk-factor in 7 patients, Cerebral aneurysm - in 2. Dissection - in 1. Encephalitis was found in 3 patients, Vasculitis - in 1, Post Varicela-zoster virus FCA - in 2, 1 patient had stroke due to Hemolytic anemia, 1 – Hypochromic microcytic anemia, 1 – Thrombocytopenic purpura, Hypocoagulation (K-vit) was a risk-factor in 2 patients, Hypertension – in 3, 3 patients were diagnosed with Moyamoya disease, 1 with Sturge-weber syndrome and 1 with MELAS. Outcome: • Death occurred in 10 patients, all of them were with hemorrhagic stroke • Neurologic deficit at discharge was found in 39 patients - in 32 with AIS and in 7 with hemorrhage stroke • Stroke recurrence occurred in 3 patients – 2 with AIS and 1 with hemorrhagic stroke. From 39 patients with neurological deficit at discharge, follow-up assessment revealed mild deficit in 6 patients, moderate deficit - in 7 and severe deficit - in 2 patients.

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Stroke and vascular disorders

ICNC-0882: Neurological involvement in infective endocarditis in children without congenital heart disease

Introduction: Neurological manifestations are seen in up 40% of cases of infective endocarditis (IE), includes cerebrovascular entities and other complications. Few publications report in children. AIM: to describe neurological features, neuroimaging and hospital discharge outcomes of pediatric patients with IE. Methods: we present three pediatric cases od neurological involvement associated with IE seen in a tertiary hospital. Results: of the three cases, 2 boys, 1 with previous rheumatic fever, median age was 9 year (range, 3 – 14). 1 patient have a positive detection pathogen in blood cultures (Streptococcus viridans). Clinical presentation were fever, abdominal pain and neurological manifestations. The median duration from diagnosis of IE to onset of neurological symptoms was 16 days (range, 1 – 48). Neurological manifestations are impairment of consciousness, seizure and focal signs. All the patients had cerebrovascular complications, 2 cases due to cardioembolism (1 case with mycotic aneurysm and additionally renal
artery aneurism demonstrated by conventional angiography) and 1 due to vasculitis. 1 patient required surgical management of heart disease due to cardioembolic complications. Outcomes of hospital discharge were 2 patient with mild hemiparesis and 1 death. Discussion: cerebrovascular complications of IE should be considered in every child with impaired consciousness and fever.

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Stroke and vascular disorders
ICNC-0884: Diagnostic approach of children with ischemic stroke – 20 years of experience
Objective: Although rare, stroke in children represents an enormous diagnostic and treatment problem. In this paper we present our experience regarding diagnosis of ischemic stroke in children. Material and methods: We performed a retrospective study on children with ischemic stroke acquired after perinatal period, admitted in our Department between 1995 and 2015. We noted: demographic data, clinical features presented at the onset, time spent till the diagnosis of stroke was established, causes of diagnosis delay, and stroke causes. All children were extensively evaluated, including neuroimaging studies, coagulation profile, heart and Doppler ultrasound, angiography. Results: 86 children, 47 males and 39 females, with ages ranging between 15 months and 17 years, were included in this study. The most frequent clinical feature at the onset was hemiparesis (71 cases). In most children the diagnosis of stroke was established in 1-7 days (41%). The most frequent causes for the delay in establishing the diagnosis were lack of awareness about stroke occurrence in children, both in parents and general practitioners, and unavailability of neuroimaging studies. Concerning the stroke etiology, the most common causes were coagulopathies (30%), infectious diseases (23%), arterial anomalies (12%); in 30% of cases we could not identify an etiology. Conclusions: Ischemic stroke is a rare condition in children, which raises difficulties in establishing the diagnosis. An extensive evaluation of these children can identify the cause of stroke in most children, but there is an important percentage of cases without an etiological diagnosis, with consequences in evaluation of the recurrence risk.

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Stroke and vascular disorders
ICNC-0885: Basal Ganglia and Internal Capsule Stroke in two young children following Mild Head Trauma
BACKGROUND Arterial ischemic stroke AIS in children is associated with diverse etiologies. Mild head trauma has been reported as a causative factor. We describe 2 young children with AIS after mild head trauma METHOD Thirty-nine children < 18 years presenting with AIS were studied. A sub-cohort with antecedent head trauma was identified and analysed for evolution and possible risk factors. RESULTS Etiological factors were identified in 33 cases, comprising infection 10, cardioembolic 7, moyamoya 6, mitochondrial disorders 3, vasculitis 2. Two infants (5%) had prior mild head trauma. The two, aged 7 months and 17 months, were previously healthy with no other risk factors. The younger infant fell backwards while being seated; the other child fell while walking. There was no loss of consciousness or drowsiness. Clinical presentation was similar: hemiparesis and facial weakness developed several hours after head trauma. Brain magnetic resonance imaging (MRI) with Gd-DTPA showed unilateral basal ganglia and internal capsule infarct. Other investigations performed as per the department’s protocol included MR-angiography, cardiac echocardiography, haematological and biochemical screening were normal. Outcome was good with fairly swift neurological recovery and no stroke recurrence. DISCUSSION: Mild head trauma is a risk factor for pediatric AIS. Exclusion of other predisposing conditions is important, including cardio-embolic disease, thrombophilia, arterial dissections. Vasospasm or intimal damage of the lenticulostriate or thalamoperforating arteries with subsequent thrombosis is a suggested mechanism. Improved understanding is needed to develop preventative stroke strategies in childhood trauma. Word count 250

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Stroke and vascular disorders
ICNC-0887: Ischemic stroke on an infant with a vegan mother - a case of hyperhomocysteinemia
Introduction: Stroke is a rare disease in childhood, affecting 2.7 / 100,000 children per year. Hyperhomocysteinemia, an independent risk factor for premature atherosclerosis, is the most common cause of stroke in pediatrics and its origin is either genetic or due to vitamin B12 deficit. Case Description: We present the case of a 10 months old infant, with a family history of a stillborn brother (unknown cause). Brought to the ER after a fall (from his own height) due to prostration and decreased spontaneous movements of the left arm. Acute orthopedic pathology was excluded and decrease of the spontaneous movements was noted in left upper limb, with afflexed posture. The first CT scan was normal, but 48 hours
Stroke and vascular disorders

ICNC-0888: Complex partial seizure as a presentation of multiple cerebral cavernous malformations in a pediatric age patient: The first individual in a family

Introduction: Cerebral cavernous malformations (CCMs) are vascular abnormalities that may cause mostly seizures, recurrent headaches, cerebral hemorrhages, focal neurological deficits and gait ataxia. They may occur as a sporadic or an autosomal dominant familial disorder (f CCM). Cases with multiple lesions that appear to be sporadic in fact could be the hereditary form of the disease. Spontaneous de novo mutation has also been reported in one apparently sporadic CCM patient with multiple lesions. Case report: An eight year old girl was admitted to our hospital with the complaint of fever and persistent vomiting. Infectious and toxic screening parameters were negative. At the 10th day of administration, she had a complex partial seizure (CPS) lasting for almost two minutes. Her neurological and fundoscopic examination was normal. Her EEG recordings revealed right frontoparietal focal discharges. Patient was seizure free after medication with levatiracetam. Her MRI revealed multiple CCMs. One of them located on the right subcortical parietal region was hemorrhagic and vasogenic edema surrounded it. Neurosurgical consultation resulted as conservative medical treatment. Genetic tests and MRI screening for silent members of the family were offered. Conclusions: The clinical presentation of multiple CCMs could be a single CPS. If a patient seems to be the first individual case of a family and have multiple CCMs; we should search the hereditary mutations of the disease. Genetic maps of the disease could help us to delineate environmental factors or modifying genes explaining the intra and interfamilial variability of fCCM.

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Stroke and vascular disorders

ICNC-0889: Basal ganglia stroke precipitated by trivial trauma; a pediatric cohort

Introduction: Acute basal ganglia stroke in children following trivial trauma associated with mineralization of lenticulostriate arteries is a distinct clinicoradiological entity. The current study describes a cohort of children with basal ganglia stroke following trivial trauma with respect to clinical, laboratory and radiological parameters. Methods: The current study was conducted in a tertiary care teaching hospital in north India. Over 1 year period (March 2014 to February 2015), 12 patients with mineralising angiopathy following trivial trauma were recognized and analysed. Results: The cohort had a median age of 12 months (range: 4-18 months) with a male to female ratio of 2:1. Majority (n=10) presented with hemiparesis while the remaining two presented with hemidystonia. Other clinical features noted were aphasia in 2 and encephalopathy in one. Radiologically bilateral basal ganglia involvement was seen in 5 children at onset and basal ganglia calcification was seen in all. All of them had history of trivial trauma before onset of stroke. Detailed work up for stroke and bilateral basal ganglia calcification was negative in all children. None of the patients have been started on long term antiplatelet agents. The median follow-up was 12 months (range: 9-20 months), during which only 2 children experienced recurrence of stroke following trivial trauma. Currently eleven patients have shown complete neurological recovery and only one has mild residual hemiparesis. Conclusion: Mineralising angiopathy should be recognised and differentiated from potentially catastrophic clinicoradiological differentials. Trivial trauma should be kept in mind as a precipitating factor to exercise caution and prevent recurrences.

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Stroke and vascular disorders

**ICNC-0890: Moyamoya syndrome in South African children with HIV-1 infection**

Abstract: A national multicentre study identified 17 South African children with vertically acquired HIV1 infection and HIV-associated vasculopathy. Of this group, five children of indigenous African ancestry had progressive vascular disease, consistent with moyamoya syndrome. The children with moyamoya syndrome presented with abnormal CD4 counts and raised viral loads. Clinical features included motor deficits, neuroregression and intellectual disability. Neuroimaging supported progressive vascular disease with preceding clinically silent disease course. Recovery was evident in one patient with improved CD4 counts. Four out of the five children presented during the era when access to antiretroviral therapy was limited, suggesting that with improved management of HIV-1, progressive vasculopathy is less prevalent. However the insidious disease course illustrated indicates that the syndrome can progress “silently”, and manifest with unsuspected phenotypes such as cognitive delay or regression. In sub-Saharan Africa where there is limited access to neuroimaging, affected children may be under diagnosed or misdiagnosed.

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**Stroke and vascular disorders**

**ICNC-0891: Stroke in children with Cardiac Disease in University Hospital**

Aim: To describe clinical, the spectrum of cardiac disorders and outcome in children with cardiac disease and ischemic stroke (IS) in a no concurrent cohort. Methods: Children younger than 18 years with cardiac disease and radiologically confirmed IS were prospectively identified and included in data base of Pediatric stroke between 2002-2013 to the Pontificia Universidad Católica de Chile4 Hospital. Results: Seventy-six children with cardiac disease and radiologically confirmed IS were identified with the median age at diagnosis of 34 months. Cardiac lesions included congenital heart disease (CHD) in 66 (87%): dTGA in 15 (20%), left heart hypoplasia in 15 (20%), Aortic coartation in 10 (13%) and fallot T in 7 (9%), cardiomypatohies/myocarditis in 7 (9%), infective endocarditis in 3 (4%). The type of stroke was arterial ischemic stroke (AIS) in 65 (85.5%), cerebral sinovenous thrombosis in 7 (9, 2%) and both in 4 (5, 3%). In AIS the territory distribution was anterior circulation in 63/69 (91%) and multiple in 37/69 (53.6%). At follow up (12-144 months), there were 25 deaths (33%) and 51 survivors (67%). 41 (54%) had persisting neurologic deficits Conclusions: Patients with heart diseases are a group at high risk of developing stroke characterized by an embolic pattern with a high rate of associated mortality and neurological sequelae.

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**Stroke and vascular disorders**

**ICNC-0892: Bacterial meningitis and ischemic stroke in newborn and infants**

INTRODUCTION: Bacterial meningitis (BM) related stroke continues to cause high rates of neurological sequelae despite advances in treatment and intensive care. OBJECTIVES: To describe clinical and neuroimaging features in a series of 16 children with BM-associated strokes. PATIENTS AND METHODS: We conducted a retrospective review of the pediatric stroke database of a single pediatric referral center between January 2002 and December 2012 and we described cases of stroke following bacterial meningitis. RESULTS: Seven newborns and nine infants were identified. Symptoms included fever (16/16), decreased level of consciousness (13/16), seizures (12/16) and food intolerance (5/16), while none had focal deficits. B Streptococcus was isolated in 6 of the newborns and E Coli in one of them. Pneumococcus and meningococcus were isolated respectively in 6 and 3 of the nine patients older than one month. The MRI showed cerebral arterial stroke in 15 cases (3 of them with cerebral sinovenous thrombosis (CSVT), 3 with arterial stenosis) and venous infarct in only one case. Thirteen of the 16 meningitis cases with cerebral infarcts were associated with poor outcomes. One patient died and eight developed cerebral palsy. Ten cases had epilepsy. Three cases had intellectual disabilities without motor disorders and 3 patients had severe sensorineural hearing loss. Only 3 patients were without sequelae after 6-9 years of follow-up. CONCLUSION: Decreased mortality in BM has not been associated with decreased neurological morbidity, probably as a result of cerebral stroke. It is necessary to know when and with which patients this complication occurs and the effect of early treatment and neuroimaging in the outcomes.
Stroke and vascular disorders

ICNC-0894: Acute encephalopathy: A novel presentation of mineralizing microangiopathy of childhood
Mineralizing microangiopathy of childhood is increasingly being recognized as an important cause for stroke following minor trauma/ fall in healthy children. It typically presents with acute onset focal neurodeficit with or without seizure following minor trauma. The neuroimaging usually shows basal ganglia stroke and computed tomography (CT) of the head shows calcified lenticulostriate arteries. Though majority of them improve with physiotherapy up to 40-50 % of these children develop recurrent stroke again following minor trauma or fall on the same side or on the opposite side. Magnetic resonance angiography is usually normal thus helps differentiating this condition from the common arteriopathies seen in this age group like focal cerebral arteriopathy and moyamoya syndrome. But presentation as acute encephalopathy and coma due to acute bilateral basal ganglia stroke following minor head trauma with good recovery has not been reported earlier. We here report two toddlers (30 months and 36 months old) of age, who presented to us with acute encephalopathy following minor trauma. The CT scan of the head showed bilateral basal ganglia hypodensities along with punctuate calcification in the putamina Bilateral putaminal hypodensities was asymmetrical pointing to a vascular cause and prompted us to do 3-D coronal reconstruction to demonstrate calcified lenticulostriate arteries thereby confirming mineralizing microangiopathy as the underlying cause for the stroke. MR angiography was normal. Cerebrospinal fluid study and CSF PCR for cytomegalovirus was negative. Both the children were put on aspirin, iron and physiotherapy programme and both showed marked recovery in two months time.

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ICNC-0895: Epilepsy in children with Vein of Galen Aneurysmal malformations (VGAMs)
Introduction: Vein of Galen aneurysmal malformation (VGAM) is a rare vascular malformation. Thalamic injuries is possible in VGAM patients and some studies suggest that Thalamic injuries can potentiate epileptiform discharges in sleep. Methods: Descriptive study by retrospective review of records of VGAM patients managed at our centre. Case description: VGAM patients who had recurrent seizures were included in this study. Patients who only had acute symptomatic seizures during the acute treatment phase with no further seizures were excluded from the study. Results: Out of 134 patients on our VGAM database twelve patients fulfilled the inclusion criteria. VGAM was diagnosed in the neonatal period (42%) in the majority. Most common mode of presentation of VGAM patients was cardiac failure (58%). Seizure onset was before 2 years in 50% and Focal seizures most common (58%). Abnormalities noted on MRI were White matter signal abnormalities (8/12), Thalamic injury (6/12). Awake and sleep records were done in 8 children. One child fulfilled the criteria for ESES. 3/8 patients showed some degree of potentiation of discharges in sleep. Conclusion: Thalamic injury is common in VGAM patients which puts them at higher risk for potentiation of discharges in sleep which was noted in half of the patients who had sleep data. Increased sleep discharges can lead to cognitive decline and therefore we recommend that sleep EEG should be part of epilepsy management in this group of patients.

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Stroke and vascular disorders

ICNC-0896: Non-invasive brain stimulation is safe in children: Evidence from 3 million stimulations
Non-invasive brain stimulation is safe in children: Evidence from 3 million stimulationsBackground. Non-invasive brain stimulation can interrogate neurophysiology and therapeutically modulate brain function. Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are the primary modalities. Despite such potential, experience in the developing brain has been limited. Methods: Our academic pediatric center established a non-invasive brain stimulation laboratory for children in 2008. Multi-disciplinary neurophysiological studies included single- and paired-pulse TMS methods. Therapeutic clinical trials used repetitive TMS (rTMS) and anodal/cathodal motor cortex tDCS. Prospectively collected safety and tolerability data on all subjects included a previously developed pediatric TMS safety and tolerability measure, child and parental interviews, and data safety and monitoring boards. Results: From 2008-2015, 293 children underwent brain stimulation (median 11.2 years, range 8 months–18 years). Most common were perinatal stroke/cerebral palsy (79), mild traumatic brain injury (49), or typically developing (86). There were no serious adverse events. Of 239 receiving TMS, tolerability between TMS (>227000 stimulations) and rTMS (>2.5M stimulations) was comparable and rated similar to a long car ride. Although >100 had brain injuries and >20 had epilepsy, no seizures occurred. Headache in ~20% was mild, self-limiting and decreased across sessions and with neuronavigation. One
adolescent with major depression withdrew from a high-frequency rTMS trial for discomfort. Of 54 children receiving tDCS, scalp itching in 40% was mild, transient, and comparable to sham with no drop-outs or decrease in motor function. Conclusions: Brain stimulation is safe and well tolerated in children. Applications in the developing brain should be advanced.

**ICNC-0898: Spectrum of Clinico-Radiological features of childhood Moyamoya Disease - A study of 35 children**

**INTRODUCTION:** Presentation of childhood moyamoya disease, a cerebral vasculo-occlusive disease, varies significantly as compared to adults. As outcome of treatment depends on neurological status at time of diagnosis rather than age, early diagnosis of myriad manifestations is key to good prognosis. **METHODS:** 35 patients of childhood moyamoya disease diagnosed by MRI, MR Angiography and DSA, were studied for various spectrum of clinico-radiological manifestations. **RESULTS:** 1. Mean age: 6.71yrs (6months-15years); F:M ratio 1.15:1. 2. Most common presenting feature – Hemiparesis-65%, Recurrent TIA-11%. 3. Remaining 24%-- unusual presentations - seizures and headache in 6% each whereas cognitive decline, visual loss, paraparetic TIA and Bihemispherical TIA (quadriparesis as presentation) in 3% each. This group of 24% required strong suspicion for an early diagnosis (very unusual presentation without any history of neurological illness) 5. MRI Brain: 69% had ischemic stroke whereas 5% had hemorrhagic stroke. Remaining 26% had a normal parenchyma; had abnormal flow voids as the only clue to diagnose moyamoya disease. 6. One patient had Boomerang Sign (isolated T2 and flair hyperintensity in splenium of corpus callosum); previously described with other etiologies like toxins, demyelination, this being the first instance with moyamoya disease. 7. Angiographically, B/I ICA (Internal Carotid Artery) involvement with sparing of posterior circulation was the most common pattern seen in 69%, B/I ICA with posterior circulation involvement in 15%, unilateral ICA affection in 16% whereas none with isolated posterior circulation involvement. **CONCLUSIONS:** Knowledge of varied manifestations must be borne in mind by pediatric neurologists for early diagnosis to achieve a favourable prognosis of this potentially treatable entity.

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**ICNC-0899: Childhood intracranial arterial dissection: Clinical course and outcome**

Objective: The aim of this study is to describe clinical course and outcome of children with intracranial arterial dissection (IAD), which is a rare cause of intracranial hemorrhage or cerebral infraction in children but more frequently diagnosed with the advances in imaging techniques. **Method:** We retrospectively reviewed children diagnosed with IAD between Jan 2006 and Feb 2015 at Asan Medical Center. **Results:** Nine patients were diagnosed with IAD at mean age 12 years (range, 6.5-18.9 years). Most common clinical presentation was hemiparesis (n = 6) which is associated with acute ischemic stroke in involving area. One patient presented with mental change was diagnosed as subarachnoid hemorrhage and died. The others presented with seizure, headache and choreatic movement without other complications. Six patients (66.7%) had anterior circulation dissection including distal ICA and MCA and two had PCA dissection and one had bilateral vertebral artery dissection diagnosed by conventional angiography. Seven patients with IAD received anticoagulation and only one experienced further attack of transient ischemic attack on mean 2.6 years (range, 0.2-8.6 years) of follow-up. Conclusion: Recent advance in vascular imaging modality contributed to the diagnosis of IAD. Childhood IAD are rare but at high risk of complications. Further long-term studies with larger population are required to clarify the long-term outcome of the childhood IAD.

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**ICNC-0900: Recurrent acute ischemic stroke in a child on Novalung treated twice with mechanical clot retrieval: a case report and review of the literature**

**Background:** The American Heart Association/American Stroke Association recently amended their acute stroke guidelines to add recommendation for thrombectomy with stent retrieval in specified cases. Case: We present the case of an 8-year-old girl who demonstrated acute stroke symptoms on two occasions, 4 days apart, while therapeutically anticoagulated on Novalung. Thrombectomy was offered in both instances since the patient had a severe persistent neurological deficit (NIHSS > 6), a clot in the proximal middle cerebral artery, anticoagulation precluded her from TPA administration, and CT showed uninfarcted brain tissue distal to the thrombus. On both occasions, the clots were
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successfully retrieved with a Trevo device. No hemorrhagic complications were observed despite continuing anticoagulation during and between the procedures. Post-procedural assessment found respective decreases in the patient’s NIHSS score from 10 to 4 and 12 to 7. Discussion: The treatment indications and immediate clinical benefits in our case are consistent with other paediatric thrombectomy cases reported. However, publication bias and the heterogeneity of reported cases make drawing conclusions about the safety and efficacy of thrombectomy in children difficult. Anticipating that recent changes to adult stroke guidelines would likely prompt paediatric stroke care providers to consider thrombectomy for their patients, our institution developed consensus-based guidelines for thrombectomy prior to the index case. This guideline served to facilitate multidisciplinary intervention and manage foreseeable risks. Conclusions: Our patient repeatedly showed immediate improvement in her NIHSS score post-thrombectomy. More notably, our case emphasizes the importance of establishing institutional guidelines before offering thrombectomy to a child.

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ICNC-0901: Arterial Ischaemic Stroke in adolescents: applicability of the cascade criteria and description of the main characteristics

Introduction: Several studies have addressed arterial ischemic stroke (AIS) in young adults and children but very few specifically looking at adolescents. The adoption of a validated classification system in adults has been critical to the study of stroke. The nearest equivalent in children is the “Childhood AIS Standardized Classification and Diagnostic Evaluation (CASCADE). Our aim was to characterize AIS in adolescents using CASCADE classification to see if AIS in older children was distinct from younger children. Methods: Retrospective analysis of case records and imaging in adolescents (10-16 years) with AIS (January 2004-May 2015). CASCADE criteria were used to stroke sub-typing. Modified Rankin scale (mRs) to evaluate prognosis and PedNIHSS to stroke severity. Results: 30 patients were identified (14 females, 16 males; mean age 13.3y). Delay in performing neuroimaging was common. Single infarcts were observed in 63%. 73% strokes involved anterior circulation. The commonest risk factor was non-atherosclerotic cerebral arteriopathy. No risk factors were identified in 26% patients. Among CASCADE stroke subtypes, type 6 (“Others”) was the most frequent, followed by type 4 (cervical arteriopathy) and type 2 (focal cerebral arteriopathy). No patient was treated with thrombolytic therapy. 70% of patients had good clinical outcome (mRs 2 or better). Conclusion: this retrospective study shows that risk factors for AIS in adolescents are similar to younger children. Cervical or cerebral arteriopathy is the commonest risk factor. Application of CASCADE classification allows comparison of stroke subtypes in different age groups which may allow development of age specific investigation and treatment protocol.

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ICNC-0902: Outbreak: An incidence spike within a population based sample of acute neonatal arterial ischemic stroke

Outbreak: An incidence spike within a population based sample of acute neonatal arterial ischemic stroke Introduction: Neonatal arterial ischemic stroke (NAIS) is a leading cause of hemiplegic cerebral palsy. Risk factors and pathophysiology are poorly understood. Epidemic increases in incidence provide an opportunity to study previously unidentified risks. Hypothesis: An increased incidence of NAIS above baseline occurred in the population in the last quarter of 2014. Methods: A population-based registry that has prospectively identified all cases of perinatal stroke since 2008. Following clinical recognition of increased NAIS cases in late 2014, incidence rates per quarter were analyzed from January 2008 to July 2015. Placentas underwent standardized, blinded pathological review when available. Results: NAIS incidence increased from 1990-2008 but was stable from registry inception (2008-2015). Quarterly incidence of NAIS was 1.67 (SD=1.2) cases since 2008 (~1:3800 live births). A significantly higher incidence of NAIS (~1:750) was seen in the fourth quarter of 2014 (p<0.05). The incidence returned to the previous baseline in the first 3 quarters of 2015. Placental pathology was available for 2/9 subjects (22%) born during the fourth quarter of 2014. Both were abnormal, demonstrating chorioamnionitis and chorionic vasculitis while one also had funisitis and the other villitis of unknown etiology (VUE). Conclusions: Periodic outbreaks of NAIS have not been previously described but may be demonstrated across longitudinal, population-based surveillance programs. Occurrence supports an acquired etiology such placenta infection and may be consistent with previously described risk factors and low recurrence.
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**ICNC-0904: Left atrial myxoma presenting as cerebrovascular stroke**

Introduction: Cardiac myxomas rarely occur in children and adolescents. In addition, at least 20% of all ischemic strokes are cardiac causes. However, early diagnosis is challenging due to non-specific symptoms of left atrial myxomas. If the diagnosis do not establish in timely fashion, severe complications that lead to devastating morbidity and mortality can develop. Here, we present a case with ischemic stroke because of cardiac myxoma. Case A 15 year-old girl admitted with a sudden onset of right-sided weakness, aphasia, headache and dizziness. Further history revealed that similar symptoms had occurred in the previous 2 years. She had diagnosed epilepsy and took valproic acid 20/mg/kg/day. After 1 year follow up, she did not undergo seizure. Therefore, the epileptic therapy was discontinued. She had got no symptom until presented with previously mentioned clinical picture to our emergency unit. Neurological examination revealed that she was aphasic and drowsy, but arousable. She could understand commands, however, she could not talk. She had right upper motor neuron facial palsy. Right-sided hemiparesis with a power of 3/5 in right upper and lower limbs was found in her motor examination. Brain magnetic resonance imaging (MRI) showed infarct area in the left hippocampus, caudate nucleus in the posterior of the internal capsule. Transthoracic echocardiography ascertained left atrial myxoma. She underwent cardiac surgery at the same day of admission and was well at postoperative period. In addition, histopathology confirmed the diagnosis. Conclusion: Stroke due to cardiac myxoma is a rare clinical entity. Cardiac causes should be considered in patients suspected neurological disorders because of its devastating clinical consequences. References: 1. Bayir H, Morelli PJ, Smith TH et al. A left atrial myxoma presenting as a cerebrovascular accident. Pediatr Neurol. 1999 Aug;21(2):569-72. 2. Akhtar J, Wasay M, Rauf J. Atrial myxoma: a rare cause of cardioembolic stroke. BMJ Case Rep. 2012 Sep 7,2012, pii: bcr2012006176. doi: 10.1136/bcr.2012.006176.3. Yuan SM, Humurula G. Stroke of a cardiac myxoma origin. Rev Bras Cir Cardiovasc. 2015 Mar-Apr;30(2):225-34. doi: 10.5935/1678-9741.20150022.

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Stroke and vascular disorders

**ICNC-0905: Moya Moya Vasculopathy in children**

Background: Moyamoya vasculopathy is a chronic progressive vaso-occlusive disease of the distal intracranial carotid arteries& their proximal branches,presenting as an important cause of recurrent strokes in children. Surgical revascularization procedures are now considered the therapy of choice. The data from Indian pediatric patients with moyamoya vasculopathy is limited to a very few studies. Study design: 41 children aged 0-18 years with moyamoya disease/syndrome (MMD/MMS) treated at our tertiary care centre from 2000 to 2014 were analysed. The demographic, clinical characteristics, imaging details, treatment given & details of surgical procedures performed were reviewed. A comparison was made between the operated & non-operated groups for functional outcome. Results: Of the total 41 patients (females-19, males-22), 33 (80.48 %) had MMD & 8 (19.5 %) had MMS. The mean age at presentation was 6.26 ± 3.79 years (range: 0.6 months-14 years). Majority of the patients had ischemic events at onset; none presented with hemorrhagic manifestations. Twenty-eight (68.29 %) patients underwent revascularisation surgery (total of 33 surgical procedures, bilateral in 5 & unilateral in 13), 13 (31.7 %) were managed conservatively. The median duration of follow-up was 2.2 ± 1.85 years (range: 4 months–7 years). Three patients (10.71 %) had immediate post-operative neurological events. The rate of recurrent ischemic events amongst the surgically treated versus conservatively managed patients was none and 2 (15.3 %) respectively on follow-up. No mortality was observed in our cohort during the follow-up. Conclusion: We agree with previous studies that Indian patients with Moyamoya vasculopathy differ from their east Asian as well as European counterparts in terms of low fatality and better outcome. The availability of expertise in revascularisation surgeries in various centres should prompt surgery as an efficient & safe treatment option.

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**ICNC-0906: The analysis of indicators of Hemostasiogramm at children with a Hemorrhagic stroke**

Introduction: The imbalance of coagulative and thrombocytic levels of hemostasis is often a prime cause of the formation of arterial embolic cerebral involvement with formation of the brain infarction focus. Objective: Confirm hematologic changes at acute cerebrovascular accident at children. Methods: The haemostatic indicators of 15 children with hemorrhagic stroke in the acute and very acute periods were analyzed. The blood sampling for laboratory investigations was performed on the 1st and/or on the 5th day of hospitalization. Results: The analysis of hemostasiological...
Stroke and vascular disorders

Epilepsy after stroke in childhood; clinical observations

Introduction. Ischemic stroke (IS) and Hemorrhagic stroke (HS) are the rare childhood disorder, have different reasons and prognosis. Methods. We investigated and observed 68 children after stroke (42 children had IS, 26 had HS). Children had a debut of strokes between one month and 14-th years old. We studied symptoms in the acute period of stroke and outcomes syndromes since one year after. Results. In the acute period of IS 15 children (36%) had seizures. Since one year after acute IS 10 patients (24%) had epilepsy. The main types of seizures were secondary- generalization (in 70% cases). In that group 7 children had a pharmacological control of the seizures, but 3 (30%) had suffer from often seizures. In the acute period of HS 18 children (70%) had seizures. In the group of HS since one year 17 patients (65%) had epilepsy. Children had different types of seizures: 5 patients had infantile spasms, 4 had generalization and 3 had secondary- generalization seizures. In group of HS 10 children (59%) had not pharmacological control of the seizures. Conclusion. After HS in childhood we had patients with epilepsy frequency than after IS (65% and 24% accordingly, p<0.05%). Children had pharmacological resistant epilepsy in two parts often after HS compare with IS (59% and 30% accordingly).

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Stroke and vascular disorders

Paramedic management of childhood arterial ischemic stroke

Introduction and objectives. Ambulance usage is the most important factor resulting in shorter time to hospital arrival in adult stroke. Prenotification and bypass to stroke centres are associated with increased thrombolysis rates. Sensitivity of paramedic stroke identification in adults varies from 44-66% but there are no published data in children. Hypotheses and aims. We hypothesised that emergency medical services call-taker (EMSDCT) and paramedic identification of childhood arterial ischemic stroke (AIS) is suboptimal and contributes to prehospital delays. Our aims were to determine sensitivity of EMSCT and paramedic diagnosis, and to describe patterns and timelines of paramedic care in childhood AIS. Methods. Retrospective study of ambulance transported children <18 years with radiologically confirmed AIS, from

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Infection is associated with a hypercoagulable state in childhood stroke

Background: Infection is an associated risk for childhood stroke. The mechanism has been attributed to an infection-induced hypercoagulable state. However, there is no clear evidence to support this. Objective: We sought to evaluate the hypercoagulable markers of children with arterial ischemic stroke (AIS) with and without a confirmed infection. Methods: This is a single center retrospective case-control study of patients with stroke from 1991-2012. Charts were reviewed of children >28 days and <18 years of age with AIS. Blood work of patients with confirmed infection was compared to the control group of children with AIS without infection. Means of the blood work results was calculated and a t-test used to determine significance. Results: Seventy-seven patients with confirmed infection and AIS were identified and consented for the study. Preliminary reviews of 10 patients with infection were compared to 10 controls matched for age and gender. Results showed an elevated WBC count (p=0.03), platelets (p=0.04), activated protein C resistance (p=0.05), Factor VIII (p=0.01), Factor IX (p=0.03), and Factor XI (p=0.02) in the infectious group compared to the controls. Other markers such as ESR, CRP, INR, PTT, protein C, protein S, antithrombin III and fibrinogen were not significantly different between the two groups. Conclusion: This study provides the evidence that infection is associated with a hypercoagulable state and may be a cause of stroke in children. Early diagnosis of infection and treatment may reduce the incidence of stroke recurrence in this population.

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Characteristics of blood showed that initial aggregation properties of thromboocytes were approximately equally lowered at all patients. Tests of an indicator of ADF-AT in dynamics showed considerable decrease of it at 14 (93%) patients. Xllα-dependent fibrinolysis fluctuated >15 min. at 13 patients (N=5-12 min.). Ortofenantrolin test showed an increase in all patients from 5 to 22mg/100 ml (N=3,38 mg/100 ml). Protein C indicators were normal except of slightly increase in one patient - 1,4 (N=0,7-1,3). In 3 cases (20%) antithrombin-III was decreased. Indicators of the factor of Villebrand were increased in one case (7%), similarly to decreased indicator in another case (7%), in other cases it was normal. Concentration of fibrinogen in blood was authentically higher in 4 (26,6%) cases. Conclusion. To determine the risk factors of hemorrhagic stroke in young children, it is necessary to study carefully all indicators of haemostasiogram in all periods of stroke.
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ICNC-0911: Decrease in cerebral oxygen saturation during the six-minute walk test in patients with pediatric Pulmonary Arterial Hypertension

Objective: To investigate the relationship between the regional cerebral oxygen saturation (rSO2) during the six-min walk test (6MWT) and demographic-clinical features of the patients with PAH due to congenital heart disease. Methods: In this observational study, cerebral oxygenation was evaluated during 6MWT in 14 patients with PAH aged ≥7 years, who were diagnosed and followed at pediatric cardiology department. In all patients, rSO2 and heart rate were measured by near-infrared spectroscopy (NIRS) (SenSmart –Nonin) for 2 minutes before-baseline, during and 2 min after the walk test. The relation between the rSO2, heart rate, SpO2 values before, during and after 6-minute walk test and clinical/laboratory features were sought. Result: Fourteen patients (mean age 13, 6 years; 9 male, 5 female) were included. A statistically significant increase in heart rate and decrease in rSO2 values of the patients during 6MWT and after the walk test compared to baseline values were found. (Baseline heart rate mean ±SD: 94.92 ±16.7; during 6MWT heart rate mean ±SD:107.87±15.3, after the walk test heart rate mean ±SD: 108.89±14.2 (p<0.005). Baseline rSO2 mean ±SD: 76.44±9.07; during 6MWT rSO2 mean ±SD:69.81±12.2, after the walk test rSO2 mean ±SD:66.94±12.6; (p<0.005). Conclusion: Exercise performance in children with PAH is very limited. The 6MWT is a simple method used to evaluate exercise capacity in adults and children with cardiac diseases. Regional cerebral desaturation may occur during daily activities in pediatric PAH patients. rSO2, SpO2 and heart rate monitoring during 6MWT may help us to identify those patients with limited cerebral oxygenation capacity thus guide us to take needed precautions.

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Stroke and vascular disorders

ICNC-0912: Pediatric moyamoya: the 17-years experience of an Italian neurology unit

Introduction: Moyamoya (MM) has currently received an increasing interest as cause of cerebral ischemic events and poor neurological outcome in children. To date, the larger series belong to Asiatic centers. Methods: Retrospective analysis of cases followed between 1998 and 2005 years. Results: 12 patients, 4 males. Age at diagnosis: 11 months-11 years (under 3 years: 6/12), 5 cases had MM syndrome; 3 familial MM disease. 11/12 patients had symptoms at diagnosis: 5 stroke (3/5 associated to focal seizure, 2/5 preceded by TIA episodes); 3 TIA. 1 case previous history of focal seizures; 3 headache. Lapse time symptom onset to diagnosis: 1 week-1,5 years. Neuroimaging at diagnosis: ischemic lesions (5); bilateral (9) unilateral (3) MM, posterior circulation involvement (3). Follow-up: 1-18 years, mean 6,5 years. 1 patient remained asymptomatic; others: focal seizures (3), TIA (3), second stroke (1), headache (4); persistent motor deficits (5); cognitive problems (6). Therapy: acetylsalicylic acid (8), plus flunarizine (4); antiepileptic drugs (4). 5 were treated surgically with indirect revascularization: 1/5 operated elsewhere suffered a severe hypoxic damage during surgery; the others experienced clinical improvement (TIA and stroke-free, controlled epilepsy) and stable/improved angiopathy. Conclusion: Our series is characterized by similar clinical presentation and outcome compared with other pediatric experiences. Interestingly, we appreciated a greater proportion of early disease onset and lower frequency of diagnostic delay from symptoms onset. Four out of five patients improved after neurosurgery, confirming the importance of a prompt surgical treatment in the attempt to modify the natural history of the disease.

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ICNC-0914: Rare neurocutaneous disorders associated

Introduction: Moya-moya syndrome is an occlusive cerebrovascular disorder of unknown pathogenesis complicating various neurocutaneous and connective tissue disorders. It is characterized by progressive stenosis of the bilateral supraclinoid internal carotid arteries, with concomitant formation of tortuous arterial collateral vessels. The steno-occlusive areas are usually bilateral, but unilateral involvement does not exclude the diagnosis. In our pediatric moya-moya clinic we follow patients with moya moya syndrome and moya moya disease (idiopathic moya moya), pre and post-surgical treatment, in collaboration with pediatric neurosurgery, neuroradiology and thrombosis and homeostasis clinic.

Objectives: In this study we describe the features of four selected moya-moya syndrome patients each suffering from a rare underlying neurocutaneous or vascular disorders. Conclusions: Moya moya syndrome should be considered in children with various neurocutaneous diseases and vascular disorders with focal neurological symptoms. The diagnosis and treatment in these children is complicated and requires a multidisciplinary team and various radiologic surgical and medical facilities.

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Syndromes & Autism

ICNC-0492: OSHA: a multidisciplinary successful protocol for autistic children treatment

OSHA program aims treating autistic children by diverting them to the average normal and to be ready for academic life. Inclusion Criteria: the age to start was <6 years, full consent of parents for program steps and instructions given and the program goes on for 1-3 years. Exclusion Criteria: Fragile X syndrome or tuberous sclerosis or other chronic non-neurological diseases METHODS: DS-5 criteria and CARS scoring for diagnosing autistic children. Language, cognitive, self-dependence, motor and social skills assessments. EEG, Vineland assessment and intellectual assessment were also applied OSHA program were done by applying many hours of rehabilitation/week for each child depending on: 1- Severity of autism: for weekly credit hours (not less than 25 hours/week) 2- Social defect: diversity of specialists 3- Language defect: diversity of plans 4- Learning defect: diversity of training places 5- Family role 65 cases (40 boys and 35 girls) were included and mean age was 3 years. Youngest was a boy aged 15 months. The mean duration of working was 16 months and shortest duration was 8 months. Full improvement was recorded in 69% (45 cases) the criteria of success 1- Young age for diagnosis and starting the treatment 2- Not associated with epilepsy 3- Cooperation between home and center 4- Love Conclusion: the OSHA program is applying many daily hours of working with autistic children. Early intervention in a Well-run program & Multi-disciplinary team work are the key for helping autistic children to reach their potential

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Syndromes & Autism

ICNC-0332: Application of Array-Based Comparative Genomic Hybridization to pediatric neurologic diseases

PURPOSE: Array comparative genomic hybridization (array-CGH) is a technique used to analyze quantitative increase or decrease of chromosomes by competitive DNA hybridization of patients and controls. This study aimed to evaluate the benefits and yield of array-CGH in comparison with conventional karyotyping in pediatric neurology patients.

MATERIALS AND METHODS: We included 700 patients from the pediatric neurology clinic with at least one of the following features: developmental delay/intellectual disability, dysmorphic features, microcephaly, multiple congenital anomalies or refractory epilepsy. Results are compared with G-band karyotyping. The results were analyzed with findings reported in recent publications and internet databases.

RESULTS: Array CGH yielded abnormal (pathogenic) results in 189 of 700 patients (27%), and normal in 511 patients (73%). CONCLUSION: Although there were relatively small number of tests in patients with pediatric neurologic disease, this study demonstrated that array-CGH is a very useful tool for clinical diagnosis of unknown genome abnormalities performed in pediatric neurology clinics

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Syndromes & Autism

ICNC-0333: The genetic characteristics of epileptic encephalopathy in children of uzbek population

Relevance. Disclosure of genetic aspects of epilepsy is necessary for a clear understanding of the etiology and pathogenesis of this disease, the search for new ways of correction. Objective: to study the molecular and genetic aspects of epileptic encephalopathy and symptomatic epilepsy in children Materials and Methods: We have analyzed 30 indicators of gene polymorphism SCN1A among 20 studied children with epileptic encephalopathy and 20 healthy children. Results: Of the total sample of patients with epileptic encephalopathy in children (n = 20) polymorphism 3184 A-G met in the homozygous state (3184 * A / * A) in 8 patients (40%) in the heterozygous state (3184 * A / * G) - 11 (56%) and homozygous genotype (3184 * G / * G) was identified in only 1 patient (4%). In healthy children (n = 20) polymorphism 3184 A-G met in the homozygous state (3184 * A / A) in 6 patients (60%) in the heterozygous state (3184 * A / * G) - in 4 (40%). Conclusion: Thus, considering all of the above it can be concluded mutations and polymorphisms in the gene SCN1A neuronal sodium channel leads to an increase in recovery time channel activity after inactivation and, as a consequence, provoke neuronal hyper excitability. We observed changes in the nucleotide sequence of the gene SCN1A that can make some contribution to the development of susceptibility to epileptic encephalopathy in children Uzbek nationality.

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Syndromes & Autism

ICNC-0493: Autism spectrum disorders: a necessary prevalence study in Santa Fe, Argentina

Introduction: Autism spectrum disorders (ASD) seem to be dramatically raising up in numbers during the last two decades. Prevalence of ASD studies in our country are none. This group of investigators is trying to determine the prevalence of ASD in children from Santa Fe, Argentina. Believing that numbers rule many of government decisions along with health administrators, educational services administrators to establish policies that could cover the multiple needs of children with autism we planned this project at FCM/UNL. Methods: Prevalence is a proportion, the study design respected principles of probabilistic sampling. Groups own attributes allow to run a study taking on account its age, gender, social level, occupation. … Following those principles a stratified sampling strategy was needed. This requires: to establish attributes, define how many attributes a population has, to know total number of population belonging to each strata, to take a random sample from each strata. The formula to calculate is: Our Prevalence Study population: children ages 18 to 36 months old, last 2010 national census Age (years) 1 2 3 TOTAL Total 6067 5852 5737 17656 Z

Expected prevalence: p=0,00885, where (1-p)= 0,99115 Accuracy: d = 0,008 (estimation error 0,8%) Infinite population: Correcting to finite population: Sample number = “n” children 1-3 years old = 512 Results: 512 children ages 18 month to 36 month old was require to a random stratified study sample to determine TEA Prevalence in our city.

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Syndromes & Autism

ICNC-0479: A case of chromosome 9 trisomy mosaicism not detected by conventional karyotyping or standard aCGH analysis method.

[Introduction] Chromosome 9 mosaic is a rare condition associated with variable features, and is difficult to diagnose by conventional karyotyping. We present a case whose trisomy was not detected by intensive karyotyping or standard aCGH analysis method. [Case] An 18-month-old dysmorphic female patient with severe psychomotor retardation was referred to our hospital. She had a history of severe IUGR, and suffered from respiratory and feeding difficulty, and recurrent pneumonia. Subtle seizures were noted during early infancy. Clinical investigation revealed bilateral hearing loss. [Cytogenetic testing] Karyotype: 46,XX [20/20 at neonate, 1,000/1,000 at 18 months]; Array CGH (Agilent CGH+SNP 180K): Complete 9 chromosome amplification [AverageLogRatio: 0.21]; Interphase FISH for ABL gene (9q34.1): 3 signals in 24.0% [240/1,000] on buccal samples, and 28.6% [20/70] on blood samples. [Discussion] We experienced a female patient whose trisomy mosaic was not detected by intensive karyotyping or standard aCGH. aCGH signals slightly shifted to the patient-side throughout chromosome 9. This aberration was not detected by standard analysis method CGH+SNP v2 provided by Agilent due to the cut-off AverageLogRatio value of <0.25. The re-calculated LogRatio of chromosome 9 was 0.21. Subsequent interphase FISH analysis revealed 24–29% trisomic cells, which confirmed the diagnosis. We speculate that trisomy 9 cells have some growth disadvantage during blood cultivation using PHA stimulation. The cut-off LogRatio value of 0.25 can only allow the detection of more than 38% trisomic cells. These practical pitfalls, and the limitations of conventional karyotyping and standard aCGH analysis in mosaic detection should be noted.

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Syndromes & Autism

ICNC-0494: Changes of event related potentials (ERPs) and depression rate in children with attention deficit hyperactivity disorder (ADHD) plus subclinical depression

Introduction: Depression is one of the most frequent comorbidity in children with ADHD. Recent studies show that cognitive event related potentials (ERPs) especially late response (P3) might serve as endophenotypes for discriminating depressed patients from healthy individuals. It was hypothesized that in depressed children the amplitude of P3 is decreased in left frontal lobe emphasizing the hypofrontality underlying ADHD. Thus the aim of our study was to assess the changes of P3 parameters in ADHD children with subclinical form of depression as well as the evidence of depression severity before- and after treatment with EEG biofeedback. Methods: We have examined 43 children with ADHD plus depression and 39 healthy individuals of the same age (Age range 9-12 years). Depression was assessed with Beck Depression Inventory (BDI-II). P3 was recorded using GO/NOGO stimulus with auditory modality. 30 session of EEG biofeedback was conducted by alpha training according to Rosenfeld protocol. Repeated measures multivariate analysis of variance was used to test the difference of P3 and BDI-II parameters before- and after treatment. Results: We have found the decrease of P3 amplitude in left frontal lobe after 30 session of EEG biofeedback training in children with ADHD plus subclinical depression (p<0.01). The same was found for BDI-II in ADHD plus subclinical depressed children.
compared with controls (p<0.01). Conclusions: According to our results we have concluded that EEG biofeedback can be used as a successful method for treatment of subclinical depression in children with ADHD. This is very important as the use of antidepressants has to be restricted due to adverse events which is extremely challenging in this age group.

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Syndromes & Autism

ICNC-0483: Maternally inherited autosomal dominant intellectual disability caused by 16p13.3 microduplication

A 16p13.3 duplication syndrome has been recently suggested to be a novel recognizable syndrome as a reciprocal microduplication disease of Rubinstein-Taybi syndrome. The CREBBP gene is believed to be the dosage-sensitive critical gene responsible for the reciprocal duplication and deletion syndrome. Descriptions so far have been de novo. Here, we report a very rare case of maternally inherited 16p13.3 duplication identified by SNP array testing. The study provides additional information that further the understanding and delineation of 16p13.3 duplication syndrome. Key words Chromosome 16p13.3 duplication syndrome, Maternal inheritance, Autosomal dominant, Intellectual disability, CREBBP

Syndromes & Autism

ICNC-0482: Presentation a phase II randomized placebo-controlled double-blind pilot clinical trial to test safety and effectiveness of Ascorbic acid and Alpha-Tocopherol on behavioural and learning problems in the Fragile X syndrome

A Phase II randomized, double-blind clinical trial to show whether the combination of 10 mg/kg/day of ascorbic acid(vitamin C) and 10 mg/kg/day of alpha-tocopherol(vitamin E) reduces hallmarks among male patients aged 6–18 years, compared to placebo treatment, as measured by the Conner’s Parent and Teacher Rating Scales, and also WISC-R scales at baseline, 12 weeks and 24 weeks. Scope: 30 male children and adolescents affected with Fragile X syndrome. Instrumentation: clinical data, blood analysis and Conner’s Parent and Teacher scores will be obtained at the base line (T0). The follow up examinations after 12 weeks (T1:15 patients in the treated group and 15 patients in the placebo group) and 24 weeks (T2:30 patients in the treated group). Group A (6 to 12 year olds) and group B (13 to 18 year olds). Mean age (SD) 11.67 (4.20) [treated subgroup: 12.13 (3.44); placebo subgroup: 11.71 (4.86)]. A significant improvement in direct scores in total manipulative and total verbal subscales were observed in group A. A significant reduction of hyperactivity/impulsive rage in the Conner’s Parent Rating Scales, and a strong response in the group of 6 to 12 years, when hyperactive symptoms are much more intense. We propose a reduction of behavioural and learning problems by antioxidant treatment in a subgroup of young patients affected with the syndrome. These symptoms can be ameliorated by a combination of antioxidant compounds such as Alpha-tocopherol and Ascorbic acid.

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Syndromes & Autism

ICNC-0495: Treatment of Pathological laughing and crying in children

Objective – Pathological laughing and crying (PLC) is characterized by involuntary and uncontrollable laughing and/or crying episodes incongruent to the patient's mood. The objective of this study was to evaluate the treatment of PLC in children. Methods – This was a retrospective study conducted at the neuropediatric clinic of our University Hospital. Inclusion criteria was age up to 18 years-old and episodes of uncontrollable laughing or crying consistent with PLC. Exclusion criteria were the presence of an underlying mood or personality disorder that could explain the abnormal emotion expression, Angelman syndrome and hypothalamic hamartoma. Results – Twelve patients met the inclusion criteria, seven boys, five girls; ages ranging from three to 18 years-old (mean = 8.4 years-old). All patients had pathological laughing; and only four had pathological crying. Treatment was considered when the family reported that PLC was disrupting the child quality of life. Only three patients needed treatment. Risperidone was highly effective in all of them, with no side effects. Conclusion – We conclude that when treatment is needed in PLC risperidone is a safe and effective option providing major improvement in quality of life.

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Syndromes & Autism

ICNC-0489: Maternal inheritance, Autosomal dominant, Intellectual disability, CREBBP words Chromosome 16p13.3 provides additional information that further the understanding and delineation of 16p13.3 duplication syndrome. Key words Chromosome 16p13.3 duplication syndrome, Maternal inheritance, Autosomal dominant, Intellectual disability, CREBBP
Syndromes and autism

ICNC-0484: Presentation Persistent T2 hyperintensity in terminal zones of brain MRI in a global delay case with IL1RAPL1 gene deletion

Introduction: IL1RAPL1 gene deletions have been associated with developmental delay and autistic spectrum disorders. (1) Persistent T2 hyperintensity in brain magnetic resonance imaging (MRI) implied myelination is processing and this phenomenon will be disappeared while the process is complete about age 3 years. (2) We reported one 3 years old boy with global delay, autistic behavior, and finally genetic confirmation with IL1RAPL1 gene deletion. Persistent T2 hyperintensity over terminal zones was noted during follow up. Case report: This child was the firstborn child of nonconsanguineous phenotypically normal parents. At age 11 months, he was admitted to our hospital for developmental delay. On general examination, nonspecific dysmorphic features were noted. A brain MRI scan revealed symmetrical hyperintensity noted in FLAIR and T2-weighted images in the "Terminal zones". On 2 years and 9 months of age, array comparative genomic hybridization was suggested and revealed one copy of deletion in the Xp21.2-p21.3 cytogenetic band, where the ILRAPL1 gene is located. Now 3 years of age, the boy has profound intellectual disability. Follow up brain MRI showed static hyperintensity over terminal zones. Discussion: To our best knowledge, less than ten families with changes affecting only the IL1RAPL1 gene have been reported. (3) Our case with global delay and autistic behaviors showed intragenic deletions of IL1RAPL1, which later confirmed being de novo. It is worthy to note that persistent T2 hyperintensity over terminal zone should alert clinical physicians to perform genetic survey in global delay cases and add knowledge to the phenotypic spectrum of IL1RAPL1 mutations. Reference 1. Hayashi T et al. PLoS One 2013;8:e66254.2. Cecilia P et al. Am J Neuroradiol 2002;23:1669-1673. Behneche A et al. Am J Med Genet A. 2011;155A(2):372-379.

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Syndromes & Autism

ICNC-0496: Preliminary evidence for a role of enterovirus 71 in Autistic Regression

Objective: Due to the increasing prevalence of Autism Spectrum Disorder (ASD) and recent epidemics of neurotropic enterovirus infections, we investigated whether there is evidence for persistent Enterovirus 71 (EV71) infection in children with autistic regression. Methods: Anti-EV71 IgM to assess ongoing EV71 infection and IgG to assess past infection were measured by ELISA in plasma samples from children with ASD who enrolled in a clinical trial 2008-2014 (N=129) and were compared to an age matched control group (N=20). IgM+ and IgG+ status in the ASD group were compared to measures of regression on ADI-R and brain alpha-[11C]methyl-tryptophan (AMT) PET findings. Results: Comparisons of the proportions of IgM+ (0% control, 5% ASD, p=1.0) and IgG+ cases (15% control, 20% ASD, p=0.766) showed no significant differences between the control and ASD groups. Within the ASD group, however, loss of language (p=0.037), language loss due to illness (p=0.025) and the combined loss language or other skills due to illness (p=0.008) were related to presence of anti-EV71 IgM. Loss of language or other skills were not related to presence of IgG (p=0.693). Whole brain AMT uptake was higher in the anti-EV71 IgM+ group (p=0.006), but not in the IgG+ group (0.087). Unilateral AMT focal increases were observed in fusiform/parahippocampal gyrus in 5/6 IgM+ cases. Conclusions: The significant relationships between anti-EV71 IgM antibody and language regression and brain AMT PET provide sufficient evidence to merit further study of IgM and the virus itself in larger collections of ASD blood and brain specimens.

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Syndromes & Autism

ICNC-0497: Efficacy of low dose Buspirone for restricted and repetitive behavior in young children with Autism Spectrum disorder

Objectives: The purpose of this study was to determine safety and efficacy of the 5HT1A serotonin partial agonist buspirone on core autism and associated features in children with autism spectrum disorder (ASD). Study Design: Children with ASD 2-6 years old (N=166) were randomized to receive placebo, 2.5 mg or 5.0 mg buspirone twice daily. The primary objective was to evaluate the effects of 24 weeks of buspirone on the Autism Diagnostic Observation Schedule (ADOS) Composite Total Score (CTS). Secondary objectives included evaluating effects of buspirone on social competence, repetitive behaviors, language, sensory dysfunction and anxiety, and side effects. Positron emission tomography (PET) measures of tryptophan metabolism and blood serotonin concentrations were assessed as predictors of buspirone efficacy. Results: There was no difference in the ADOS-CTS between baseline and 24 weeks among the three treatment groups (p=0.400). However, the ADOS Restricted and Repetitive Behavior score showed a time by treatment effect (p=0.006); the 2.5 mg buspirone group which showed significant improvement (p=0.003), whereas placebo and 5.0 mg buspirone groups showed no change. Children in the 2.5 mg buspirone group were more likely to improve if they had fewer foci of increased brain tryptophan metabolism on PET (p=0.018) or if they showed normal blood serotonin (p=0.044). Adverse events did not differ significantly among treatment groups. Conclusions: Treatment with 2.5 mg buspirone in young children with ASD might be useful adjunct therapy to target restrictive and repetitive behaviors in conjunction with behavioral interventions, which are effective in improving social communication and adaptive behavior.

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ICNC-0498: Reduction of non-verbal IQ in preschool children with Sickle Cell Anaemia

Background: Children with sickle cell disease (SCD) are at-risk for stroke and cognitive difficulties. Intellectual quotient (IQ) has been reported to decrease in school-age children with SCA with increasing age even when there is no evidence of stroke. One previous study looked at IQ in children with SCD <6 years without evidence of stroke (n=26), however they combined genotypes, did not look at age-effects, and did not use matched controls. The current study aims to investigate whether there are IQ differences between SCD patients and ethnicity, age-matched controls, as observed for school-age children, and if this is predicted by increasing age and other disease-related factors.

Method: Twenty-two children with SCA between 3-5 years, with no history of stroke, were compared with a matched comparison group. The Wechsler Scales were administered to obtain IQ. Results: The patient group were, on average, 3-4 points lower than the comparison group in all three domains, similar to the average 4.3 point difference reported for older children with SCA in a recent meta-analysis. However, there were no significant differences between the two groups on verbal (99.9v103.8), non-verbal (97.8v100.9), or full scale IQ (98.6v101.5). Patients showed a significant decline in non-verbal IQ with age (r=-.549, p=.008), but not with other measures of disease severity and socio-economic status. Conclusion: This study shows evidence for a widening gap in non-verbal IQ even at this early stage of development, placing emphasis on the importance of early neuropsychological assessment in children with SCA.

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References:
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ICNC-0499: Attention deficit/hyperactivity disorder and urinary nonylphenol levels: a case-control study in Taiwanese children

Introduction: Animal studies had suggested that endocrine-disrupting nonylphenol (NP) exposure might promote motor hyperactivity, likely by causing deficits in dopaminergic neurons. The aim of this study was to explore the association between child NP exposure and ADHD while controlling for several of the most studied covariates, such as lead levels and dopamine-related gene polymorphisms.

Methods: A case-control study was conducted on clinically diagnosed ADHD; and the Swanson, Nolan and Pelham, Fourth Revision (SNAP-IV) questionnaire was used to identify normal controls, ages 4-15 years. Participants were examined for urinary NP concentrations, blood lead levels, and selected single-nucleotide polymorphisms of two dopamine-related genes (D4 dopamine receptor gene, DRD4, and dopamine transporter gene, DAT1). Socio-demographic variables, maternal lifestyle factors during pregnancy and family medical history were obtained using a questionnaire.

Results: A total of 97 children with doctor-diagnosed ADHD and 110 normal controls were enrolled. The blood lead levels of both groups were similar (1.57±0.73 vs. 1.73±0.77 μg/dL, p=0.15). No significant difference in the urinary NP concentrations was found between ADHD and control subjects (4.52±3.22 μg/g cr. vs. 4.64±2.95 μg/gcr., p=0.43). Allelic association trend tests showed that rs752306 of DRD4 was significantly associated with ADHD (p<0.01). The regression model indicated no increased odds of having ADHD with NP exposure after adjustment for confounding variables.

Conclusion: This study indicated that NP exposure might not promote ADHD in children, even though children in Taiwan had relatively high levels of NP compared to those reported previously and in other nations.

Key words: Nonylphenol; ADHD; Blood lead level; Gene polymorphism; Children

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ICNC-0500: A possible association between elevated serum levels of brain-specific auto-antibodies and reduced plasma levels of docosahexaenoic acid in autistic children.

Polyunsaturated fatty acids (PUFAs) are not only essential for energy production, but they also exhibit a range of immunomodulatory properties that progress through T cell mediated events. Autoimmunity may have a pathogenic role in a subgroup of autistic children. This study is the first to investigate the relationship between serum levels of anti-myelin basic protein (anti-MBP) brain-specific auto-antibodies and reduced plasma levels of PUFAs in autistic children. Plasma levels of PUFAs (including linoleic, alphalinolenic, arachidonic “AA” and docosahexaenoic “DHA” acids) and serum anti-MBP were measured in 80 autistic children, aged between 4 and 12 years, and 80 healthy-matched children. Autistic patients had significantly lower plasma levels of PUFAs than healthy children. On the other hand, ω6/ω3 ratio (AA/DHA) was significantly higher in autistic patients than healthy children. Low plasma DHA, AA, linoleic and linoleic acids were found in 67.5%, 50%, 40% and 35%, respectively of autistic children. On the other hand, 70% of autistic patients had elevated ω6/ω3 ratio. Autistic patients with increased serum levels of anti-MBP auto-antibodies (75%) had significantly lower plasma DHA (P b 0.5) and significantly higher ω6/ω3 ratio (P b 0.5) than patients who were seronegative for these antibodies. In conclusions, some autistic children have a significant positive association between reduced levels of plasma DHA and increased serum levels of anti-MBP brain-specific auto-antibodies. However, replication studies of larger samples are recommended to validate whether reduced levels of plasma PUFAs are a mere association or have a role in the induction of the production of anti-MBP in some autistic children.

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ICNC-0485: Clinical spectrum of distal 1q21.1 microdeletion

Introduction: The distal 1q21.1 microdeletion can be detected by molecular methods that determine the copy number of sequences within the deleted region, including chromosomal microarray analysis. This entity has an autosomal dominant inheritance with variable findings that most commonly include mild-moderate developmental delay, mild dysmorphic facial features, microcephaly, eye abnormalities, cardiac defects, genitourinary abnormalities, seizures, intellectual disability and behavioral abnormalities. Manifestations vary widely from asymptomatic to severe affected patients.

Methods: We describe the clinic features of 5 patients diagnosed of distal 1q21.1 microdeletion in our center.

Results: Four of five subjects have a head circumference under 2 DS, four have mild dysmorphic features and four have speech disorder. Three patients have an attention deficit hyperactivity disorder and two have a mild-moderate mental retardation. One patient presented transient muscle tone alterations and tics and another one presented transient
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dystonic movements. One case has short stature and skeletal abnormalities and in other case renal examination found a vesicoureteral reflux. Family genetic studies have allowed to find two carriers with less clinical manifestations.

CONCLUSIONS: We found that microcephaly, mild dysmorphic features, speech disorders, attention deficit hyperactivity disorder and mild-moderate mental retardation are features we usually found in patients with distal 1q21.1 microdeletion. This entity has a high variable expression and that’s why there is not a clinically recognizable syndrome. Usually carriers have less severe clinical manifestations.

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Syndromes & Autism
ICNC-0486: Selective single base deletion in BCL11A gene is associated with severe oral, speech and manual dyspraxia: A case report.

Introduction: Phenotypic similarities of the 2p15p16.1 micro-deletion syndrome include growth retardation, microcephaly, optic nerve defects, anomalies in brain anatomy, kidney defects, dysmorphic features, intellectual disability, and gross motor impairments. Size of the deletions range from 0.2 to 5.7 Mb, commonly including the BCL11A gene. Case description: We report the detailed psychometric evaluation of a 7 year-old boy with moderate intellectual delay (IQ of 53), mild facial dysmorphism and persistent saliorrhea. He presented severe expressive speech disorder, combined with oral and manual dyspraxia. Results: A brain MRI (1.5 Tesla) and an 180K CGH-array (Bluegnome) returned normal results. Exome sequencing demonstrated a de novo cytosine deletion in exon 4 of BCL11A that led to apremature stop codon. Discussion: BCL11A is situated in a region referred to as dyslexia susceptibility candidate region 3. In mice, this has recently been shown to control cell polarity and radial migration of upper layer cortical neurons, with deletions resulting in hypoplasia of the superficial neo-cortex. To our knowledge we report the first case of a de novo single base deletion in BCL11A. Our patient presented with symptoms strikingly similar to a patient recently described by Peter et al. (Peter et al., 2014) who presented 2p15p16.1 micro-deletion syndrome limited to a full BCL11A deletion. Conclusion: Although further research is still required, we propose to include BCL11A analysis in the genetic workup of patients presenting with childhood apraxia of speech associated or not with mild tomoderate intellectual deficiency. Peter, B. et al. (2014). De novo micro-deletion of BCL11A is associated with severe speech sound disorder. Am. J. Med. Genet. A 164A, 2091–2096.

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Syndromes & Autism
ICNC-0502: Cardiovascular autonomic dysfunction in children with Rett syndrome; a cross sectional study

Introduction: Autonomic dysfunctions are common in children with Rett syndrome. They usually manifest with agitation, persistent screaming, constipation, gastroesophageal reflux, apnoea, hyperventilation and breath holding spells. Cardiovascular autonomic dysfunctions are known which at times may result in fatal arrhythmias. Many of these events are mistaken as seizures and treated with antiepileptics which may precipitate arrhythmias. Methods: The current study was conducted in a tertiary care teaching hospital in North India over a 6 month period. MeCP2 mutation positive, 24 children with Rett syndrome and 24 healthy age matched girls, were evaluated for cardiovascular autonomic dysfunction (heart rate variability (HRV), head up tilt (HUT) test and cold pressor test (CPT)). Results: The mean age in years was 9.06 (+/- 3.4) and 9.75 (+/- 3.13) for patients and controls respectively. The HRV contributed independently by parasympathetic and sympathetic nervous system was significantly reduced in cases as compared to controls (p=0.033 and p=0.001 respectively). There was significant sympathovagal imbalance with sympathetic overactivity in cases as compared to controls (p=0.001). CPT and HUT could be done in 16 RTT patients (due to poor cooperation) and in all 24 controls. The change in blood pressure during CPT and HUT was not significantly different in cases and controls. Conclusion: Children with Rett syndrome were observed to have significant cardiovascular autonomic dysfunction in the form of sympathetic overactivity, parasympathetic underactivity and sympathovagal imbalance compared to their age and gender matched healthy controls. This has important therapeutic and outcome related implications.

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ICNC-0503: BDNF in children with epilepsy
Objective: assessment of serum BDNF levels in children with epilepsy. Materials and methods: We assessed serum BDNF levels via immunoenzymatic method in 23 children, aged between 3 month and 3 years old, presenting epilepsy with CNS perinatal hypoxic-ischemic antecedents, and 25 healthy controls. Results: Our results show decreased serum BDNF in 3 months old children who developed epilepsy as compared to the control group (p < 0.001). BDNF levels were much lower as the neurophysiological changes (rxy = -0.72, p <.05) and imaging (rxy = -0.68, p <.05) were severe. We also noticed higher rates of growth of BDNF levels in children with epilepsy at the age of 1 year (18.5%) compared to healthy children (1.5%), but in absolute values the study group still presented lower BDNF levels compared to controls (rxy = 0.876, p <0.001). Conclusions: Serum BDNF levels were significantly lower in children with structural epilepsy (aged 3 month – 3 years) in comparison to controls, correlating with neurophysiological and neuroimaging changes. This result highlights the role of BDNF in epileptogenesis. BDNF levels also increase during the child’s growth, thus suggesting its involvement in neurodevelopmental processes. The negative correlations between BDNF levels and the severity of the epilepsy and structural abnormalities of brain tissue suggest its interest as a neuronal lesion biomarker.

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Syndromes & Autism

ICNC-0504: Behavioral disturbances in children with epilepsy
Children with epilepsy have an increased risk of presenting various behavioral problems. Objective: The aim of this study was to determine the influence of behavioral disturbances on the quality of life of children with epilepsy. Materials and methods: study group included 241 children, aged 3 months - 5 years, diagnosed with structural epilepsy (consequences of perinatal hypoxic-ischemic encephalopathy). Behavioral disorders were defined according to the criteria of ICD-10 and DSM-V. Results: Behavioral disorders were observed in 163 patients with structural epilepsy (67.6% 95CI 64.59-70.61), predominantly expressed by hyperactivity (19.4%), inattention (22.3%), conduct disorder (22, 1%) and bouts of aggression (36.2%). The age of onset of behavioral disorders ranked between 2 and 3 years old. Behavioral disorders correlated with the severity of epilepsy (rxy = 0.49, p<0.05). Conclusions: behavioral disorders are often observed in children with epilepsy, they are characterized by a clinical variability and correlate with the severity of the epilepsy. Thus behavioral disorders can be considered as risk factors and require psychiatric and psychotherapeutic treatment.

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Syndromes & Autism

ICNC-0505: Amygdala functioning to developmental disorder and psychic trauma in children
Objective: A new multidisciplinary research project studying developmental brain damage in medical and educational settings and using the Miyazaki perinatal network system has been supported by a Grant from the Japanese Government (website:www.med.miyazaki-u.ac.jp). This work explores what is known about cognitive processes involved in emotion and temperament and at the same time it clarifies the processes and anatomical structures involved in emotion, temperament and behavior. We aimed to clarify if emotion and its neural substrates require further study for long term (20-years). Method: Social communication in nonhuman primates and humans is strongly affected by facial information from other individuals. Many cortical and subcortical brain areas are known to be involved in processing facial information. In this study we used a long-term incentivized experiment to study this experience of emotion derived from observation of facial information in others. Results: Nearly 2,000-participants were enrolled. Data showed that there was a gender difference in the conscious experience of emotion (and therefore in amygdala functioning) induced by facial information (joy, anger, and pathos) and this gender difference appeared when the participants are aged older than 3 to 20 years. Conclusion /Discussion: We discuss the reasons for particular decisions being made and highlight any important learning points or lessons. In this study, we summarize the process of emotion generation, the functions of the amygdala, the conscious experience of emotion, its regulation, dysregulation, and a proposed approach to child psychic trauma.

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Syndromes and Autism

ICNC-0334: Phenotypic spectrum of PRRT2 mutations in Taiwanese families

Introduction Benign familial infantile epilepsy (BFIE) occurs between 6 months and 2 years old. Paroxysmal kinesigenic dyskinesia (PKD) is characterized by choreoathetoid and/or dystonic movements without alteration of consciousness, which onset in the first two decades. Mutations in PRRT2 gene have been identified as the major cause for BFIE, PKD and infantile convulsions and choreoathetosis (ICCA). Herein, we studied seven Taiwanese families with PRRT2 mutations and expanded the associated phenotype. Methods We performed mutation analysis using Sanger sequencing of all coding exons of PRRT2 gene in seven families with BFIE, or familial PKD. Results Three PRRT2 mutations, including two novel mutations were identified in 16 patients from seven families. 12 patients (75%) had the hot spot mutations c.649-650insC, p.R217fs*8. Three patients from one PKC family had a novel c.696_696del CA, p.H232Qfs*10 frameshift mutation. One familial PKC proband had missense mutation c.893T>C, p.L298P. Among the seven families, six patients (38%) had PKD and seven patients (44%) had BFIE. We also found three patients (19%) presented with late onset epilepsy around school age (7-10 years) instead of BFIE with/without PKD. The late onset epilepsy was usually self-limited and pharmaco-responsive. Conclusion We identified seven Taiwanese families with PRRT2 gene mutations. Most of them have the reported common hot spot mutation (p.R217fs*8), while two families with novel mutations (p.L298P, p.H232Qfs*10) were also found. Our study suggested that the spectrum of PRRT2 related phenotype is broader than previous conceived. In addition to BFIE, PKC and ICCA, late onset benign epilepsy without BFIE was also observed.

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Syndromes & Autism

ICNC-0487: 3p Deletion Syndrome

Introduction: 3p Deletion syndrome is a rare condition and has been proposed as a contiguous gene syndrome with the spectrum of defects depending upon the size of the deleted segment. Since the first case was reported in the medical literature by Verjal M and De Nef J in 1978, around 50 people with pure 3p25 deletion involving no other chromosome have been referred and the phenotype has been established. Objective to describe a new case of 3p syndrome Case Description: the patient suffered from developmental delay, dimorphic physical features, BPES (A complex disorder with blepharophimosis, ptosis, and epicanthus inversus) and growth retardation. The clinical findings of our case were severe. G-banded chromosome analysis revealed a de novo heterozygous deletion of the short arm of chromosome 3: 46, XY, q1±, del (3) (p25).Thirty metaphases were examined for numerical as well as structural abnormalities. Mother, father and sister had normal karyotype. Over time, mental and physical retardation became evident. Brain were structurally normal by MRI (Magnetic Resonance Image) Electroencephalogram was disorganized and slow without paroxysm Conclusion: Recognize the syndrome 3p in a patient allows to identify others syndromes that have BPES and mental retardation like Odho and Young Simpson.

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Syndromes & Autism

ICNC-0506: The availability of services for children with Autism Spectrum Disorder in a Saudi population

Background: Children with autism spectrum disorder should be evaluated and placed in specialized multidisciplinary programs to increase the likelihood of a favorable outcome. Delay is reported in the provision of such services, mostly due to the under-developed service system. We aimed to study the availability of various services in our region. Methods: A cross sectional study was conducted involving health care workers at various governmental and private autism centers. A structured 30-item questionnaire was designed to assess their demographics, training, experience, and the availability
of various services at their centers. Results: 12 autism centers were included and 136 employees participated in the study. Seventy-eight (57%) participants mentioned that their center lacks important and needed services. These included programs for home care and outreach (59%), family recognition incentives and rewards (51%), integrative educational programs (39%), and occupational therapy (16%). Access for outside referral for these services was available in only 24% of cases. They cited several major obstacles in providing adequate service including; family involvement (24%), child’s behavioral problems (13%), increased number of students (9%), and work environment and space (5%).

Conclusions: Significant deficiencies exist in the availability of autism services in our region. Access for referrals for important services is also limited. We identified several areas that can be targeted to help develop, promote, and improve the provided services to children with ASD.

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Syndromes & Autism

ICNC-0335: Hyperacusis in Japanese children with Williams Syndrome
Introduction: Williams syndrome (WS), which is caused by a approximately 1.5-Mb chromosomal microdeletion at band 7q11.23, is a multisystem disorders manifested by a wide range of medical diseases and a unique behavior and cognitive profile. One of the unique behavioral phenotype of WS is hyperacusis. We evaluated hyperacusis and its connection with the behavioral and social phenotypes in Japanese children with WS.

Methods: Participants included 47 persons with genetically confirmed classic-length WS deletions (15 boys, 32 girls) aged 5 and older. Participants’ parents completed the following survey: Clinical presentation, Hyperacusis questionnaire (HQ), Fear survey schedule for children revised (FSSC-R), Child/adult behavior checklist (%CBCL/ABCL), Short sensory profile (SP), and social responsiveness scale 2 (SRS-2).

Results: Mean score on the HQ was 16.70 (S.D. = 9.83). Of the participants 24.5% scored above the suggested cut-off for hyperacusis, compared to 2.5% in Khalfa’s et al. study (2002). Cluster analysis identified the presence of two clusters varying in level of HQ. WS in the hyperacusis positive group demonstrated poorer sensory modulating, more problem behaviors, and more difficult social responsiveness than children in the hyperacusis negative group.

Discussion: This study demonstrated the possible connections between hyperacusis and the behavioral and social phenotypes of WS. Considering that hyperacusis of WS develop from infancy, it may impact on the day-to-day functioning of individuals with WS.

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Syndromes & Autism

ICNC-0508: Long-term memory in ADHD children
Introduction: It is known that children with ADHD have impairments in cognitive abilities. The investigation of these deficits can to shed light on the nature of this disorder. The goal of this research was to examine the hypothesis that children with ADHD have a weakness in long-term memory. Methods: The experimental group included 14 Russian-speaking children with ADHD at age 7-9-years. The control group included 14 typically developing children. The children from experimental and control group were matched for IQ, gender and age. Children from both groups were assessed with NEPSY using Memory for Faces subtest. This subtest is designed to assess the ability to learn the faces. A delayed task assesses long-term memory for faces. Two-way ANOVA was used to reveal group differences in reproducing the faces in immediate and delayed conditions. Results: We have not revealed significant differences between children from experimental and control group in the recalling the faces in immediate condition. However, the interaction of condition type and group was significant. ADHD children were less successful in recalling the names in delayed condition. Conclusion: Children with ADHD have weakness in long-term memory for faces. In view of the obtained results, it can be assumed that children with ADHD have specific deficit in the long-term memory. It is necessary to check this result using different type of memory tasks.

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Syndromes & Autism

ICNC-0336: NGS-based epilepsy gene panel test in early-onset or intractable childhood epilepsy

Background and Purpose: The genetic causes of epilepsy are presumed to be multifactorial and are important in childhood epilepsy including generalized epileptic syndromes. Recent studies revealed that various genetic mutations linked to genetic epileptic syndromes and provided information about the mechanism of epileptogenesis, prognosis, and adequate treatment. In this study, we try to detect genetic mutations through epilepsy gene panel using next generation sequencing (NGS) in early-onset or intractable epilepsies in childhood.

Methods: We retrospectively reviewed the medical records of 48 patients (female : male = 24 : 24) with childhood-onset intractable epilepsy at tertiary university hospital between June 2014 and July 2015. The patients with symptomatic etiologies such as structural brain lesions were excluded in this study. We designed customized NGS-based epilepsy gene panel containing total 111 genes which included 38 candidate genes for genetic generalized epilepsy syndromes and 73 genes for other genetic epilepsy. The gene panel included the coding exons, and intron-exon boundaries using bidirectional sequencing.

Results: The mean age of seizure onset was 2.6 ± 3.18 years (range, 3 days to 12 years) and 38 patients (79.2%) had the first seizure at less than 5 years of age. Twenty-eight patients (58.3%) had severe developmental delay and six had psychiatric disorders. Three sibling cases were included and 24 patients had a family history of epilepsy (n = 12) or febrile seizure (n = 12). In 18 patients (33.3%), we identified mutations which were known to be associated with genetic epilepsy disorders: SCN1A (n = 5, 31%), SCN3A (n = 4, 25%), SCN8A, PCDH19, PRRT2 (n = 2, 13%), ARX, KCNQ2, and FOXG1. In six children with presumed as Dravet syndrome clinically, five were confirmed to have a SCN1A mutation and the other one had a PCDH19 mutation. Two families were revealed to have SCN3A and PRRT2 mutation respectively. Eight patients with mutation were sporadic cases without family history. Conclusions: Our data demonstrated the clinical efficacy of NGS-based epilepsy gene panel for screening in not only patients with clinically suspicious of specific syndrome but also sporadic cases. NGS-based epilepsy gene panel makes another step forward in diagnosis and new therapeutic approaches of childhood intractable epilepsy.

Keywords: intractable epilepsy, epilepsy gene panel, next generation sequencing, children

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ICNC-0473: Early detection of disabilities by parents

In this presentation we will discuss early detection of disabilities by parents and careers using a user friendly developmental milestone chart. The aim is to show what the child should be doing at specific ages and parents can observe their child’s achievements and compare them with the chart. The parents will be able to detect concerns which might point to developmental delay, autism and motor developmental concerns which might point to early diagnosis of cerebral palsy by professionals. Parents will be in a position to monitor their own child’s development and seek early help from professionals. The Child development chart will be eventually computerised and parents will be in a position to video progress and store the achievement of milestones and show them to others and professionals.

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ICNC-0512: Children with Autism on music therapy clinical study

Objective: To study the intervention effect of music therapy in the treatment of children’s autism and observe the clinical effect of the therapy in improving the attention, social communication, and sensibility and emotion of the children with autism. Methods: 30 cases of children with autism from 2008 to 2009, come to outpatient of Nanhai Obstetrics and Pediatric Hospital Affiliated to Guangzhou University of Chinese Medicine, who answered for American DSM IV autism diagnosis were chosen. There are 26 male cases and 4 female cases in this group. 8 cases aged from 3 to 7 years old, 22 cases aged from 1 to 3 years old. 10 cases had cerebral anoxia history during neonatal perinatal. 20 cases had no reasons. Patients were treated with music therapy, by way of passive listening, active participation, improvisation and relaxation suggestion, 6 times a week, 30~35 min each time, running for three weeks and then resting for 10 d. 60 times as a course of treatment. Compared the attention, social communication, emotion and sensibility of children with autism before, process and after music therapy. The behavioral development, musical development and emotional development of the 30 cases of children with autism before, process and after music therapy were graded and analyzed with the method of paired-samples T-tests. Results: The grades of the behavioral development, musical development and emotional development of children with autism after music therapy treatment were improved comparing to those before the treatment. The grades in the course of treatment were improved comparing to those before. The grades after treatment were improved comparing to those in the course of treatment. There were no adverse reactions in the course
of treatment. The grades of the behavioral development before treatment was 18.80±5.21, in the course of treatment was 21.13±5.45, after the treatment was 25.33±5.64; The grades of the musical development before treatment was 8.87±3.18, in the course of treatment was 12.50±3.51, after the treatment was 19.23±4.94; The grades of the emotional development before participation was 5.50±4.33, in the participation was 10.20±4.24, after the participation was 15.13±4.08, before refuse participation was -8.27±1.72, refusing participation was -5.40±1.91, after refuse participation was -2.07±1.70; The differences of each corresponding level before and after treatment were highly statistically significant (p<0.05). Conclusion: Music therapy for autistic children can extend their attention time and span, increase their eye contact, improve their language abilities, reduce stereotyped behaviors and also mobilize their positive emotions. Through the music, music therapy can gradually walk into children’s soul as a free communication medium: first, music can directly open the close emotions of children. music perception experience can ignore the language expression, to meet nonverbal self-expression needs of children with autism; second, children will pay attention to communicate with music related person after being familiar with music; third, children found self-confidence.

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Syndromes & Autism

ICNC-0513: Effects of quality of life of autistic disorder children's parents
Objective: To investigate quality of life in parents of Autistic Disorder children. Method: SF-36 was used to measure parent's quality of life of 90 children with Autistic Disorder and 120 normal children. Results: The quality of life of patients in normal children was higher than in Autistic Disorder group in Physical (90.84±11.46), Role-Physical (54.22±42.10), Bodily Pain (72.36±23.40), General Health (67.53±21.20), Vitality (60.14±25.00), Social Functioning (71.95±26.60), Role-Emotional (53.38±41.70), and Mental Health (67.23±20.00) with the difference being significant (96.16±13.32, 90.09±19.56, 89.53±24.80, 92.92±20.80, 86.39±15.45, 95.63±25.40, 22.2±30.28). The differences of each corresponding level before and after treatment were highly statistically significant (P<0.05). The quality of life of patients in normal children High functioning Intelligence group was higher than in Autistic Disorder group. The quality of life of patients in low functioning Intelligence group are worse than High functioning Intelligence group. Conclusion: Children with Autistic Disorder took grievous influence on parent's quality of life. Compared with High functioning Intelligence group, the low functioning Intelligence Children's Parents quality of life were even worse. Keywords: High functioning Autism Disorder; low functioning Autism Disorder parents; quality of life.

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Syndromes & Autism

ICNC-0514: Effects of quality of life of autistic disorder children
Objective: To investigate quality of life in Autistic Disorder children. Method: PedsQL4.0 was used to measure quality of life of 200 children with Autistic Disorder and 120 normal children. Results: The quality of life of Autistic Disorder group was lower than normal group in the scores of physical functioning were (62.30±25.05), emotional functioning were (53.57±26.69), social functioning were (44.63±27.91), and school functioning (38.69±30.60). The total scores of PedsQL were (49.86±23.32), with the difference being significant (90.16±13.32, 79.09±19.56, 86.39±15.45, 82.75±16.03, 85.23±14.2, P<0.01). Conclusion: Children with Autistic Disorder took grievous influence on quality of life.

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Syndromes & Autism

ICNC-0474: The smallest 8q21.11 deletion: from submicroscopic chromosomal rearrangements to gene-tailored therapy
Introduction: Array CGH is the first-line diagnostic test in children with global developmental delay (GDD) and intellectual disability (ID), which together with dysmorphia has up to 20% diagnostic yield. We further underline the diagnostic value of this submicroscopic chromosomal test and emphasize the treatment options based on the deleted/duplicated genes involved, particularly true when the involved segment is of small size. Case Description: Here we report 9 year old boy with GDD, ID, hypotonia, mild ptosis, fatigue, especially evident after physical activity and ataxia. The patient has dysmorphic face: high forehead, small mouth, hypertelorism, wide nasal bridge, short philtrum, low-set ears, high palate and misaligned teeth. He also has mild pectus deformation, widely spaced and inverted nipples, blood vessels that are clearly visible under the skin in chest area and bilateral chiroptorhism. Methods: Array CGH was performed using the Agilent 8x60K oligonucleotide array platform and the obtained results were analyzed with Agilent CytoGenomic Edition.
Syndromes and Autism


Microdeletions of various sizes in the 2p16.1p15 chromosomal region have been grouped together under the 2p16.1p15 microdeletion syndrome. Children with this syndrome generally share certain features including microcephaly, developmental delay, facial dysmorphology, urogenital and skeletal abnormalities. We present a child with a de-novo interstitial 1665kb duplication of 2p16.1p15. Clinical features of this child are distinct from those of children with the 2p16.1p15 microdeletion syndrome, specifically the head circumference which is within the normal range and mild intellectual disability with absence of autistic behaviors. Microduplications many times bear milder clinical phenotypes in comparison with corresponding microdeletion syndromes. Indeed, as compared to the microdeletion syndrome patients, the 2p16.1p15 microduplication seems to have a milder cognitive effect and no effect on other body systems. Limited information available in genetic databases about cases with overlapping duplications indicates that they all have abnormal phenotypes. The involvement of genes in this location including BCL11A, USP34 and PEX13, affecting fundamental developmental processes both within and outside the nervous system may explain the clinical features of the individual described in this report.

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Syndromes & Autism

ICNC-0475: The association between Cortical Tubers and Autism Severity in Tuberous Sclerosis Complex

Introduction: Tuberous Sclerosis Complex (TSC) is an autosomal dominant disorder characterized by the presence of cortical tubers1 and high prevalence rates of autism spectrum disorders (ASD)2. Previous studies suggested tuber burden to be an important predictor for an ASD diagnosis3–7. To date, no studies have investigated the association between tuber count and ASD severity. Furthermore, the role of intelligence has been insufficiently studied.Methods: In a sample of 52 TSC patients (24 boys, 0-17 years) intelligence and ASD severity (measured with the Autism Diagnostic Observation Scale (ADOS)8) were assessed. Tuber count and location were manually recorded, using FLAIR or T2 weighted images from a 1.5T Siemens scanner. Regression analyses were performed.Results: Total tuber count was positively related to ASD severity (β=0.44, p=0.003). The association was strongest for the domain ‘Restricted and Repetitive Behaviors’ (RRB) (β=0.53, p<0.001), but also present for ‘Social Affect’ (SA) (β=0.33, p=0.031). Tuber count in all separate lobes was also related to ASD severity, with tuber count in the frontal and temporal lobes only and strongly related to the domain RRB (both β=0.51, p<0.001), while parietal and occipital tuber count were related to both SA and RRB. When IQ was added as a covariate, only frontal and temporal tuber count remained significantly associated to RRB severity.Conclusion/Discussion: Children with more cortical tubers displayed more severe ASD symptoms. Intelligence was identified as an important confounding/explanatory factor in this association. However, regardless of intelligence, children with more frontal and temporal tubers displayed more severe restrictive and repetitive behaviors.References1. Crino PB. Evolving neurobiology of tuberous sclerosis complex. Acta Neuropathol. 2013;125(3):317-32. 2. Curatolo P et al. Neurological and neuropsychiatric aspects of tuberous sclerosis complex. Lancet Neurol. 2015;14(7):733-45. 3. Huang CH et al. The relationship of neuroimaging findings and neuropsychiatric comorbidities in children with tuberous sclerosis complex. J Formos Med Assoc. 2014;114(9):849-54. 4. Numis AL et al. Identification of risk factors for autism spectrum disorders in tuberous sclerosis complex. Neurology. 2011;76(11):981-7. 5. Bolton PF et al. Neuro-epileptic determinants of autism spectrum disorders in tuberous sclerosis complex. Brain. 2002;125:1247-55. 6. Asano E et al. Autism in tuberous sclerosis complex is related to both cortical and subcortical dysfunction. Neurology. 2001;57(7):1269-77. 7. Bolton PF et al. Association of tuberous sclerosis of temporal lobes with autism and atypical autism. Lancet. 1997;349:392-5. 8. Lord C et al. Autism Diagnostic Observation Schedule, Second Edition (ADOS-2). Manual (Part I). Los Angeles: Western Psychological Services; 2012.
Methods: We tested 101 healthy child volunteers (6 to elucidate normal development of the finger tapping movement in children and to evaluate clumsiness in child. Clumsiness, however, has not been evaluated objectively, especially in children. The purpose of this study was to

ICNC

Locations” and “Connecting Words” showed significantly lower percentages of expressed words. The averaged percentage of expressed words in each area were calculated for each patient. The averaged percentage of the numbers of expressed words to those of the words listed in the inventory were calculated for each patient. The average percentages of expressed words in each area were compared. Results: The areas “Prepositions and Locations” and “Connecting Words” showed significantly lower percentages of expressed words. Conclusion/Discussion: Spatial vocabulary is delayed in Japanese as in European languages. The development of spatial area, is especially delayed in English and other European languages. Examining whether similar findings exist in other languages, Japanese, would improve our understanding of the influence of cognitive function on language acquisition. Method: The caregivers of eight children with WS (4 girls) who had been followed at our institute were included in this study. The caregivers were asked to answer the MacArthur communicative development inventory (Word and Grammar version) every 2 or 3 months. The responses at the time when the number of total expressive words of a patient first became more than 431 for boys and 497 for girls (the level of 36 month-old typically developing children) were obtained. The words listed in the inventory are 711 in total and are divided into 24 areas. In each area, the percentage of the numbers of expressed words to those of the words listed in the inventory were calculated for each patient. The average percentages of expressed words in each area were compared. Results: The areas “Prepositions and Locations” and “Connecting Words” showed significantly lower percentages of expressed words. Conclusion/Discussion: Spatial vocabulary is delayed in Japanese as in European languages. The development of connecting words was also found to be delayed in the present study, which is a new finding that needs to be evaluated further.

ICNC-0476: The acquisition of Japanese vocabulary in children with Williams Syndrome

Introduction: In Williams syndrome (WS), the development of vocabulary in the area of the cognitive difficulty, the visuo-spatial area, is especially delayed in English and other European languages. Examining whether similar findings exist in a non-European language, Japanese, would improve our understanding of the influence of cognitive function on language acquisition. Method: The caregivers of eight children with WS (4 girls) who had been followed at our institute were included in this study. The caregivers were asked to answer the MacArthur communicative development inventory (Word and Grammar version) every 2 or 3 months. The responses at the time when the number of total expressive words of a patient first became more than 431 for boys and 497 for girls (the level of 36 month-old typically developing children) were obtained. The words listed in the inventory are 711 in total and are divided into 24 areas. In each area, the percentage of the numbers of expressed words to those of the words listed in the inventory were calculated for each patient. The average percentages of expressed words in each area were compared. Results: The areas “Prepositions and Locations” and “Connecting Words” showed significantly lower percentages of expressed words. Conclusion/Discussion: Spatial vocabulary is delayed in Japanese as in European languages. The development of connecting words was also found to be delayed in the present study, which is a new finding that needs to be evaluated further.

ICNC-0516: Children with developmental disorders, such as ASD and ADHD tend to suffer clumsiness in daily life

Assessment: Children with developmental disorders, such as ASD and ADHD tend to suffer clumsiness in daily life. Clumsiness, however, has not been evaluated objectively, especially in children. The purpose of this study was to elucidate normal development of the finger tapping movement in children and to evaluate clumsiness in children with DD. Methods: We tested 101 healthy child volunteers (6-12 years of age) and 3 children with DD for fine motor function using a finger-tapping digital device equipped with two magnetic sensors each taped on the thumb and index finger. The device
measures the distance between the thumb and index fingers during finger tapping movements and has been reported previously as a useful tool for evaluation of fine motor movements in adults with movement disorders. Tests were conducted for 10 seconds by the following tasks: left- and right-hand simultaneous tapping, left- and right-hand alternative tapping, left- and right-hand tapping with/without metronome set at 2-4 Hz. Volunteers were divided into three age groups: 6-8 years of age, 9-10 years of age and 11-12 years of age groups, and normal developmental values of finger tapping movement were determined to compare the findings of children with DD. Results: In bilateral simultaneous and alternative tapping task, tapping numbers rise as their age increase significantly. On the other hand, tapping in children with DD tended to be associated with errors in movement coordination. Conclusions: Our device is suitable for assessment of children and adults and can detect movement difficulties in children with DD. Snt of fine motor development in children using magnetic sensors

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Syndromes & Autism
ICNC-0517: Study of neurofeedback technique as an innovative rehabilitative method for management of Egyptian children with attention deficit hyperactivity disorder
Introduction: Attention-Deficit/hyperactivity disorder is the most common neurobehavioral disorder of childhood that affects social and academic performance of children. Pharmacological treatment is the first line choice in many guidelines but the fear from adverse effects and presence of non responders directed researchers to find other alternative interventions. Neurofeedback was one of these alternative interventions that many studies discussed its effectiveness. Methods: Forty six children with combined type ADHD were included in the study. They were divided into two groups, group I (n= 22) who were trained with Neurofeedback and group II (n=24) who remained on ADHD medications. Pre and post treatment assessment was done by Conners’ Parents Revised Scale CPRS-TR: to assess behavioral symptoms severity and EEG neurofeedback analysis for the selected brain waves amplitudes (Theta, Beta 1 and Theta/Beta ratio). Results: The study proved that there are no significant difference between the both groups according to the improvement in the severity of behavioral symptoms or the EEG neurofeedback analysis but neurofeedback was superior to medication in reduction of the oppositional, anxiety and psychosomatic symptoms. No significant change happened in the EEG neurofeedback analysis in neurofeedback group while theta/beta ratio was significantly changed in the medication group. Conclusions: The study showed that neurofeedback has a similar effect to ADHD medications on reducing the severity of behavioral symptoms and can be used as a part of the rehabilitative program of those children.

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Syndromes & Autism
ICNC-0518: The efficacy of “Son-Rise” program for development of social and communication skills of a sample of children with autism
Introduction: The Son-Rise Program is an intensive, child-centered parent-mediated approach for autism intervention. It incorporates strategies to promote child-initiated social interactions using training as a core element and to be based at home. Methods: This study examined efficacy of Son-Rise program for development of social and communication skills of children with autism. Parents of 10 children with autism were enrolled in an intensive training on Son-Rise program techniques for 24 days including 7 consecutive stages: program overview, start up program, maximum impact, new frontiers, preparation and implementation of individual program. Children were evaluated before and after using Childhood Autism Rating Scale and by specific evaluation form using the four components of the program’s Developmental Social Model. An age and sex - matched control group was included. Results: The study showed significant changes between the pre-and post-treatment CARS scores among the study group as well as between the study group and the control group. Also, significant improvement was observed in the study group with regard to the four components of the social developmental model of the program. In addition, follow up CARS scores were significantly different during the follow up evaluation from the initial evaluation. Conclusions: SRP is an important and effective training program for children with autism with its unique principles that stress on the role of parents in facilitating social communication with their children.

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Syndromes & Autism

ICNC-0477: Clinical features associated with an 18.11 Mb deletion of chromosome 13q encompassing the MIR17HG locus

A characteristic facial appearance with systemic affection has been described in patients with microdeletions of the long arm of chromosome 13, with an extensive phenotypic spectrum that varies according to the location and size of the deletion region. Common manifestations include microcephaly, short stature, and brachymesophalangy. Here we describe a 24 months-old male patient who presented to our Pediatric Neurology Clinic with a history of severe developmental delay, short stature and microcephaly. Upon examination he was noted to have dysmorphic features, brachydactyly of his fingers and toes and empty scrotum. His head circumference was 41 cm (<1st centile) and his height was 72 cm (<1st centile). MRI showed a short, thin corpus callosum. The karyotype formula was 46, XY, del (13)(q22q32). A comparative genomic hybridization microarray was completed and a ~18 Mb deletion at 13q22.2q31.3 including MIR17HG was found. MIR17HG encodes the miR-17–92 polycistronic miRNA cluster which it is involved in growth and skeletal development. Clinically, this patient shows the characteristic digital anomalies and short stature often seen in this deletion. This report further highlights the capacity of high-molecular cytogenetic methods in the evaluation of children with idiopathic developmental delay and intellectual disability.

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Syndromes & Autism

ICNC-0519: Using Transcranial Magnetic Stimulation to measure Neuronal Plasticity and Inhibition in adolescents with Neurofibromatosis type 1

Introduction: Cognitive deficits in children with Neurofibromatosis type 1 (NF1) seem to arise from increased neuronal plasticity through increased activity of inhibitory interneurons. This increased inhibition in NF1 arises from attenuated activity of the hyperpolarization-activated cation current 1 (HCN1). Lamotrigine, an anti-epileptic and HCN1 agonist, restores inhibition and rescues behavioural deficits in NF1 mice. Lamotrigine is therefore currently tested as a possible treatment for cognitive deficits in adolescents NF1 patients in the NF1-EXCEL trial (ZonMw nr: 113303003). To concurrently evaluate the effect of Lamotrigine on neuronal level, we measure neuronal plasticity and inhibition using transcranial magnetic stimulation (TMS). Methods: The NF1-EXCEL study is a randomised, double blind, placebo-controlled clinical trial. In total 60 adolescent patients (age 12-18) will be included. The intervention is lamotrigine (200mg daily) or a placebo during half a year. The primary outcome is performal IQ. Intracortical inhibition and neuronal plasticity are measured with TMS. Inhibition is assessed using a paired pulse TMS protocol, named short intracortical inhibition (SICI). Neuronal plasticity is assessed using paired associative stimulation (PAS) TMS. Results: We could analyse TMS baseline measurements of the first 16 out of 22 included participants. SICI was measured in 15 participants, showing an inhibition of 80% (±15%; p<0.001). PAS could be measured in 13 participants, showing a potentiation of 95% (±127%; p=0.04). The participants reported low anxiety preceding the measurements and low discomfort during the measurement. Conclusion: TMS is a well-tolerated and feasible method to assess intracortical inhibition and neuronal plasticity in adolescents with NF1.

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Syndromes & Autism

ICNC-0520: Effectiveness of home based sensory interventions along with standard therapy versus standard therapy alone in children with Autism spectrum disorders having sensory processing abnormalities: A Randomized trial

Introduction: Majority of children with Autism spectrum disorders (ASD) have associated sensory processing abnormalities. Clinic based Child centered Sensory Integration Therapy, despite its emerging positive outcome, has feasibility and financial restraints in developing countries. Home-based sensory intervention is a novel initiative to circumvent these practical difficulties. This study was done to look for feasibility and effectiveness of home based sensory intervention in children with ASD having sensory processing abnormalities. Methodology: Children aged between 3-12 years diagnosed with ASD as per DSM–V, were screened for sensory processing abnormalities using short sensory profile-2 in Advanced Pediatric center, PGIMER. Children with sensory processing abnormalities were randomly assigned to Sensory intervention (SI) or Standard therapy (ST) group. Children with progressive neurological or metabolic disorders, active epilepsy and structural brain abnormalities were excluded. SI group received structured
sensory interventions and standard therapy for 3 months; ST group received speech therapy and applied behavior analysis. Demographic details, Sensory assessment by Child Sensory Profile-2, Childhood Autism Rating Scale and IQ/SQ were recorded. Effectiveness outcome measures, Parent rated 10-item Likert scale, PedsQL, Children’s global assessment scale (CGAS) were assessed at inclusion and 3 months. The trial was registered in CTRI. (CTRI/2015/12/006418) Results: Of the 150 children screened, Sensory processing abnormalities were seen in 32.66%. 30 children were recruited with 17 in SI arm and rest in ST arm. At 3 months, Children in SI arm had better outcome in Parent rated 10-item Likert scale and improvement in social responsiveness, non-verbal communication, stereotypic behavior and overall functioning. Conclusions: Our study illustrates the potential beneficial role of home-based sensory interventions in children with ASD having sensory processing abnormalities.

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Syndromes & Autism
ICNC-0343: Isolated megalencephaly caused by a de novo mutation in the AKT3-gene
Introduction: Megalencephaly can be caused by mutations in the PTEN-gene (PTEN Hamartoma Tumor Syndrome) or NSD1-gene (Sotos syndrome). Recently, activating mutations in the PI3K-AKT pathway have been associated with other brain overgrowth syndromes like Megalencephaly-Capillary Malformation-Polymicrogyria syndrome (MCAP) and the Megalencephaly-Polymicrogyria-Polydactyly-Hydrocephalus syndrome (MPPH). In this case report we describe the clinical characteristics of a girl with isolated megalencephaly and developmental delay. Case description: The girl was born after an uneventful pregnancy of 36+4 weeks, with a birth weight of 2530 gram (-0,5 SD) and a head circumference of 36 cm (+0,8 SD). At the age of two months the head circumference was +3.8 SD, further increasing to +6.5 SD from the age of 2.5 years onwards. Body length follows the -1 SD and weight/length the +2 SD curve. She has a moderate cognitive, motor and speech delay. At the age of five years no epileptic seizures were present. Facial dysmorphisms included frontal bossing with scaphocephaly, low-set posteriorly rotated ears, short eye slits and a deep nasal bridge. No signs of polydactyly, hemihypertrophy or cutaneous capillary malformations were present. Also no focal neurological abnormalities were seen at neurological examination. The MRI of the brain showed no signs of ventriculomegaly, cerebellar tonsillar ectopia or polymicrogyria. SNP-array showed a normal female profile. Exome sequencing revealed a de novo pathogenic missense mutation in the AKT3-gene (c.1393C>T, (p.Arg465Trp)). Conclusion: Mutations in the AKT3-gene should be considered in children with isolated megalencephaly with developmental delay.

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Syndromes & Autism
ICNC-0850: A child with 14q31.3-q32.11 deletion presenting with congenital left auditory neuropathy, hemifacial weakness and insensitivity: involvement of FOXN3?
Introduction: An interstitial deletion in the middle and distal part of chromosome 14 is a rare chromosomal abnormality characterized by a spectrum of phenotypic manifestations, including microcephaly, failure to thrive, face and head abnormalities. Case description: We present the detailed medical history and clinical evaluation of a 5 year-old girl that presented features of a left congenital peripheral facial paralysis, including microcephaly, failure to thrive, face and head abnormalities. At the age of 3 months the head circumference was +3.8 SD, further increasing to +6.5 SD from the age of 2.5 years onwards. Body length follows the -1 SD and weight/length the +2 SD curve. She had a moderate cognitive, motor and speech delay.

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ICNC-0522: How to improve the diagnosis of autism spectrum disorders (ASDs)?
There were no formally accepted protocols or guidelines for diagnosis of ASDs in Croatia, whether by medical association or state institutions. Children with suspected ASDs are firstly seen by neuropsychiatrists, and after that by their personal indication future diagnostic procedure were applied and early treatment is usually postponed for variable period of time. Therefore, during the last five years we implemented a strict protocol regarding diagnostic procedure in children with suspected ASDs at our institution. This protocol includes multidisciplinary approach starting with neuropsychiatric examination and diagnostic procedure, followed by psychiatric and psychological evaluation. Diagnostic procedures include routine blood investigation, screening for metabolic diseases, hearing and visual screening by specialist, electroencephalography during sleep and brain magnetic resonance. Data regarding children diagnosed with ASD during the last four years were analysis. There were 64 children, 57 boys and 7 girls. The number of children increased from year 2011 - 8 children diagnosed to year 2015 - 26 children diagnosed. The average age of children with confirmed diagnosis was 3.5 years. Comparing this with our previous results, we decreased the average age of ASDs diagnosis for one year. Our results confirm the already known fact that in the last decade we witnessed a growing number of children with autistic spectrum disorders. More importantly, we showed that simple intervention in organizational health management can improve earlier recognition of ASD which consequently improves inclusion in the early intervention treatment.

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ICNC-0490: Homozygous Variant in B9D1 associated with Joubert Syndrome: A case report
Background: Joubert Syndrome is characterised by hypotonia, developmental delay and a distinctive brainstem malformation known as the ‘molar tooth’ sign on brain imaging. We present a novel case of homozygous c.220C>T mutation in the B9D1 gene associated with this disorder. Case: A male infant born to consanguineous parents presented at the age of 2 weeks with head thrusting and poor visual behaviour, later on recognised as oculomotor apraxia. He was born at term in good condition. An initial brain MRI was normal. Due to ongoing developmental delay at the age of 4 years, he underwent a second brain MRI which demonstrated a ‘molar tooth’ appearance of his brainstem. Mutation analyses of the 27 genes known to cause Joubert Syndrome was subsequently undertaken. A novel homozygous mutation was identified in the B9D1 gene (c.220C>T). A heterozygous pathogenic variant in TTC21B (c.2258C>T) was also detected. Discussion: Joubert Syndrome is an autosomal recessive ciliopathy. The c.220C>T mutation in B9D1 gene has not been reported in literature as being associated with Joubert Syndrome. However, other mutations in B9D1 have been reported in cases of mild Joubert Syndrome as well as a Meckel Syndrome phenotype. It is interesting that the proband also carries a heterozygous pathogenic mutation in TTC21B. Conclusion: Initial imaging in Joubert Syndrome may not demonstrate the classical ‘molar tooth’ findings. Our patient’s clinical manifestation may be contributed to by mutations in two different genes, one of which is a novel homozygous mutation. This is likely to be an example of oligogenic inheritance.

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ICNC-0524: Rett syndrome in Kazakhstan: description of three clinical cases
Rett syndrome is a neurodevelopmental disorder characterized by loss of acquired skills after a period of normal development in infant girls. The responsible gene, encoding methyl-CpG binding protein 2 (MeCP2), was recently discovered. In our clinic were examined three girls aged 4 years with autistic behavior. The debut of the disease in all cases kept in the range of 14 months, 18 months and 24 months respectively, when parents began to notice clearly the loss of previously acquired speech, social and motor skills. Seizures occurred in two patients. The debut of seizures was observed in two patients in the age of 3 to 4 years. Character of attacks ranged from affective–respiratory to tonic-clonic seizures. Seizures appeared spontaneously or at fever above 38 degrees. In all three cases during EEG monitoring revealed epileptic changes in the frontal and temporal lobe. Neuroimaging results as different manifestations of variability from nonspecific posthypoxic changes of white matter to the local unit of cysts in the temporal lobe or diffuse atrophy of the cortex and cerebellum. The diagnosis of Rett syndrome in all three cases was established after the age of three. Up
to this point, all patients were observed with different diagnoses - infantile autism, ataxic form of cerebral palsy, cerebellar ataxia syndrome (Louis-Barr virus). An analysis of three clinical cases showed that there is a late diagnosis of Rett syndrome, which led to a prolonged unjustified treatment, instead of early behavioral rehabilitation of children with Rett syndrome.

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Syndromes & Autism

ICNC-0525: Diagnostic evaluation of the developmental level in Mexican children identified at risk of delay through the Child Development Evaluation (CDE) Test

BACKGROUND: The Child Development Evaluation or CDE Test was developed in Mexico as a screening tool for child developmental problems. It yields three possible results: normal, slow development or risk of delay. The modified version was elaborated using the information obtained at the validation study, and its properties “on the field” are not known.

OBJECTIVE: To establish the diagnostic confirmation of developmental delay in children 16-59 months old previously identified as risk of delay through CDE Test in primary care facilities. METHODS: A population-based transversal study was conducted in one State of Mexico. CDE test was administered to 11,455 children 16-59 months old from December/2013 to March/2014. The eligible population was the 6.2% (n=714) who were identified at risk of delay at CDE Test. For the inclusion in the study a block randomization stratified for sex and group of age was performed. Each participant included in the study had a diagnostic evaluation using the Battelle Development Inventory, 2nd Edition.

RESULTS: From the 355 participants with risk of delay included, 65.9% were male and 80.2% from rural areas. 6.5% were false positives (Total Development Quotient >90) and 6.8% didn't have any domain with delay (Domain Developmental Quotient <80). The proportion of delay for each domain was: Communication 82.5%; Cognitive 80.8%; Social-personal 33.8%; Motor 55.5%; and Adaptive 41.7%. There were significant differences in the percentages of delay both by age and by domain/subdomain evaluated. CONCLUSION: In 93.2% of the participants it was corroborated at least developmental delay in one domain evaluated.

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Syndromes & Autism

ICNC-0526: Population-based study of child developmental screening in Prospera beneficiaries younger than 5 years old in Mexico

Background: Child Development Evaluation CDE test (Prueba EDI), a screening tool designed and validated in Mexico, classifies child development as normal (green) or abnormal (yellow or red). Population-based results of child development level with this tool are not known. Objective: Evaluate the developmental level of children aged 1-59 months living in poverty (PROSPERA program beneficiaries) through application of the CDE test. Methods: CDE tests were applied by specifically trained and standardized personnel to children <5 years old who attended primary care facilities for a scheduled appointment for nutrition, growth and development evaluation from November 2013 to May 2014. Results: There were 5,527 children aged 1-59 months who were evaluated; 83.8% (n = 4,632) were classified with normal development (green) and 16.2% (n = 895) as abnormal: 11.9% (n = 655) as yellow and 4.3% (n = 240) as red. The proportion of abnormal results was 9.9% in children <1 year of age compared with 20.8% at 4 years old. The most affected areas according to age were language at 2 years (9.35%) and knowledge at 4 years old (11.1%). Gross motor and social areas were more affected in children from rural areas; fine motor skills, language and knowledge were more affected in males. Conclusions: The proportion of children with abnormal results is similar to other population-based studies. The highest rate in older children reinforces the need for an early-based intervention. The different pattern of areas affected between urban and rural areas suggests the need for a differentiated intervention.
Syndromes and autism

ICNC-0851: VLDLR Gene Mutation in a 8-year old girl with Ponto-Cerebellar Hypoplasia

Very low density lipoprotein receptor (VLDLR) is part of the reelin (RELEN) pathway, which guides neuroblast migration in the cerebral cortex and cerebellum. RELEN and VLDLR are important genes for cerebellar development, which play a key role in gait. VLDLR gen mutations cause autosomal recessive, congenital, non-progressive cerebellar ataxia and mental retardation syndrome with or without quadripedal locomotion associated with cerebellar hypoplasia and mild cerebral gyral simplification. Here, we present a 8-year old girl who presented with delayed gross motor retardation, ataxia, frequent falls and intellectual disability. The prenatal, natal and early postnatal periods of the patient were uneventful. She was born at term with normal birth weight, height and head circumference. She had a history of bilateral inguinal hernia repair at 2 months old and surgery for strabismus at 2 years old. Cranial magnetic resonance imaging showed severe cerebellar and brainstem atrophy. Physical examination at 8-year old showed generalized hypotonia, hyperextensibility at elbow, metacarpophalangeal and distal phalangeal joints, sacral dimple and ataxia. She had some dysmorphic features such as narrow forehead, narrow and long face, abundant eyebrows, prominent nasal root, bulbous nasal tip, long philtrum. She can walk approximately 10 meters independently, and speak 8

Syndromes & Autism

ICNC-0852: A case of TUBA1A mutation presenting with cortical malformation and ponto-cerebellar hypoplasia

Tubulin gene family have an essential role in neuronal migration, axonal guidance, and necessary for development of the central nervous system. TUBA1A gene is a member of tubulin gene family, coding for alpha I tubulin that constitutes subunit of microtubule. TUBA1A gene mutation is a relatively rare cause of lissencephaly. The most consistent feature of lissencephaly spectrum due to TUBA1A mutation is severe cerebellar and brainstem abnormalities and agenesis of corpus callosum with congenital microcephaly. Here, we present a 3 5/12-year old boy who presented with delayed gross mental-motor retardation and congenital microcephaly. He was born at term with normal height and weight. Parents were consanguineous. Cranial magnetic resonance imaging showed dilated ventricular system with irregular margins, pachygria, sulcation insufficiency, atrophy of cerebellar vermis and hemispheres, pontine atrophy, and hypoplastic corpus callosum. Physical examination at last examination showed generalized hypotonia, hyperextensibility at elbow, tapering fingers, mild digital clubbing, truncal obesity, and bilateral cryptorchidism. He had some dysmorphic features such as narrow forehead, deeply located eyes, dysplastic earlobes, small nose and mouth, hypoplastic ala nasi, short philtrum, and thin upper lip. He can hold his head, sit unsupported for a short time, and can not speak. He had no eye contact. Whole exome sequencing showed TUBA1A gene mutation. TUBA1A gene mutation should be considered in the differential diagnosis of patients with ponto-cerebellar hypoplasia and non-progressive cerebellar ataxia.

Syndromes & Autism

ICNC-0341: A Turkish girl with 16p11.2-p12.2 microdeletion syndrome

Introduction The development of new diagnostic methods such as array Comparative Genome Hybridization (array-CGH) has allowed the detection of numerous new microdeletion syndrome. 16p11.2-p12.2 microdeletion is a newly discovered syndrome characterized by minor facial anomalies, feeding difficulties, significant delay in speech development, and
recurrent ear infections. Here in we describe a Turkish girl with delay in speech development, malnutrition and minor dysmorphic futures who was diagnosed as 16p11.2-p12.2 microdeletion syndrome with array-CGH analysis Case Report

The patient was a girl now 5 years of age, born from healthy non-consanguineous parents. She admitted to our unit with complaint of feeding difficulties, mental motor retardation, and minor craniofacial anomalies at 2 years of age. The family history was non-contributory. Pregnancy and delivery were unremarkable. Physical examination revealed severe malnourished child with minor facial dysmorphic features. Neurologic examination revealed generalized hypotonia with brisk deep tendon reflexes and there was no speech development. Laboratory analyses revealed a normal complete blood count and normal blood chemistry values, including levels of lactate, pyruvate, and ammonia. Tandem mass spectrometry of serum and urine organic acid analysis was normal. Magnetic resonance imaging and electroencephalography were normal. Cardiac echocardiography and renal ultrasonography revealed also no abnormalities. Since the cytogenetic analysis was normal, array-CGH analysis was performed and which identified 16p11.2-p12.2 microdeletion. Discussion/Conclusion 16p11.2-p12.2 microdeletion syndrome should be searched with array-CGH analysis for in patients presenting with mental motor retardation with prominent speech impairment, feeding difficulties and minor dysmorphic futures.

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Syndromes & Autism

ICNC-0285: Ethical leadership in paediatric neurology

Introduction: The field of ethical management in healthcare organizations examines the ethics of managers in the public health care profession of doctors: through administrative ethics and professional ethics. In paediatric neurology ethical clinical aspects are well recognized. In recent years neuroethics includes a modern context for ethics in neuroscience; ethical, legal and social policy implications of neuroscience and with aspects of neuroscience research. Advances of neuroscience challenges long-held views of the self and the individual’s relation to society. The objective of the study is: What is meant by ethical management? What challenges come up when reconciling the administrative work and ethical demands of the profession? What dilemmas arises in the process of prioritization? Another objective is to analyse empirical data so as to contribute to developing a system of ethical management. Methods: A survey was conducted in autumn 2015. The target group was 50 paediatric neurologists in leading positions. The results were complemented by questions about individual values and attitudes concerning health care system. Ethical dilemmas were described. The results are to be statistically analyzed. Results: Preliminary results: paediatric neurologists experience ethical cohesion although measuring profitability is stressing and diminishing resources make work demanding. Ethical dilemmas are part of daily management. Conclusion: No remarkable value conflicts were observed. Seedhouse D et al. Practical Medical Ethics. Wiley & Sons. Toronto 1992 Alfandre D et al. Ethical Dilemmas and Suggestions for Practical Management. Am J Med 2015 Oct 29 (epub)

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Syndromes & Autism

ICNC-0527: Comparative study between school and motor performances in children of two private schools

Abstract Introduction: during schooling age, motor skills widen, with possible connection between motor development and school learning. Objective: to evaluate and compare the motor skills of children with good and poor school performance. Methodology: school children aging 6 to 11 participated divided into two groups; G1 (poor school performance) and G2 (good school performance), evaluated through the Motor Development Scale (MDS) and the Nine-hole Peg Test. Results: G2 presented higher score in the MDS (100.43±10.36) and less time spent for execution of the Nine-Hole Peg Test. (Dominant Hand 00:22:62±00:03:13; Non-dominant hand 00:24:5±00:03:48) when compared to G1, which showed values of (92.86±8.11) and (Dominant Hand 00:22:69±00:03:87; Non-dominant Hand 00:24:18±00:01:53) respectively. In statistical analysis, a meaningful difference was found in positive age, body scheme and spatial organization with P<0.05. Conclusion: results point to a direct relation between poor school performance and difficulty in motor skill and dexterity, elucidating a connection between motor and cognitive performance. Keywords: Child development, learning and motor skills.

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Syndromes & Autism

ICNC-0342: Results of medical genetic studies of patients with febrile seizures in Uzbekistan
Syndromes and Autism

ICNC-0478: Casuistry of Phelan Mcdermid Syndrome in our hospital

INTRODUCTION: Intellectual disability (DI) needs a complex study, its prevalence is about 3% of the population. In sporadic cases without physical features, we make karyotype, fragile X and study of subtelomeric regions. Deletions or duplications in these regions cause an genetic imbalance and cause DI, and are studied by FISH or MLPA. The 22q11.2 deletion syndrome (PMS) is a rare disease with DI and is detected by MLPA or arrays, we describe the cases founded in our area in the last 20 years. Case 1. girl, 15 years old, with psychomotor retardation and autism. Premature 32 SG with hypotonia. At 3, 5 years they consulted by language delay, inattention and hyperactivity. Male, healthy parents. Physical examination, laboratory tests with metabolic proves, EEG and cranial MRI were normal. 46, XX karyotype. Study of X fragile and Sd Angelman negatives. Subtelomeric deletions by MLPA shows a deletion of 22q subtelomeric zone (more than 300 kb affecting genes, SHANK3 included) Case 2. girl, 9 years old, with psychomotor delay, after DI (IQ 65), cortical dysplasia and epilepsy. Parents and sister not affected. Diagnosed by microarrays array (hg18) 15q11.2 (21, 236, 096 to 21, 901, 624) x3 with paternal imprinting and arr (hg18) 22q13.33 (49, 470, 357-49, 565, 875 ) x1 with terminal deletion.CONCLUSIONS: ID and autism can be caused by mutations in SHANK3 on chromosome 22q. Loss of one copy of SHANK3 results in 22q13 deletion syndrome or Phelan-McDermid syndrome (PMS) and causes a monogenic form of autism and/or ID.

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Syndromes & Autism

ICNC-0344: The use of Targeted Capture and Massively Parallel Sequencing in atypical leukoencephalopathy

Introduction: Leukoencephalopathy is a disease with high clinical heterogeneity, especially for genetic leukoencephalopathy which may involves in multiple genes, the etiological diagnosis is difficult for neurologists. With the development of next-generation sequencing technology, we designed the personalized chip which contains 118 genes reported to be associated with leukoencephalopathy. To our knowledge, this is the first study to undergo targeted capture and massively parallel sequencing (MPS) for leukoencephalopathy. Methods: A pilot study of 48 Chinese patients with atypical leukoencephalopathy was performed. These patients were recruited into our cohort according to the inclusion and exclusion criteria, then we screened for them using the personalized chip and made the validation among their parents using Sanger sequencing. Results: A total of 39.6% (19/48) of the patients exhibited pathogenic mutations. Including four associated with metachromatic leukodystrophy, three associated with vanishing white matter leukoencephalopathy, three associated with mitochondrial complex I deficiency, one associated with globoid cell leukodystrophy, two associated with megalencephalic leukoencephalopathy with subcortical cysts, two associated with Pelizaeus-Merzbacher disease, one associated with X-linked adrenoleukodystrophy, one associated with Zellweger syndrome, one associated with amyotrophic lateral sclerosis and one associated with Alexander disease. In this study, twelve pathogenic mutation sites were identified for the first time. Conclusion: Our data supported the combination of targeted capture and MPS technology with clinical and genetic diagnosis, allowing the identification of atypical leukoencephalopathy, highlighting its usefulness for rapid and comprehensive genetic testing in the clinical. These results expand our knowledge of the genetic and clinical spectra of leukoencephalopathy.

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Syndromes & Autism

ICNC-0345: Hematopoietic stem cell gene therapy mediated correction of metabolic and phenotypic abnormalities in a MNGIE mouse model

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) disease is caused by severe deficiency of thymidine phosphorylase enzyme activity and toxic accumulation of the substrates deoxy-thymidine and deoxy-uridine. Early onset of devastating clinical manifestations characteristic for MNGIE regularly involve the nervous and gastrointestinal systems. Allogeneic hematopoietic stem cell transplantation is in principle curative but resulted in high transplant related mortality rates or MNGIE-related complications. Hematopoietic stem cell gene therapy (HSC-GT) may provide a single curative intervention for a wide range of metabolic disorders. In the present preclinical study we evaluated clinically applicable lentiviral vectors (LVs) overexpressing the native cDNA or the codon optimized (TPco) sequence driven by PGK promoter for syngeneic ex vivo HSC-GT in a large cohort of MNGIE mice. Transplantation of HSCs transduced by LV-PGK-TP(co) resulted in sustained expression of TP in blood cells and the affected organs with a prominent reduction in the levels of toxic metabolites up to 11 months after transplantation. In addition, we describe, for the first time, disease phenotypes in MNGIE mice which were fully corrected by HSC-GT. LVs displayed the expected tendency to integrate within highly expressed genes with integration pattern similar to those of SIN-LV vectors in other disease models; long-term follow up of primary and secondary recipients did not reveal demonstrated LV integration related malignancies. We conclude that HSCs mediated ex vivo gene therapy provides stable TP expression and long-term biochemical and phenotypic correction in MNGIE mice without overt genotoxicity, establishing the feasibility of an initial clinical trial in early diagnosis MNGIE patients.

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Syndromes & Autism

ICNC-0528: Attention deficit hyperactivity disorder-related symptoms improved by allergic rhinitis treatment in children

Introduction: Increased prevalence of attention deficit-hyperactivity disorder (ADHD) and higher ADHD scores, compared to controls, in children with allergic rhinitis (AR) have been reported. This prospective follow-up study aimed to investigate whether elevated ADHD scores in children with AR can be decreased by AR treatment.Methods: Sixty-eight drug-naive children with AR (aged 6-14 years) were enrolled and evaluated by AR symptom score, ADHD symptom scores, and computerized continuous performance test, before and after AR therapy. Thirty-one age-matched controls and 13 children with pure ADHD were also enrolled for comparison. The relationship between AR and ADHD score change was analyzed by a partial correlation test. Univariate and multivariate linear regression models were applied to investigate possible predictors for the improvement of ADHD scores by AR treatment.Results: AR symptom scores in children with AR decreased significantly after treatment (p < 0.001), and their ADHD scores also decreased significantly (p < 0.001). An improved AR symptom score was positively correlated with improved detectability (rp = 0.617, p = 0.001) and commission error (rp = 0.511, p = 0.011). Significant predictors for the improvement of ADHD scores included age, AR drugs, AR subtypes, and multiple atopic diseases (ps < 0.05).Conclusion: Higher ADHD scores in children with AR did decrease significantly with AR treatment. For children with AR and borderline ADHD symptoms, which do not meet full ADHD diagnostic criteria, we recommend initially treating their AR, and monitoring improvement of ADHD symptoms.

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Syndromes & Autism

ICNC-0346: A Case with BDMR and Epilepsy caused by de novo terminal deletion of 2q37 including the gene...
HDAC4
Brachydactyly-mental retardation syndrome (BDMR) is often associated with a deletion involving chromosome 2q37. HDAC4 gene, which is encoded on 2q37, is known to regulate gene expression during development of many tissues including bone. Defect of HDAC4 gene is known to be responsible for BDMR, which presents developmental delay, seizure, intellectual disabilities, behavioral abnormalities, skeletal abnormalities (including brachydactyly type E), autism spectrum disorder, and obesity. A 6-month-old female patient without any specific familial history was brought to the University Hospital due to developmental delay. She did not reveal any notable abnormality at birth and at the time of initial visit. On her age of 17 months, complex partial seizure recurring 3-4 times every week developed. EEG showed frontal spike and slow wave discharges. After anticonvulsant medication, there was decline in frequency of seizure attack, but she experienced seizure until her age of 5. Synchronous bifrontal spike or polyspike and slow wave discharges were still present at the age of 17. Initial brain MRI and chromosomal study showed negative findings, but her hand radiograph showed brachydactyly type E. Recently, whole exome sequencing was performed, which revealed de novo terminal deletion of 2q37 including gene HDAC4. Now she is 21 years old. She has profound mental retardation, which was measured as 24 by K-WAIS. Social Maturity Scale was correspondent to 2.27 years. Here we report a case representing with BDMR caused by de novo deletion of 2q37 including gene HDAC4, combined with mental retardation, epilepsy, autistic feature, brachydactyly type E, and obesity.

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ICNC-0347: Microcephaly and global developmental delay: biallelic variants in ALDH18A1 without cutis laxa
Introduction: ALDH18A1 encodes delta1-pyrrolin-5-carboxylate synthase (P5CS) that catalyses the first common step in proline and ornithine biosynthesis. Biallelic mutations in ALDH18A1 have been implicated in a neurocutaneous syndrome with cutis laxa, microcephaly, cataract and developmental delay. We report a patient with compound heterozygous variants in the ALDH18A1 gene without cutaneous manifestations. Case report: The patient, a two and a half years old girl was born at 37 weeks gestation with a weight of 1950 g to healthy, non-consanguineous Caucasian parents. Delivery was uncomplicated. She had generalized hypotonia and resting tremor in the head and hands. Failure to thrive and delay in motor and cognitive development were noticed. Postnatal deceleration of head growth was observed. Cutaneous manifestations or cataract were not seen. Brain MRI revealed moderate hypoplasia of the corpus callosum. Routine chromosomal analysis and metabolic tests were normal, except a transient elevation in blood lactic acid. CSF glucose and lactic acid were also in the normal range. MECP2, CDKL5- and FOXG1-related disorders were excluded. Whole exome sequencing revealed compound heterozygosity for two variants (c.-28-2A>G, c.383C>A, p.Arg128His) in the ALDH18A1 gene. These variants were also detected in the parents in heterozygous states. Discussion: The variants found in the ALDH18A1 gene may lead to P5CS deficiency and alterations in proline, ornithine, citrulline and arginine biosynthesis. Neurological symptoms can occur without cutaneous manifestations suggesting that normal P5CS activity is required for development of the nervous system. The pathophysiology of P5CS deficiency in the brain is still unknown, changes in the mitochondrial function are supposed.

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White matter disorders and neuroradiology

ICNC-0811: Posterior Reversible Encephalopathy Syndrome: Single center report of Mid-Term follow up

Purpose: Posterior reversible encephalopathy syndrome (PRES) is a syndrome presented with convulsion, vision abnormalities, altered mental status, focal neurologic deficit, nausea, vomiting and headaches in the presence of an underlying etiology. The diagnosis can be confirmed by support of radiological studies. The aim of this study is to describe the clinical and radiological features and outcomes following PRES in paediatric patients. Materials and Methods: Patients diagnosed with PRES were analyzed retrospectively for the clinical symptoms and the underlying etiology. Demographic data were recorded. Magnetic resonance images (MRI) and electro-encephalography (EEG) findings were evaluated to relate with clinical symptoms. Results: Total of the 17 patients (4 male-13 female) were evaluated. Mean age was 11.2±3.5 (5-19). Underlying etiologies required 7 cases with acute lymphocytic leukaemia (ALL), 2 cases with non-neoplastic haematological diseases, 5 cases with nephrological diseases and 1 case with metabolic disease. Presenting symptoms were seizure in 14 cases, confusion in 2 cases and hypertension in all cases. T2 hyper-intense images of MRG were presented in occipital-parietal (88%), parietal (82.3%), temporal (58.8%), thalamus (11.7%), frontoparietal (5.8%) diffusion tension. Presenting symptoms were seizures (88%), change of consciousness (17%), headache (11.7%) and vision impairment (23%). All of the cases had hypertension, 47% of the cases had been undergone steroid treatment. All of the cases had recovery time shorter than <2 days except one (he died). Conclusion: PRES in children is more common with haematological malignancies than non-haematological and renal diseases associated with hypertension. Seizure is the most common acute manifestation and MRI changes may be resolving.

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White matter disorders and neuroradiology

ICNC-0927: Central Nervous System (CNS) demyelinating diseases in childhood: a report of 11 cases

Introduction: Demyelinating diseases in children and adolescents can be a challenging diagnosis, especially at onset because of different presentation, small number of affected subjects and lack of large cohort studies. Materials and methods: 11 cases were retrospectively evaluated along a period of 4 years. Clinical (neurological examination), laboratory (biochemical, cerebral spinal fluid (CSF) analysis) and neuroimaging (cranial and spinal magnetic resonance imaging (MRI)) findings were reviewed. Patients were followed during a period ranging from 10 months to 4 years. Results: We evaluated 6 males and 5 females, mean age at onset 9 years (range 2.7-13), with those presenting symptoms: headache, gait impairment, vomit and drowsiness. Neurological findings at admission were: weakness (73%), osteoarticular hyporeflexia (36%) or hyperreflexia (18%), altered sensitivity (18%), nystagmus (9%), balance disorder (18%), hypotonia (9%), hemiparesis (9%), clumsiness (18%) and cranial nerves deficit (9%). CSF examination performed in 73% revealed presence of oligoclonal bands in 5 patients. MRI at admission was performed in all case revealing multiple and heterogeneous lesions. Clinical evaluation and MRI findings permitted us to make diagnosis of Acute Disseminated Encephalomyelitis (ADEM) in 55%, Multiple Sclerosis (MS) in 18%, Clinically Isolated Syndrome (CIS) in 18% and Transverse Myelitis (TM) in 9%. Conclusions: In this report we intend to remark that in demyelinating diseases, especially in paediatric patients, certainly diagnosis needs a long follow-up with periodic clinical and neuroradiological evaluations

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White matter disorders and neuroradiology

ICNC-0774: Lack of bilateral thalami involvement in one familial acute necrotizing encephalopathy 1 (ANE1)

Background: Familial and recurrent acute necrotizing encephalopathy (ANE) due to mutations in the RAN Binding Protein 2 (RANBP2) gene has been recently reported (ANE1) and is inherited as autosomal dominant.(1) Early magnetic resonance imaging (MRI) criteria require high T2 signal in both thalami to diagnosis of ANE1.(2) To date, only few ANE1 families have been described. Method: We reported two siblings who both presented with episodes of typical clinical presentation and one with atypical radiological presentation (lack of bilateral thalami involvement). Both received steroid and gammaglobulins therapy. We analyze the genetics of RANBP2, and describe clinical and radiological features in this family. Results: The family included 2 symptomatic individuals (2 siblings with encephalopathy) and five asymptomatic obligate carriers (including one carrier later died of nasopharyngeal carcinoma). MRI showed typical necrotizing lesions in bilateral thalami in one case and sparing in the other case. RANBP2 gene screening identified pathogenic heterozygous c.1966A>G (p.I656V) mutation. Secondary episodes led to death in one child and severe handicap in the other siblings. Conclusion: ANE1 due to RANBP2 mutations has a large clinical heterogeneity and implicated associated
not only encephalopathy but might associated with carcinogenesis. The brain MRI finding in our family supported the revised clinic-radiologic criteria for ANE1 proposed by Neilson et al.(1,3). Based on our familiar cases and review the literature, the expanding clinco-radiological phenotype is needed in order to early genetic diagnosis since symptomatic management of infections may be beneficial, possibly in association with steroid or gammaglobulins. Reference: 1. Neilson DE et al. Curr Opin Pediatr 2010;22:751-757 2. Mizuguchi M. Brain Dev 1997;19:81-92 3. Mizuguchi M et al. Acta Neurol Scand 2007;115:45-56

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White matter disorders and neuroradiology

ICNC-0775: Providing insights into the mechanism of action of CIMT; an fMRI based study
Introduction Modified Constraint Induced Movement Therapy (mCIMT) has been shown to have beneficial results and safety in children with hemiparetic cerebral palsy by several researchers. The current study intended to describe cortical reorganization after modified Constraint Induced Movement therapy (mCIMT) in children with hemiparesis using functional Magnetic Resonance imaging (fMRI). Methods This longitudinal study was conducted in a tertiary care teaching hospital in North India. Overall 19 children between 6 and 15 years of age having hemiparetic cerebral palsy were evaluated at baseline, within 1 week and 8 weeks of completion of 28 days of mCIMT. The evaluation included upper limb assessment using Wolf Motor Function Test (WMFT) and fMRI. Those analysing fMRI data were blinded to WMFT scores and vice versa. Results The median age was 10 years (range: 7 to 15 years), 10 subjects (52.6%) had right hemiparesis while 9(47.3%) had left hemiparesis. The fMRI changes in terms of BOLD cluster activation, Laterality index and Ipsilateral cerebellar activation ratio between all the three visits were statistically not significant. WMFT scores improved at first follow up compared to baseline which was sustained in the second follow up (p<0.05). Conclusion The current pilot study showed no definite pattern of activation. However, it established the feasibility of performing fMRI based studies in children with hemiparetic cerebral palsy. In future, studies should be planned with enough sample size and prolonged CIMT for definite conclusive evidence.

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ICNC-0791: Leukoencephalopathy with Subcortical Cysts in a child with Congenital Cytomegalovirus Infection
Introduction: MRI brain demonstrating leukoencephalopathy with subcortical cysts is often implicate of megalencephalic leukoencephalopathy with subcortical cysts (MLC), a rare, heterogenous, genetic condition. This MRI appearance has also been reported in other conditions including Aicardi-Goutières syndrome (AGS) and cystic leukoencephalopathy without megalencephaly. The emerging pathological concept of type 1 interferonopathies might shed light on this link. There have been limited reports of congenital CMV (cCMV) infection causing leukoencephalopathy with subcortical cysts.
Case Description: We report a case of cCMV infection, which presented with delayed motor development and imaging suggestive of MLC. At 12 months, T2-weighted MRI demonstrated widespread increased signal intensity of cerebral white matter and subcortical cysts at the fronto-parietal junction. Head circumference was between the 25th and 50th centile and hearing was normal. Genetic testing for the MLC1 and HEPACAM, as well as RNASET2 and GFAP genes, was negative. TORCH screen at 16 months demonstrated positive CMV IgG, negative IgM. PCR amplification of a neonatal blood spot was positive for CMV. Conclusions: 1. cCMV has a broad spectrum of neuroradiological phenotypes and may display leukoencephalopathy with subcortical cysts. cCMV infection is an important differential diagnosis to consider in non-progressive white matter disorders, including MLC. 2. AGS and RNASET2-deficient cystic leukoencephalopathy may share a common pathological mechanism with cCMV.

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White matter disorders and neuroradiology

ICNC-0800: Kept in mind Susac Syndrome
Introduction Susac syndrome (SS) is a triad of encephalopathy, branch retinal artery occlusion (BRAO) and sensorineural hearing loss. This is the result of microvascular occlusions of brain, retina, inner ear and also it is a disorder of autoimmune endotheliopathy. SS usually effects young women between the age of 20-40. Susac syndrome can be
misdiagnosed as multiple sclerosis (MS) or acute disseminated encephalomyelitis (ADEM) because of similar findings. CaseA 15 year old female patient presented in June 2015 with vomiting and severe headache. Her cerebral MRI was performed and revealing multiple lesions in the corpus callosum. CSF findings was normal. Initially diagnosed as MS and 1000 mg/day steroids was given. She started to describe hallucinations. Than treated by 5 times plasmapheresis without response. EEG was diffusely slow with 2-3 Hz delta rythm at frontal regions. On audiologial examination showed that she had left ear sensorineural hearing loss. Ophthalmological evaluation revealed BRAOs especially on the right eye. By these findings she is diagnosed as Susac Syndrome and treated by IVIG and aspirin. Conclusion Susac syndrome must be kept in mind in differential diagnosis of multiple sclerosis and ADEM.

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White matter disorders and neuroradiology

ICNC-0777: Airway size, hypoxia and brain structure in sickle cell anaemia
Background There is evidence that low daytime and overnight haemoglobin oxygen saturation (SpO2) is associated with risk of overt and covert stroke, subtle abnormalities on magnetic resonance imaging (MRI) and cognitive difficulties in children with sickle cell disease (SCD). We hypothesized that the size of the airway, measurable using MRI, is associated with overnight SpO2 and with brain infarction. Methods Airway measurements (i) adenoid width, (ii) adenoid length (iii) anterior-posterior (AP) width of the airway at C2 and (iv) length of the airway from the soft palate to the base of the tongue were made on MRI (Siemens) in 2 cohorts of children with SCD: (1) the East London cohort (ELC; n=54) studied on a 1.5T MRI from 1991-2001 with overnight home oximetry (2) the London Sleep Asthma cohort (LSAC; n=22) who had full polysomnography from 2006-2011 and a 3T MRI during 2015-16. Results In the ELC, adenoidal width correlated inversely with minimum overnight SpO2 (r=-.288; p=.03) but was lower in those with infarction (p=.01). In the LSAC, airway length correlated with minimum overnight SpO2 (r=.514, p=.04) and was shorter in SCD patients without infarction than controls (p=.084) but not SCD patients with infarction (p=.08); analysis of diffusion tensor imaging and brain and airway volume is underway. Discussion Measurement of the adenoids and airway on MRI may be useful in screening for low overnight SpO2. Unexpectedly, wider adenoids and shorter airway length were associated with absence of cerebral infarction in SCD, possibly reflecting early protective preconditioning by hypoxia and/or infection.

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White matter disorders and neuroradiology

ICNC-0947: Megalencephaly with polymicrogyria and periventricular laminar heterotopia: newly recognized migration disorder
Introduction: Megalencephaly-related migration disorders include megalencephaly-capillary malformation (MCAP) and megalencephaly-polymicrogyria-polydactyly-hydrocephalus (MPPH) syndromes. Both syndromes are partly overlapping disorders and are proved to due to the gene mutations in PI3K-AKT signal pathway. In proposal diagnostic criteria for two syndromes, it is noted that the brain heterotopia is absent. We report the patient with megalencephaly with polymicrogyria and symmetrical laminar heterotopia in periventricular region. Patient description: A female patient was born at term after a normal pregnancy and delivery. Macrocephaly was noted at 1 month of age. At 6 months of age, she was referred for global developmental delay and enlargement of head circumference (49.0 cm, +3.5 SD). Magnetic resonance imaging revealed bilateral generalized polymicrogyria prominently in temporal regions and extensive laminar heterotopia in periventricular region symmetrically with posterior dominancy. She developed intractable focal seizures at 9 months of age, and subsequently they evolved to epileptic spasms. Total callostomy at 22 months of age reduced drop attacks but she showed profound developmental delay. Cytogenetic analysis: Chromosome G-band analysis showed 46,XX. Whole exome sequencing from patient’s peripheral leukocytes identified no pathogenic mutation in neuronal migration related genes. Discussion: Neuroimaging of our patient reveals extensive symmetrical heterotopias in addition to MPPH like images, suggesting the previously unrecognized migration disorder. Showing megalencephaly suspects existence of genetic factor, however, genetic analysis could not elucidate the genetic background of this patient. Further comprehensive genetic analysis such as whole genome sequence or somatic mutation analysis of affected region would provide the clue to genetic background of this patient.

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ICNC-0396: Acute-onset encephalopathy and Leukoencephalopathy in children: Inflammatory or toxic? A case series from two tertiary care centres in India

Background: Etiopathogenesis and neuroimaging features of children with acute-onset encephalopathy and leukoencephalopathy is poorly understood. Study methods: Ten children with acute-onset encephalopathy and supratentorial leukoencephalopathy at two tertiary care pediatric centres over 4 year period were reviewed. Results: Mean age was 46 months (range 9-96). Nine had fever (1-4 days), followed by encephalopathy (GCS range 3-13) and seizures at admission. Six had status epilepticus (4 refractory SE and one non-convulsive status epilepticus). Also shock in 5, sepsicaemia in 5, mechanical ventilation in 7. Mean hospital stay was 18.3 days (3-30 days). MRI of all children showed extensive leukoencephalopathy involving frontal and parietal lobes (all), and temporal and occipital lobes (nine each). 2 children had sparing of peri-rolandic white matter. None had cortical grey matter involvement, 4 had basal ganglia involvement. Thalamic, cerebellar involvement was rare (one each). All had restricted diffusion of affected regions. One had minimal Gadolinium enhancement of white matter. 8/9 had normal CSF with negative HSV-PCR, and negative autoimmune antibodies in 4 children. Nine had febrile encephalopathy of unclear etiology, while one child had organophosphate poisoning. Five received IV Methylprednisolone. One died during hospital stay. At follow-up (1-36 months), 8/9 were seizure-free, all had significant improvement in motor milestones, 8 had variable cognitive impairment. All were requiring rehabilitation. Discussion & Conclusion: The acute-onset leukoencephalopathy is a distinct clinico-radiological entity affecting children of all ages, with fever, seizures and encephalopathy, diffuse supratentorial leukoencephalopathy. Toxic/inflammatory mechanisms are likely. Exact pathophysiology are to be elucidated.

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ICNC-0779: Childhood-onset cerebellar atrophy: clinical spectrum and approach to diagnosis

Introduction: Childhood-onset cerebellar atrophy is associated with a heterogeneous group of disorders. Diagnosis is often challenging. We have reviewed 157 patients with confirmed cerebellar atrophy or cerebellar hypoplasia on magnetic resonance imaging (MRI) presenting to a tertiary care hospital over a 20-year period. The spectrum of presenting clinical features and associated diagnoses has led to the development of a proposed diagnostic approach. Methods: Retrospective analysis of case records in children (0-18 years) with confirmed cerebellar atrophy or hypoplasia on MRI presenting between 1994 and 2014. Clinical features, detailed neuroimaging findings and diagnostic investigations were analysed. Results: 86 females and 71 males were identified. The mean age at presentation was 16 months. A diagnosis was established in 43% of patients. Mitochondrial disorders were the most common diagnoses, followed by infantile neuroaxonal dystrophy and ataxia telangiectasia. Chromosomal abnormalities were identified in 8% of patients, and not all showed a static course. 57% of patients were undiagnosed. The most common presenting feature was developmental delay in 119 patients (75%), followed by balance/gait difficulties (30%) and seizures (14%). Detailed MRI evaluation guided further investigations. Significant abnormalities in electromyography and nerve conduction studies, electroencephalogram, or electroretinogram and visual evoked potentials were found in almost 50% of patients. A genetic diagnosis was confirmed in 24% of patients. A diagnostic approach has been developed. Conclusion: Many children with cerebellar atrophy remain undiagnosed. Although new genetic techniques have increased the diagnostic yield, a careful evaluation of clinical features and detailed analysis of brain imaging should guide further investigations.

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White matter disorders and neuroradiology

ICNC-0780: Self-paced modification increases specificity and applicability of pediatric language fMRI: a feasibility study

Introduction: We have previously developed an fMRI task battery (synonyms and vowel identification tasks) for assessing the language domain in children. However, using a fixed stimulus presentation time seemed to be suboptimal in the presence of below- or above-average language abilities, as the task is perceived to be either too fast or too slow. This
must be expected to impair cooperation, which is critical in pediatric fMRI. Therefore, in this feasibility study in healthy adults, we modified these language tasks by using a self-paced paradigm, and also evaluated the impact of using a block- versus an event-related statistical approach. Methods: Twenty adult subjects were included. They performed the synonyms and the vowel identification tasks during fMRI performed on a 1.5 T Siemens MR-scanner. Functional data analysis was performed using SPM8. One sample t-tests were used in order to assess group activation patterns obtained using a block- or an event-related statistical approach, while results from the two statistical approaches were compared by paired t-tests. For all analyses, significance was assumed at a voxelwise p ≤ 0.05, FDR-corrected for multiple comparisons and an additional cluster-level FWE-correction at p ≤ 0.05. Results: The self-paced modification allowed our participants to process stimuli more than 2.5-times faster than originally implemented, likely increasing task adherence. A higher specificity of the event-related analysis was confirmed by stronger left inferior frontal and right cerebellar activation. Conclusion: We suggest that a self-paced modification of an fMRI language battery is promising when aiming to investigate language functions in subjects with above- or below-average language abilities.

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ICNC-0781: Diffusion tensor imaging in glucose transporter 1 deficiency syndrome

Introduction: Although MRI findings are considered nonspecific in glucose transporter 1 deficiency syndrome (GLUT1-DS), delayed myelination or white matter signal abnormality are seen in some patients. We performed diffusion tensor imaging (DTI) to assess white matter abnormality in patients with GLUT1-DS. We also studied longitudinal change of DTI.Methods: We studied 6 patients with GLUT1-DS. Age at the scan was 3 to 18 years (mean 10.7 years). DTI was acquired using 3T MRI (3.0T Trio, Siemens) and fractional anisotropy (FA) images were constructed. The FA images of patients were compared with those of 45 controls aged 2 to 16 years (mean 9.9 years). Three patients had DTI 2 or 3 times. Statistical analysis of FA images was carried out using tract-based spatial statistics (TBSS) implemented in FSL (The Oxford FMRIB Software Library). Regions with significant differences were identified with threshold: p<0.05. Mean FA values in the skeleton with significant difference on TBSS were calculated and longitudinal change was evaluated in 3 patients.Results: TBSS showed widespread FA reduction in the cerebral white matters, brain stem, and cerebellum of patients. FA reduction persisted in 3 patients with repeated scans. A patient in whom ketogenic diet was started at 3 years old, FA reduction was less at 6 years old than that at 3 years.Conclusion: Widespread FA reduction suggests delayed myelination or white matter damages caused by glucose deficiency in CNS. Ketogenic diet from infancy possibly improves white matter abnorality in GLUT1-DS.

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ICNC-0782: Recurrent Idiopathic Intracranial Hypertension due to extreme dilation of Virchow–Robin spaces: first case report

Introduction Virchow-Robin spaces (VRS) are normal perivascular spaces within the brain parenchyma and frequently clinically silent. The precise pathophysiological mechanism is poorly understood. Dilated VRS have been described in patients with various neurological disorders, such as mental retardation, memory impairment, epilepsy, headaches, and macrocephaly. To our knowledge, this is the first report of dilated VRS in a patient with idiopathic intracranial hypertension (IH). Case report A four year old boy, born at term following unremarkable perinatal period with subsequent normal neurological development has been referred to our outpatient clinic with papilledema without any complaint. On physical examination, head circumference was 52 cm (90 percentile). His neurological examination was unremarkable except bilateral papilledema. Brain magnetic resonance imaging (MRI) showed enlarged VRS throughout the occipital periventricular white matter with signal hyperintensities in T2-weighted images. His lumbar puncture showed an elevated
opening pressure (480mmH2O) with normal content of cerebrospinal fluid (CSF). Laboratory investigations for IIH were normal. The patient was initially treated with topiramate. After six months, papilledema resolved and CSF pressure was normal (180mmH2O). The patient readmitted with papilledema after one year. There were no additional findings on physical examination. Brain MRI at the age of five years revealed similar findings. CSF pressure was high (600mmH2O) with normal content. Acetazolamide therapy was started. Discussion This is the first case report of recurrent IIH in a patient with dilated VRS. Better awareness and prompt diagnosis of this unusual but predisposing entity will provide a good outcome without any sequela in its management.

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White matter disorders and neuroradiology

ICNC-0932: Familial risk of multiple sclerosis and other autoimmune diseases in children

Objective: To assess the prevalence of autoimmune diseases in first-degree relatives of pediatric patients with multiple sclerosis (MS). Methods: We analyzed medical records of 116 pediatric patients with definite MS (33 boys, 83 girls) in order to identify patients who suffer from another autoimmune disease and patients whose relatives suffer from MS and other autoimmune diseases. Results: Four out of 116 (3.45%) patients with MS suffered from other autoimmune disease (autoimmune thyroid disease in 2 cases; idiopathic thrombocytopenic purpura in 1 case, autoimmune hepatitis in 1 case). There were 9 (7.8%) cases of familial multiple sclerosis: 5 in first-degree relatives, 1 case of multiple sclerosis in second-degree relatives, 3 cases of multiple sclerosis in third-degree relatives. Two patients had 2 relatives with MS. One patient had 1 first-degree relative who suffered from neuromyelitis optica (NMO). The most frequent autoimmune diseases in patients’ relatives were autoimmune thyroid disease (4 cases) systemic lupus erythematosus (2 cases), granulomatosis with polyangiitis (1 case), and rheumatoid arthritis (1 case). Conclusions: Our results show that autoimmune diseases cluster within families of children with MS. This supports the hypothesised that MS and some other autoimmune diseases might arise on a

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White matter disorders and neuroradiology

ICNC-0933: Efficacy and safety of interferon beta therapy in children with multiple sclerosis: prospective study of 84 patients

Introduction: Approximately 2-10% of all multiple sclerosis (MS) patients experience their first symptoms before the age of 16. The relapse rate in children with MS is higher than in adult-onset disease. Currently, disease modifying therapies with interferon beta are approved for children. Aim: To report the efficacy and safety of interferon beta therapy in a prospective study of 84 children with MS. Methods: A cohort of 84 patients with MS (27 boys, 57 girls), who started disease modifying therapy with INF beta was prospectively followed. Medical data including the relapse rate, time to MRI progression, time from disease onset to therapy, and safety parameters were analyzed. Results: Mean follow-up was 20 (1-121) months. Average age at MS onset was 13.9 (5-17.6) years. In 77 patients (91%) therapy was well tolerated. In 22 patients (25%) therapy was stopped due to lack of efficacy. The time interval between first symptoms and initiation of treatment ranged from 1 month to 8 years. Treatment was inefficient in 7, 17, 25, and 35% of patients who started treatment within 6 months, 7 to 12 months, 13 to 18 months, and later than 19 months after the onset of disease, respectively. Conclusions: Interferon beta therapy is effective and safe in children with MS. Longer time gap

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White matter disorders and neuroradiology

ICNC-0784: Neuroimaging in patient with mucopolysaccharidoses

INTRODUCTION: Mucopolysaccharidoses (MPS) represents a heterogeneous group of inherited lysosomal storage disorders characterized by defective degradation of long-chain complex carbohydrates. The aims of this article are to describe the neuroimaging findings in patients evaluated in our hospital with this diagnosis.METHODS:We analysed retrospectively the 10 children who had been diagnosed with MPS between 2007 and 2014: 7 had type I (4 with Hurler syndrome and 3 with Hurler-Scheie syndrome), 1 had type III or Sanfilippo syndrome and 1 had type IV or morquio syndrome. We describe Cranial and spinal MRI in this patients.RESULTS: Cranial and spinal MRI imaging revealed a broad spectrum of changes in patients with MPS. The most prominent brain features,in almost all patients,are enlargement of PVS(perivascular spaces) , white matter changes(85% in MPS I,100% in MPS III and without involvement in MPS IV) ventriculomegaly(60% in MPS I,100% in MPS III and MPS IV ), cortical atrophy(60% in MPS I,100% in MPS III and MPS IV).
III and MPS IV) and in spinal neuroimaging, canal stenosis (71% in MPS I, 100% in MPS III and MPS IV) are usually present. CONCLUSIONS: Neuroimaging finding in MPS patient including dilated Virchow-Robin perivascular spaces, white matter abnormalities and ventriculomegaly however is not specific for definite diagnosis of MPS but should be consider in evaluation of patient whith non specific neurodevelopmental delay. We find a correlation between these findings and clinical severity of MPS. Key Word: Mucopolysaccharidoses, Neuroimaging, MPS, MRI, , white matter changes

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White matter disorders and neuroradiology

ICNC-0507: Neuroimaging as a biomarker in the diagnosis of neurodegeneration with brain iron accumulation (NBIA): a retrospective observational study

Introduction: Neurodegeneration with brain iron accumulation (NBIA) refers to a heterogeneous group of disorders with increased focal brain iron deposition with neuronal loss and gliosis. In this series, we describe the clinical phenotype, neuroimaging findings, and genotype in a cohort of children and adolescents with NBIA. Methods: Clinical data, neuroimaging characteristics and genetic evaluation of twenty children with a diagnosis of NBIA during the period January 2012–July 2015 were carried out. Results: The average age at onset of symptoms was 47.45 months (SD 43.31) and average age at presentation was 90.10 months (SD 42.42). Consanguinity was present in 40% of cases and 25% had positive family history. Frequency falls, gait disturbances, motor regression, speech disturbances, extrapyramidal symptoms, dystarthis, spasticity, hyper reflexia and extensor plantar response were observed in 65–100%. Visual disturbances were evident up to 45%. Based on the neuroimaging findings, diagnosis of pantothenate kinase associated neurodegeneration (PKAN) was established in 6, beta propeller associated neurodegeneration (BPAN) in 1, mitochondrial membrane associated neurodegeneration (MPAN) in 1, infantile neuronal axonal dystrophy (INAD) in 10 and undifferentiated in 1 case. Genetic analysis was performed only in 10 patients (pathogenic variations of PLA2G6 in 4, PANK2 in 3, WDR45 in 1 and C19ORF12 in 2 patients). Novel disease causing variants were identified in 5 children. Radiological categorization was in 100% concordance with genetic diagnosis. Conclusion: Neuroimaging is a sensitive biomarker and has tremendous utility in the evaluation of brain iron disorder. Neuroimaging abnormalities may help to distinguish subtypes of NBIA and guide in targeted genetic studies to facilitate a more definitive diagnosis.

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White matter disorders and neuroradiology

ICNC-0321: Olfactory development and dysgenesis in fetus and neonate

Introduction: Discrimination of odorous molecules in amniotic fluid is demonstrated after 30 weeks gestation; fetuses exhibit differential responses to maternal diet. Neonatal olfactory reflexes enable reliable testing. Olfactory nerves project from nasal epithelium to telencephalon before olfactory bulbs form. Neurons of the olfactory bulb arrive via the rostral migratory stream. Olfactory bulb synaptic glomeruli and concentric laminar architecture are unlike other cortices. Olfaction is the only sensory system without thalamic projection because of its own intrinsic thalamic equivalent. Olfactory bulb, tract and epithelium are repositories of progenitor cells. Methods: Post-mortem immunocytchemical study of olfactory system was performed in 24 normal fetuses and neonates of 16-42wk gestation and 8 abnormal brains. Results: Olfactory maturation is incomplete at term for synaptogenesis and myelination. A transitory olfactory recess of the lateral ventricle involutes postnatally but dilates in fetal hydrocephalus. Malformations of the olfactory bulb are diverse, ranging from arrinencephaly to enlarged bulbs to fusion and dysplastic architecture, including genetic/metabolic diseases. Conclusions: Olfactory immaturity does not preclude function. Olfactory dysplasias can be diagnosed not only neuropathologically but also by clinical examination and pre- and post-natal imaging. Cranial nerve 1 should be included in the neonatal neurological examination.

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White matter disorders and neuroradiology

ICNC-0786: Pediatric Lhermitte-Duclos disease

INTRODUCTION: Lhermitte-Duclos disease (LDD) is a rare condition in pediatrics. It is defined as a tumoral lesion of the cerebellar cortex with slow growth and unknown etiology. Clinical manifestations are diverse, from asymptomatic cases to patients with cerebellar dysfunction signs, non-communicating hydrocephalus and cranial neuropathy. AIM To describe
the clinical and imaging characteristics of two pediatric patients with pathologically confirmed LDD. MATERIAL AND METHODS Two patients, a male aged 11 and a female of 14 years old are described. The first patient presented a progressive onset bifrontoparietal headache and vomiting. The second case showed a subtle left central isolated facial paralysis of one year of evolution. RESULTS Lumbar puncture was performed in both patients. One of them presented mild pleocytosis, butbacteriological, virological and cytology for neoplastic cells investigation were negative. In the other patient, cerebrospinal fluid was normal. Cerebral MRI showed hyperintense cerebellar lesion on T2, FLAIR, DWI sequence and drop on the ADC map. After administration of intravenous contrast, a faint leptomeningeal enhancement of interfoliar spaces appeared. Both injuries produced partial collapse of the fourth ventricle. Spectroscopy with fail in NAA neuronal marker. LDD diagnosis is confirmed by biopsy. Currently both patients are asymptomatic. CONCLUSION The LDD is an entity of high clinical heterogeneity. The presence of cerebellar lesions in NMR with "tigroid" pattern on T2 should be considered highly suggestive and specific to this pathology. The diagnosis can be confirmed through histopathological analysis.

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White matter disorders and neuroradiology

ICNC-0501: Genetic heterogeneity in 26 infants with a hypomyelinating leukodystrophy
T2 hyperintensity of brain white-matter lesions detected by magnetic resonance imaging (MRI) include a heterogeneous group of diseases. Persistent T2 high intensity in combination with T1 iso- or high intensity of white matter in infants indicates a lack of normal myelination, that is, hypomyelination; however, the precise diagnosis of hypomyelinating leukodystrophy based solely on MRI findings can be difficult, especially in the early stage of the disease. We studied 26 patients who were diagnosed with hypomyelinating leukodystrophy according to MRI findings and clinical features to uncover their genetic etiology through chromosomal analyses, targeted gene analyses, and array comparative genomic hybridization (aCGH) assay. Then, for the 17 patients with unexplained hypomyelination by traditional analyses, whole-exome sequencing (WES) was performed. The presumptive diagnoses were confirmed in 61.5% of the enrolled patients (16/26) and involved 9 different genetic backgrounds. The most frequent backgrounds were 18q deletion syndrome and Pelizaeus-Merzbacher disease, with an incidence of 12% (3/26) for both. The diagnostic rate of chromosomal analyses, targeted gene analyses, and aCGH was 31% (8/26), and one patient was clinically diagnosed with Cockayne syndrome. Using WES, the following causative genes of hypomyelination were identified in seven individuals (35%, 6/17): TUBB4A, POLR3B, KCNT1, and MCOLN1, and some of those genes are pathogenic for not only hypomyelination but also dysmyelination or delayed myelination. Our findings suggest heterogeneous genetic backgrounds in patients with persistent white matter lesions. These data also indicate that WES may be a rapid and useful tool for identifying the underlying genetic causes of undiagnosed leukodystrophies.

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White matter disorders and neuroradiology

ICNC-0934: Gallbladder and the risk of polyps and carcinoma in metachromatic leukodystrophy
Objective: Metachromatic leukodystrophy (MLD) is an inherited neurodegenerative disorder caused by deficiency of arylsulfatase A. Consequently, sulfatides accumulate, ultimately leading to demyelination of both PNS and CNS. Gallbladder abnormalities, such as polyps, as a consequence of sulfatide accumulation in the gallbladder, have been described in case studies. The presence of a gallbladder carcinoma, normally occurring at an average age of 56-63 years, in a 32-year-old MLD patient prompted us to study the relationship between MLD and the development of gallbladder polyposis and carcinoma. Methods: 34 MLD patients (average age 16-7 years, age range 2 to 39 years) screened for gallbladder abnormalities by ultrasound were evaluated. In the case of cholecystectomy, findings at pathology were reviewed. Results: Only 8/34 (23%) patients had a normal gallbladder at ultrasound. Gallbladder polyps were visible in eight (23%) patients. Cholecystectomy was performed in eleven (32%) patients. In these, pathology revealed various abnormalities, including hyperplastic polyps, intestinal metaplasia, prominent Rokitansky-Aschoff sinuses and sulfatide storage. Conclusion: These results suggest that gallbladder involvement is the rule rather than the exception in MLD. Moreover, the high prevalence of hyperplastic polyps, a known precancerous condition, and the exceptionally young presentation of a fatal gallbladder carcinoma suggest that MLD predisposes to neoplastic gallbladder abnormalities. As novel therapies for this patient group are emerging leading to increased life expectancy, we recommend screening for gallbladder abnormalities by ultrasound in order to prevent early death.

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Opinion of Prof. Dr. V came as negative. Our next possible diagnosis was Vanishing white matter. Hence Molecular testing done following Megalencephalic Leucodystrophy. Hence DNA of the child was tested for mutations in MLC 1 gene by sequencing which the child had lost all her acquired milestones. The child was examined in detail. Our initial diagnosis from her a missed abortion in her second pregnancy. The second child was born at term with no immediate neonatal complications. The child had attained normal neuroregression. She was referred for her second child’s evaluation at 8 months of her life. Her first child was born at term with no immediate neonatal complications, except treated for respiratory distress on day 2 of life. She had global developmental delay with seizure disorder since 8 months of age. On examination she had mild dysmorphism and his MRI images were dilated lateral ventricles and inferior horns with large anterior temporal cysts. The white matter abnormalities were not diffuse and was not swollen ruling out the possibility of Megalencephalic Leukodystrophy with cyst. she was tested negative for MLCI gene. On repeating the MRI images again we noted dilated lateral ventricles and inferior horns with large anterior temporal cysts. The white matter abnormalities were not diffused and was not swollen ruling out the possibility of Megalencephalic Leukodystrophy with cyst. A possibility of Congenital cytomegalovirus brain infection was suspected. As a differential Aicardi Goutiers syndrome was thought of and gene analysis was negative. Inview of the MRI findings and RNASET2 gene was analysed which revealed a novel homozygous pathogenic mutation and parents were also found to be heterozygous for the same confirming the diagnosis of Cystic leukoencephalopathy without megalencephaly in this family.

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White matter disorders and neuroradiology
ICNC-0935: A case of RNASET2-deficient cystic leukoencephalopathy, identified in India with homozygous novel Mutation in the RNASET2 gene.
Objective: We report data on a South Indian family with two children affected with Cystic Leukoencephalopathy with homozygous novel Mutation in the RNASET2 gene. Design: Case report. RNASET2-deficient cystic leukoencephalopathy is a non-progressive leukoencephalopathy disorder that occurs without megalencephaly. Not more than 50 cases have been reported till date. We present a third degree consanguinous couple, with 2 male children affected with similar presentation of severe psychomotor delay at infancy with seizure disorder. First child’s antenatal period was uneventful, he was born of normal full term delivery. Noted to have poor activity and feeding & treated for sepsis in the neonatal period. He had global developmental delay with recurrent episodes of respiratory infection and eventually succumbed at the age of 3yrs & 6months. No investigations were available from this child. Second child was brought to our center at the age of 2yrs & 6 months for genetic evaluation. Ueneventful antenatal period, born at term, no immediate neonatal complications, except treated for respiratory distress on day 2 of life. She had global developmental delay with seizure disorder since 8 months of age. On examination she had mild dysmorphism and his MRI images were suggestive of Megalencephaly with leukodystrophy with cyst. she was tested negative for MLCI gene. On repeating the MRI images again we noted dilated lateral ventricles and inferior horns with large anterior temporal cysts. The white matter abnormalities were not diffused and was not swollen ruling out the possibility of Megalencephalic Leukodystrophy with subcortical cysts. A possibility of Congenital cytomegalovirus brain infection was suspected. As a differential Aicardi Goutiers syndrome was thought of and gene analysis was negative. Inview of the MRI findings and RNASET2 gene was analysed which revealed a novel homozygous pathogenic mutation and parents were also found to be heterozygous for the same confirming the diagnosis of Cystic leukoencephalopathy without megalencephaly in this family.

White matter disorders and neuroradiology
ICNC-0936: An Indian family with two children with history of neuroregression: Classical history, MRI findings, Molecular and prenatal diagnosis of Vanishing White Matter disease
Objective: Our Case report is on an Indian family with two children with Vanishing white matter disease. Design: Case Report A fourth degree consanguineous couple was referred to genetic clinic as two of their children had similar history of neuroregression. She was referred for her second child’s evaluation at 8 months of her life. Her first child was born at term with no immediate neonatal complications. The child had attained normal milestones till 7 months of her life. Later she lost the milestones she acquired following a illness. She was investigated and she died at 1 year of life. Mother had a missed abortion in her second pregnancy. The second child was born at term with no immediate neonatal complications. The child had attained normal developmental milestones till 7 months of her life. Following a viral illness, the child had lost all her acquired mile stones. The child was examined in detail. Our initial diagnosis from her MRI was Megalencephalic Leucodystrophy. Hence DNA of the child was tested for mutations in MLC 1 gene by sequencing which came as negative. Our next possible diagnosis was Vanishing white matter. Hence Molecular testing done following opinion of Prof. Dr. Van der Knaap from Amsterdam, Netherlands. The child was found to harbor homozygous mutation (c.584G>A,p.Arg195His)in the gene EIF2B5, which is commonly called “cree founder mutation”. This mutation is
associated with severe variant of the disease. The second child also died at 11 months of her life. The parents were heterozygous for the same mutation. Prenatal diagnosis in the subsequent pregnancy showed a heterozygous variant in the fetus. Conclusion: Children with classical clinical history and MRI findings of Vanishing white matter should have a molecular confirmation which will help the family for prenatal diagnosis.

White matter disorders and neuroradiology

ICNC-0937: Aicardi Goutieres - A close mimicker of congenital infection: Case series with 3 children and 4 families
Aicardi Goutieres is an autosomal recessive encephalopathy caused by mutation in any one of the six genes - TREX1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, or ADAR. We report three children in whom we could diagnose AicardiGoutieres by the characteristic radiological findings and subsequent molecular confirmation. In the last family using the characteristic radiological finding alone Aicardi goutieres was suspected and molecular confirmation was also done. In two families prenatal diagnosis was done in subsequent pregnancies Case 1: Child was evaluated at 8 months of life as she did not acquire any milestones had scissoring of legs and nystagmus. CT Brain showed calcification in periventricular areas, basal ganglia and cerebellum. The child succumbed at 3 years of age. The second child also presented with a similar history. She was evaluated at 5 months of age due to delay in achieving milestones. The parents had noted rash like lesions on the fingers of the child on and off. Her CT imaging also showed periventricular and basal ganglia calcifications. On examination the child had microcephaly and hypertonia. In view of the history, clinical and radiological findings Aicardi Goutieres was suspected and the molecular testing was done. This showed a frameshift mutation in TREX1 gene confirming the diagnosis. Parents were also found to be heterozygous and subsequent prenatal diagnosis showed that the fetus was unaffected Case 2: A live term baby was delivered by LSCS. The baby was apparently normal till 23 days when she presented with high grade fever, nystagmus and seizures. Subsequently baby was very irritable and did not attain any milestones. CT Brain showed multiple periventricular calcification and MRI showed leukodystrophy and this pointed to a diagnosis of Aicardi Goutieres syndrome. Molecular testing confirmed AGS due to mutation in RNASEH2C gene and parents were found to be carriers. The child succumbed at 10 months of age. Case 3: This child was born to third degree consanguineous couple and was being evaluated for global developmental delay. The child was born by normal delivery at term with a birth weight of 3kg. The child was evaluated around 6 months as he did not attain head control yet. At that time CT brain showed periventricular calcification. MRI at 2.5 years showed cystic changes in temporal lobe. These features raised the suspicion of Aicardi Goutieres and molecular screening confirmed AGS as he was found to have mutation in RNASEH2C gene. Parents were found to be carriers and testing in subsequent pregnancy revealed an affected fetus and the family opted not to continue the pregnancy Case 4: This was third degree consanguineous couple who had come for genetic counseling regarding future pregnancies. They had lost two children. The first child was born at term with a birth weight of 2.5 kg. The baby had microcephaly at birth. The baby developed seizures by 55 days of life. The baby had tachypnea, pallor and intermittent apneic spells. CT Brain showed extensive calcification in the basal ganglia, periventricular and subcortical areas. MRI brain showed leukodystrophy with cystic changes in temporal region. Baby succumbed by 2.5 months. Ultrasound in second pregnancy showed microcephaly and intraventricular calcification at 31 weeks. There was also evidence of fetal anemia. A female baby was delivered at term with birth weight of 2.1 kg. Baby did not cry well after birth, was lethargic and died after seven days of life. In view of the history a strong suspicion of Aicardi Goutieres was entertained and carrier screening for the couple was performed and they were found to be carriers for mutation in TREX1 gene thereby confirming the diagnosis.

White matter disorders and neuroradiology

ICNC-0938: Anxiety, depression and stress in parents of children with communication and behavioural disorders

Aim: Aim of the study was to evaluate anxiety, depression and stress in the parents of children with communication and behavioral disorders to design appropriate intervention programs. Materials and Methods: This study was a hospital based prospective observational study. 110 parents of children with communication and behavioral impairment were randomly enrolled for the study. The children were provisionally diagnosed by the Neurologist, Speech language pathologist and Psychologist. Depression Anxiety and Stress Scale-21 (DASS) and Parental stress scale were used to identify the anxiety, depression, and stress in the parents. Results: The mothers were more affected compared to fathers. Unemployed mothers, with two or more children showed high psychological distress. Psychological problems of the mothers were more if affected children were female. When the affected children were administered behavioral intervention techniques and mothers learned coping skills, the mothers showed improvement in DASS Scores and Parental Stress Scale scores. Conclusion: Our study emphasizes the importance of psychological care of parents of

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White matter disorders and neuroradiology

ICNC-0939: Impact of perceptual reasoning deficits on academic achievement in normal school children

Aim: 1. To examine the deficits in verbal and non verbal intelligence in children presented with poor academic performance. 2. To compare perceptual reasoning ability (predictor of non verbal learning disorder) of these children against their academic achievement.

Materials and Methods: This is an observational study conducted in a tertiary care hospital in India. Thirty two children of age 6-15 years of both sexes, who presented with a complaint of decline in academic performance and were assessed with Malin’s Intelligence Scale for Indian Children (MISIC) and National Institute of Mental Health and Neurosciences’ (NIMHANS) index of specific learning disabilities. Exclusion criteria: Children with physical and mental growth problems, epilepsy, developmental disabilities, birth injuries, pre natal injury and traumatic brain injury were excluded from the study. Results: NIMHANS index of specific learning disabilities brought out reading, writing, arithmetic difficulties in the study population. All these children had impairment in object assembly test of MISIC compared to other subtests which clearly indicated deficit in perceptual reasoning ability. Conclusion: Nonverbal learning disorder can cause poor academic achievement. This was brought out by showing impairment in object assembly test using MISIC in our study.

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White matter disorders and neuroradiology

ICNC-0789: Measures of Ventricles and Evans’ index; from neonate to adolescence

Objective: Ventricles sizes are important for early diagnosis of hydrocephalus or follow-up after ventriculostomy. Measurements of ventricle may change with age especially in childhood age. Providing of normative data about ventricle diameters is aimed with this study.

Patients and Methods: Among 14854 cranial MRI performed between 2011-2013, 2755 images of Turkish children aged 0-18 were acquired. After exclusions 517 images were left. Four radiologists were educated by pediatric radiologist. Twenty images were assessed by all radiologists for pilot study then seen that there was no inter-observer variation. Results: There were 10-22 children in each age group. The maximum width of the third ventricle was 5.54±1.29 mm in males in 1 age group, and 4.98±1.08 mm in females in 2 age group. Evans’ index was lower than 0.3 and consistent with literature. Third ventricle / Basilar Artery width ratio was found >1 and <2 in all age and both gender group. Conclusion: Our study demonstrated the ventricle size data of children in various age groups from newborn to adolescent. Ventricle volume to cerebral parenchyma ratio seems to decrease with age. It is thought that these data can be applied in clinical practice especially in early diagnosis of hydrocephaly. Running title : Ventricle diameters in childhood

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White matter disorders and neuroradiology

ICNC-0790: MRI Measurements of Corpus Callosum in childhood; Determination of normative values

Key words: Children, Corpus Callosum, MRI Measurements, Normative Data. Synopsis: Even mild structural disorders of CC may be important in the diagnosis of neurological diseases or syndromes in childhood. Therefore, it’s important to determine the reference values of CC dimensions in healthy children. These data can be applied in clinical practice.
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Objective: Corpus callosum (CC) has an important role in ensuring the transfer of information between homologous regions of hemispheres. Radiological anatomy of CC may contribute to diagnostic evaluation in children with neurological or syndromic diseases. Although some previous studies are present about the dimensions of CC in different populations, but there isn’t enough study examining the reference sizes of CC in childhood. The aim of this study was to identify the normal dimensions of CC subregions using MRI in healthy children of all age groups and gender. Methods: Among 14852 cranial MRI performed between 2011-2013, 2753 images of children aged between 0-18 were acquired. After exclusions 493 images (boys/girls; 246/247) were included. The thickness of the genu, corpus, isthmus, splenium and antero-posterior diameter of CC is measured on MRI. Results: We demonstrated CC dimensions data of children from newborn to adolescent. Conclusions: We think that it is important to determine the reference values of CC dimensions in healthy children to in order to be detected deviation from normal. It is thought that these data can be applied in clinical practice.

ICNC-0940: Delay of MRI abnormalities in pediatric acute disseminated encephalomyelitis

Introduction: Acute disseminating encephalomyelitis (ADEM) is an inflammatory demyelinating disease affecting the central nervous system mainly in young children. New or enlarging MRI lesions can occur even during clinical recovery. This is a potential problem as the 2012 IPMSSG diagnostic criteria for pediatric multiple sclerosis (MS), state that MS diagnosis can be made when new clinical symptoms occur with new lesions on MRI at least three months after onset. Here we aim to study the timing of MRI abnormalities related to the evolution of clinical symptoms in our Dutch pediatric ADEM cohort. Methods: Children less than 18 years old with ADEM, selected from our database of acquired demyelinating syndromes, were eligible when at least one follow-up brain MRI was available and the first MRI was performed within three months after onset. In case of a multiphasic disease course, only MRIs obtained before the second attack were assessed. Changes in MRI abnormalities and clinical status were categorized as 1) improvement, 2) deterioration and 3) unchanged. If MRI lesions deteriorated, this was further specified as ‘new lesions’ and/or ‘enlargement of lesions’. Results: Forty-two patients fulfilled our inclusion criteria. During clinical recovery, in the first three months, new lesions and/or enlargement of existing lesions were observed in half of the cases. In contrast, MRI abnormalities rarely deteriorated after three months after onset. Conclusions: Our results indicate that a brain MRI should be performed three months after onset as a reference for further follow-up imaging, in order to avoid an incorrect MS diagnosis after a first episode of ADEM.

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ICNC-0942: Expanding the phenotype of COL4A1 mutation-related disorders

Introduction: COL4A1 mutations, first described in 2005 as a cause of porencephaly, are now known to affect the heart, kidneys, eyes, muscle as well as the brain. Most patients (>60%) develop signs antenatally or soon after birth. We present a paediatric case presenting at 11 years with previously undescribed symptoms associated with COL4A1 mutations, as well as the symptoms of his likely affected father and siblings. Case description: The index case is an 11 year old boy presenting with headaches and dizziness. The headaches occurred 2 to 3 times a week lasting a few minutes, and were stabbing in nature. He complained of constant dizziness. There was a background history of being ‘clumsy’. Antenatal scans and history were normal, congenital cataracts were operated on as a baby. Neurological examination was normal except for mild co-ordination difficulties. MRI Brain scan showed periventricular white matter changes. Father had a diagnosis of clinically isolated syndrome (CIS) when he presented with unilateral weakness and numbness, MRI showed white matter changes. He and another daughter (being investigated for haematuria) also had cataracts. The index case was heterozygous for a novel missense COL4A1 mutation highly likely to be pathogenic. Genetic testing of the other members of the family is in process. Conclusion: Discussion: COL4A1 mutations can present with non-specific neurological symptoms and even CIS. A history of cataracts and MRI white matter changes should prompt genetic testing for this condition even in later life.

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ICNC-0943: Follow-up and genetic study of 43 Chinese children with type I Alexander disease
Objective. Alexander disease (AxD) is a rare hereditary leukodystrophy caused by mutation in glial fibrillary acidic protein (encoded by GFAP). The purpose of this study was to follow-up patients with AxD to determine the rate of progression and to identify new mutations. Methods: Brain MRI of patients fulfilled the criteria of typical AxD (Type I AxD) proposed by van der Knaap. 43 children with genetic AxD were followed up for 0.33 to 13.80 years. Results: The characteristic phenotype of these patients was developmental delay (86.05%), seizures (95.34%), macrocephaly, and paroxysmal deterioration. Regression of motor function became obvious after 5 to 8 years of age. p.Arg239 and p.Arg79 were hotspot mutations in Chinese patients. Conclusions: The common phenotypic features of type I AxD are developmental delay, seizures, macrocephaly, and paroxysmal deterioration. Regression of motor function became obvious after 5 to 8 years of age. p.Arg239 and p.Arg79 in GFAP were hotspot mutations in Chinese patients.

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ICNC-0944: Characteristics of pediatric multiple sclerosis: A report of the Turkish Pediatric Multiple Sclerosis Study Group
Introduction: We aimed to describe clinical, neuroimaging, and laboratory characteristics in a cohort of Turkish children with multiple sclerosis (MS) diagnosed according to recently promoted criteria. Method: Data of 188 pediatric MS patients collected from 25 different MS centers throughout the Turkey were analyzed. Results: There were 120 (64%) girls and 68 (36%) boys. The median age at onset was 14 years. There was a family history of MS in 6% of patients. Sensory disturbances (45%), brain-stem syndromes (36%), motor symptoms (34%), and optic neuritis (27%) were commonly encountered initial manifestations. The disease onset was polysymptomatic in 55% of patients. Eighteen children had facial paralysis, and 10 children had epileptic seizures at the time of first clinical attack. Twenty (11%) children were initially diagnosed with acute disseminated encephalomyelitis (ADEM). The mean interval between the first two attacks was 10.4 months. Oligoclonal bands were identified in 68% of patients. Serum 25-hydroxyvitamin D levels were lower than normal in 69% of patients. MRI showed periventricular (96%), juxtacortical (61%), brain stem (62%), cerebellum (52%), and spinal cord (67%) involvement. Visual evoked potential (VEP) abnormalities were found in 52% of all children, and in 32% of patients with no previous clinical optic neuritis. A longer period between the first two attacks, a higher rate of initial diagnosis of ADEM, and a higher rate of previous infection/vaccination were found in children ≤11 years old when compared to adolescents. Conclusion: Initial presentation with encephalopathy, facial paralysis, and seizures were noticeable in this series of pediatric MS. A high rate of vitamin D deficiency and subclinical VEP abnormalities were associated paraclinical findings. Key words: pediatric multiple sclerosis, vitamin D, visual evoked potentials

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**ICNC-0945: Phenotype of 20 cases of unrecognized infantile Leukoencephalopathy**

Introduction To summarize the phenotypic features of an unrecognized leukoencephalopathy in infants sharing similar clinical features. Methods Clinical and follow-up data of 20 patients with unrecognized infantile leukoencephalopathy were collected from January 2006 to October 2015. The average follow-up duration was 22 months. Results (1) The average age of onset was 10 months. All had acute onset and rapid motor function regression. Until the last follow-up, the average duration of the disease course was 30 months, and the average age was 3.3 years. Patients' condition became stable, and motor function gradually improved 1–2 months after onset. (2) MRI was characterized by implicating deep white matter, presented with low signal in T1WI, high signal in T2WI and FLAIR in the periventricular area. DWI showed patchy high signal in some of the lesions. The last follow-up MRI with the average duration of the disease course 16 months, showed decrease of the original lesions in 93% of patients, and white matters atrophied in 57%; Regional linear or spot high signals were in DWI in 93%, which was much smaller than before. The MRI features were similar to those of reported mitochondrial leukoencephalopathy (such as EARS2, DARS, APOPT1). (3) Metabolic screening was negative. Next generation gene screening for leukodystrophies and most of mitochondrial nDNA/mtDNA was performed. Mutations in NDUFS1 and NDUAF5 were identified only in 2 patients. Conclusions These patients with leukoencephalopathy caused by unknown pathogenic gene were probably mitochondrial leukoencephalopathy. This study provided evidence for further exploration of new pathogenic genes causing leukoencephalopathy.

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