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EP2116

Mucopolysaccharidosis type III: Tunisian experience

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Introduction: Mucopolysaccharidosis III (MPS III) or Sanfilippo syndrome is a rare and misdiagnosed lysosomal storage disorder characterized by cognitive decline, a distinct behavioral disturbances and relatively mild somatic disease. The aim of this study was to present clinical and neuroimaging features of MPS III in a Tunisian series.

Methods: Eleven children with biochemically confirmed MPS III were followed up (2005-2013). Clinical and neuroimaging features were analyzed.

Results: Eleven children (3 males and 8 females) were included. Mean age was 12.9 years (5-21). Mean age at onset was 3 years (0-4.7). Mean age at diagnosis was 9.9 years (4-18). Main clinical features were: developmental and/or speech delay (10/11), developmental and/or speech regression (7/11), cognitive decline (6/11), behavioral abnormalities (11/11) with predominance of agitation (9/11), hyperactivity (7/11), irritability (6/11), aggressivity (4/11) and autistic-like behavior (3/11). Somatic features were relatively mild with delayed appearance: dysmorphic features (11/11), hepatomegaly (7/11), splenomegaly (3/11), deafness (4/11). Brain MRI performed in 7 patients was normal in 1 patient and showed cerebral atrophy and periventricular signal abnormalities in 6 patients.

Conclusions: The diagnosis of MPS III should be evoked in children with developmental or speech delay and/or behavioral abnormalities. Early diagnosis is important in this devastating, progressive disorder, for genetic counseling and development of potential therapeutic options.

Disclosure: Nothing to disclose

EP2117

Ring chromosome 15 in a family diagnosed as neurofibromatosis

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Introduction: Neurofibromatosis type I (NF1) is characterized by café au lait spots, fibromatos tumors of the skin and there is an increased susceptibility to tumor development. NF1 is an autosomal dominant disorder with an incidence of about 1 in 3,000. Less than 50 patients with ring chromosome 15 syndrome have been reported up to now. Most cases occur sporadic. The transmission of a ring from a mother to a child has been reported twice.

Methods: An infant was diagnosed as NF1 due to multiple café au lait spots. His mother had some spots and hemihypertrophy of a leg.

Results: Chromosomal analysis, array comparative genomic hybridization and targeted High Throughput Sequencing revealed the genetic cause of their symptomatology.

Conclusion: To our knowledge, this is the third time a maternally transmitted ring chromosome 15 has been described. Ring chromosome 15 has been reported to cause café au lait spots and may be confused with NF1 especially when there are family members with similar symptomatology.

Different genetic investigations may be of importance even in seemingly straightforward clinical NF cases.

Disclosure: Nothing to disclose
EP2118

Mosaic ring chromosome 18 in a child with mental retardation and delayed speech

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Introduction: In ring chromosome 18 [r(18)] one or both ends of chromosome 18 are lost and joined forming a ring-shaped figure. Thus, r(18) patients can show features of 18q- and/or 18p- syndrome, depending on the size of the 18p and 18q deleted regions. R(18) is characterized by developmental delay, mental retardation, facial dysmorphisms and major abnormalities. Mosaic r(18) cases are more seldom and usually have more subtle clinical findings.

Methods: A male infant with microcephaly and delayed speech was genetically investigated.

Results: Chromosomal analysis and array comparative genomic hybridization (aCGH) revealed the r(18) mosaicism, the size of the deletions and the breakpoints.

Conclusion: Genotype phenotype correlation in mosaic r(18) syndrome have rarely been described, 12 times in literature, and the exact size of the deletions have only been described twice before. Clear breakpoint delineations are necessary for genotype - phenotype correlations and for delineating the related neurocognitive and behavioral aspects.

Disclosure: Nothing to disclose

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EP2119

Neuroprotective effects of N-acetyl-l-cysteine in human oligodendrocyte progenitor cells and in neonatal rats with hypoxic-ischemic encephalopathy

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Introduction: Hypoxic-ischemic encephalopathy (HIE) is one of the most devastating neurological diseases in children exhibiting diverse neurobehavioral symptoms. Previous studies on the candidate compounds attained from neuronal culture displayed controversial results in animal models or in humans. Since oligodendrocyte progenitor cells (OPCs) are the target cells of demyelinating HIE, it was expected that compounds displaying protective activity against hypoxic cytotoxicity in OPCs would be effective in animal models.

Methods: Human OPCs (F3.Olig2) were incubated with various concentrations of N-acetyl-l-cysteine (NAC) and potassium cyanide, and the cytoprotective effects of NAC were assessed by MTT and apoptosis assays. Male rats were subjected to hypoxia-ischemia surgery at postnatal day 7 (PND7), intraperitoneally administered with NAC (100 mg/kg) once a day, and their physical functions were measured at PND20, 30 and 40. To evaluate the integrity of host myelins, brain sections were stained with Luxol fast blue and antibodies to myelin basic protein.

Results: NAC decreased potassium cyanide cytotoxicity of F3.Olig2 cells in MTT assay, and especially suppressed apoptosis by regulating Bcl2 and p-ERK. NAC administration recovered motor functions such as the using ratio of forelimb contralateral to the injured brain, locomotor activity, and rota-rod performance of HIE animals. It was also confirmed that NAC attenuated demyelination in the corpus callosum, a white matter region vulnerable to HIE.

Conclusions: The results indicate that NAC exerts neuroprotective effects in vitro and in vivo by preserving OPCs, via regulation of anti-apoptotic signaling.

Disclosure: Nothing to disclose
EP2120
High frequency of additional cerebral involvement in adrenomyeloneuropathy (AMN)
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Introduction: X-linked Adrenoleukodystrophy (X-ALD) is an inherited disorder of peroxisomal metabolism associated with mutations in the ABCD1 gene, resulting in damage to central and peripheral nervous system and endocrine organs. Adrenomyeloneuropathy (AMN) was considered a relatively mild phenotype with only incidental additional cerebral demyelination. However, in 2001 it was reported that 13/68 male patients with AMN (19.1%) developed additional brain involvement during a follow-up interval of 9.5±5.5 years. We studied the frequency of additional cerebral demyelination in AMN patients in the Netherlands.

Methods: Consecutive AMN patients without cerebral demyelination from the Dutch X-ALD cohort, seen between January 1, 1992, and January 1, 1999, were included. Primary endpoints were demonstration of brain involvement, death, or the end of our study. Three levels of certainty were used to classify cerebral demyelination; confirmation by MR-Imaging, detailed information from treating physicians, or information obtained from their families. Results were compared with a study carried out in 2001, using the differences and their 95% confidence intervals.

Results: Seventeen out of 27 AMN patients (63%) developed additional cerebral demyelination 10.2±6.9 years after onset of myelo(neuro)pathy. Mean survival was 3.4±2.9 years. Additional brain involvement was higher in the Dutch AMN patients (difference 44%, 95% CI 0.23 - 0.64).

Conclusions: Additional cerebral demyelination in AMN may be even more frequent than previously reported. Survival is just as poor as in Childhood Cerebral ALD. Therapies that can halt relentlessly progressive cerebral demyelination in these patients are needed.

Disclosure: Nothing to disclose

EP2121
How evolutionary anthropology informs the evolution of inhibitory interneurons in the cerebral neocortex
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Introduction: Inhibitory interneurons (INS) play a role in postnatal brain development, increasing signaling to maintain balance between excitatory/inhibitory in cortex networks; balance is imperative to generate behaviorally-relevant patterns.

Methods: This paper explores inhibitory INS’ evolution/their significance in cerebral-neocortex development.

Results: Energy metabolism sets humans apart from primates, maintaining neural tissue’s high cost: evolutionary increases in synaptic signaling/connectivity/glial cells/glial:neuron unexpected 46% greater density, p< 0.001. INS’ energy efficiency exceeds excitatory neurons’: 85% energy consumption associated with excitatory glutamate recycling, using both glycolytic/glycogenolytic processes, only glycolytic ATP for INS’ synaptic cleft recycling. Key in evolution’s INS’ origins is recruitment of other mechanisms for primates’ cortices’ greater number/diversity; lampreys’ (450Mya) INS’ circuits devoid of sense organs/pallium/geniculate eminence (GE); gnathostomes’ (350Mya) INS’ tangential migration from GE to pallium, highly conserved; INS’ competence to enter neocortex subventricular zone (SVZ) established in amniotes (310Mya); competence to enter cortical plate from GE, mammalian unique (185-210Mya). 40Mya primates’ INS’ number/diversity/complexity increased more than excitatory neurons’: a pre-existing mechanism’s boosting, a bipartite process: INS’ progenitors migrating radially.

Conclusions: Evolutionary ancient INS are vitally important to brain function as local integrators of cerebral neocortex activity and……. to our preeminent human identity.

Disclosure: Nothing to disclose
EP2122
Systemic juvenile lupus erythematosus long lasting remission of severe neurological symptoms after treatment with Rituximab
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Introduction: Systemic Lupus erythematosus (SLE) has a much higher incidence in Asian and African populations than in Western countries. Up to 50% of patients suffer from neuropsychiatric symptoms of different pathogenesis.

Case presentation: We report a 13-year-old girl who was diagnosed with SLE with rheumatic symptoms. She rapidly developed confusion, focal epileptic seizures with secondary generalization and left sided hemiparesis combined with high fever and tachycardia. Initial showed right hemispheric cortical dwi-positive lesions in the MCA territory. During the following 8 weeks extensive progression of MRI lesions to subcortical regions in both hemispheres with additional microbleeds could be demonstrated, no arterial occlusion, no typical vasculitic changes, no meningeal enhancement. CSF was without significant pathology. Aggressive treatment with highdose corticosteroids and iv Immunoglobuline G was started, followed by one cycle of iv cyclophosphamide and plasmaexchange. The patient deteriorated with respiratory failure, increase of liver enzymes, severe thrombopenia and anemia, colitis and secondary infectious complications. After stabilization of vital functions and weaning from the respirator Rituximab was given with no side effect. The patient recovered tremendously without any persistent motor dysfunction, she was able to resume schooling and has no neuropsychological deficits except occasional headache and fatigue. A second dose of Rituximab was applied 6 months later after an increase of CD 20 lymphocytes. Under a low dose corticosteroid treatment the patient has been free of new somatic and neuropsychiatric SLE manifestation since two years.

Conclusion: Rituximab was well tolerated and longterm effective in this case of juvenile SLE with life threatening cerebral lupus vasculopathy. Further studies have to establish the therapeutic significance of Rituximab in severe neuropsychiatric Lupus.

Disclosure: Nothing to disclose

EP2123
Stereotypes as a marker of autism severity
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Introduction: The new classification of autism spectrum disorder on DSM-V emphasizes the importance of the severity of this condition. Stereotypies have been related with the severity of autism, but few studies analysed the association between them. The aim of this study was to explore the association between the frequency and type of stereotypies and autism severity scores and comorbidities.

Methods: A series of consecutive patients from a paediatric neurology clinic with ASD and stereotypies were selected. The diagnosis of ASD was based on ADOS and ADI-R scales, and DSM-V criteria. Severity was obtained from ADOS and DSM-V criteria. Standardized video recording of the patients were obtained with consent. Two independent researchers performed the classification.

Results: We evaluated 15 autistic patients, 80% males, with a median age of 7.6 years-old (range:3.8-15.7). The median intelligence quotient (IQ) or general development quotient (GDQ) was 45 (range:32-68) and 51 (range:32-81) respectively. The ADOS median severity score was 7 (range:7-10). The median number of motor stereotypies per 10 minutes was 6 (range: 2-20) and 87% of patients presented also visual or vocal stereotypies. The frequency of motor stereotypies increased with ADOS severity score (p=0.028), social communication DSM-V severity score (p=0.025), absence of intelligible speech (p=0.029) and lower IQ (p=0.035).

Conclusions: This study suggests that motor stereotypies are more frequent on autistic patients with more severe autism and lower IQ. This highlights the necessity of understanding the neurobiology of stereotypies and the nature of their relation with ASD.

Disclosure: Nothing to disclose
EP2124

A diffusion tensor MRI study of pediatric patients with severe non-traumatic brain injury

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Introduction: We applied DT MRI to analyze damage to the supra- and infra-tentorial districts in pediatric patients with vegetative state (VS) or minimally conscious state (MCS) and their correlations with clinical scales of disease severity.

Methods: Seven pediatric patients in a VS and six in a MCS, suffering from severe acquired brain injury due to non-traumatic origin and 10 pediatric healthy controls underwent a DT MRI scan and patients were assessed using the Glasgow Coma Scale and Disability Rating Scale. We obtained fractional anisotropy (FA), mean (MD), axial (AD) and radial diffusivities (RD) from the corpus callosum (CC), inferior (ICP), middle (MCP), and superior (SCP) cerebellar peduncles.

Results: Compared to controls, patients had lower FA of the CC and SCP, and higher MD, AD and RD of the CC and cerebellar peduncles. Compared to acute patients, those in the chronic stage had lower FA and higher MD, AD and RD of the anterior part of the MCP. Differences of FA, MD and RD between supra- vs. infra-tentorial compartments differentiated patients from controls. Furthermore, the difference of FA between supra- vs. infra-tentorial compartments distinguished VS from MCS patients (p<0.01). Significant correlations were found between DT MRI indexes and clinical scales (r ranging from -0.77 to 0.73).

Conclusions: In pediatric patients with VS/MCS due to non-traumatic origin, the severity of clinical disability correlates with structural damage to both infratentorial and the long-range cortico-cortical tracts, suggesting that global, rather than focal damage, contributes to the clinical severity of these patients.

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EP2125

Leukoencephalopathies in inborn errors of metabolism: the Tunisian experience

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Introduction: Leukoencephalopathies (LE) in inborn errors of metabolism (IEM) are common. They are due to primary defect of myelination or to metabolite toxicity toward myelin. Diagnostic approach may be complex. The aims of our study were to describe clinical and radiological characteristics and to determine main etiologies of LE with IEM.

Methods: A prospective study (2004-2013) included patients with LE and IEM. All patients had cerebral MRI. White matter abnormalities were analyzed, and correlated to clinical and electrophysiological findings. Biochemical tests were performed according to the presumed etiology.

Results: 55 patients (24 males, 31 females) were included. LE was classified into demyelination (decreased T1 signal) (30/55) and hypomyelination (normal T1 signal) (25/55). In the demyelination group, the main clinical features were psychomotor milestones loss (21/30) and peripheral neuropathy (17/30). Lysosomal storage diseases were diagnosed in 21/30 cases with predominance of metachromatic leukodystrophy (10/30). In the hypomyelination group, the main clinical features were psychomotor milestones loss (21/30) and peripheral neuropathy (17/30). Lysosomal storage diseases were diagnosed in 21/30 cases with predominance of metachromatic leukodystrophy (10/30). The hypomyelination group presented often with psychomotor delay (17/25). The main etiology was respiratory chain defect (9/25).

Conclusions: Analysis of MRI patterns of LE is a diagnostic clue to orientate biochemical tests of IEM. A structured and multidisciplinary diagnostic approach is crucial to identify etiologies and to allow genetic counseling.

Disclosure: Nothing to disclose
EP2126

PEDOT-PSS modified silk electrode for neural activity measurement

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A poly(3,4-ethylenedioxythiophene)-poly(styrenesulfonate) (PEDOT-PSS) is one of the implantable conductive polymer candidates for improving the biocompatibility of the electrode. Our previous results using a PEDOT-PSS modified microelectrode array (PPM-MEA) indicated continuous monitoring of neural cell development and network formation. We also reported the differentiation conditions of neural stem cells (NSCs) from rat embryo striatum could be monitored with this electrode array. Here we report the formation of flexible electrodes using silk fiber for implantable electrode. Polymerization of the fiber with the conductive polymer indicated higher biocompatibility and allowed us for longer measurement. Brain neural activities of mouse and chick were measured with this electrode for more than six months. Flexible characteristics of the electrode would be important for stable contacts to neurons. Stimulation experiments with this electrode will be reported. As the PEDOT-PSS modified silk electrode is a soft and biocompatible measurement method, the usage of this electrode could be a useful tool not only for implantable and stable activity monitoring, such as primary evaluation of physiological conditions of the neurons, but also for the reconstruction of neural pathway.

Disclosure: Nothing to disclose

EP2127

Childhood neuroferritinopathy caused by novel mutation in the PLA2G6 gene – better prognosis? Case report of a family

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Introduction: Childhood neurodegeneration with brain iron accumulation (NBIA) presents with heterogeneous clinical manifestation. We describe a family, where progressive neurological symptoms affected three girls with autosomal recessive inheritance. The aim of our investigations was to classify the genetic background of NBIA. Genetic tests revealed novel mutation in PLA2G6 gene.

Methods and patients: We report a Caucasian family with three affected girls out of 5 children. Two of the patients were identical twins and their younger sister. Earliest symptoms presented at the age of 2-3 years as gait disturbance, speech difficulties, followed by mental deterioration, cerebellar ataxia, pyramidal involvement. All of them developed bulbar dysfunction, vertical gaze palsy combined with saccadic eye movements. Symptoms showed continuous progression. All of the patients became wheelchair dependent.

Results: PANK2 and PLA2G6 gene mutation were tested in one of the twins. There was no pathologic mutation of PANK2, but heterozygous variants in exon 13 of the PLA2G6 gene were detected. One of the mutations (c.1798C>T p.R600W), is known as probably disease-causing, the other variant (c.1864C>T p.P622S) can lead to moderate differences between proline and serine. These abnormalities can be concluded as the cause NBIA in the investigated family. Segregations analysis revealed that father and the healthy young brother are heterozygous for R600W mutation while mother and the unaffected sister are heterozygous for P622S mutation.

Conclusions: Genetic tests revealed previously unreported heterozygous variants in exon 13 of the PLA2G6 gene without pathogenic mutation of PANK2, leading to better prognosis than previously reported variants.

Disclosure: Nothing to disclose