Oral presentations

O-1
Caveolin 3 Gene and mitochondrial tRNA Methionin Gene in Duchenne Muscular Dystrophy

E. Abdel-Salam, I.E. Abdel-Meguid, S. Korraa[1]
Department of Pediatrics, Genetics Unit, Faculty of Medicine, Cairo University; [1] Department of Radiation Health, National Centre for Radiation Research and Technology, Atomic Energy Authority

It was recently reported that Duchenne muscular dystrophy (DMD) patients and mdx mice have elevated levels of caveolin-3 expression in their skeletal muscles. However, it remains unknown whether this increased caveolin-3 levels contribute to the pathogenesis of DMD. Also mitochondrial DNA mutation in the tRNA methionin (tRNA Met) gene has been shown to be associated with muscle weakness, severe exercise intolerance, lactic acidosis and growth retardation. Since DMD is X-linked maternally inherited disease, mitochondrial mutation in tRNA(Met) gene can be suspected to be the cause for the inefficient splicing of dystrophin gene during its expression and can be implicated as the cause of dystrophin inactive protein.

Results gave further proof to decreased expression of inducible nitric oxide synthase (iNOS) mRNA, which leads to increased expression in caveolin 3 mRNA in lymphocytes of DMD patients compared to controls. However using SSCP, there was no evidence for tRNA(Met) gene mutation among DMD patients, and only one patient presented a mutation in the caveolin gene compared to controls.

O-2
Consequences of birth trauma in children: myotonic neurovascular and mental disorders. Diagnosis and comprehensive neurorehabilitation

O. Safonicheva, M. Safonicheva
First Moscow State Medical University, Moscow, Russia

Rehabilitation of the children with mental and physical disorders for improvement of their adaptation to modern society is an actual medical and social problem.

Cooperative work of doctors, psychologists, teachers and parents of the pupils of special correctional school N° 81 in Moscow was approved by the Ethical Committee of medical and pharmaceutical universities. Forty-five pupils of primary school (range 8-12 years) with impaired intellectual development, cognitive disorders, syndrome of hyperactivity and attention deficiency were examined. All the children had the birth trauma in their history. Clinical neurological examination and palpation were conducted to identify the role of myotonic syndromes in the cranio-vertebral region and biomechanically significant disturbances in the cervical spine that affect the cerebral blood flow. A neuropsychological study was used to examine the cognitive sphere and the state of brain activity. EEG-neurophysiological examination of children was carried out to assess the state of brain activity, the definition of cortical areas responsive to the effects of stress factors, as well as hemispheric interactions, as correlates of memory processes, learning, etc. The NEC-method was used to study the cerebral metabolism and adaptation possibilities. Color duplex scanning (ultrasonic scanner Sono Scape 1000) was conducted to identify hemodynamically significant tortuosity of the proximal extracranial parts of internal carotid and vertebral arteries. Tortuosities of the vessels slow down the circulation and lead to vertebro-basilar insufficiency in the corresponding cerebral region.

The main complains observed in children were headache, fatigue and meteopathies. Neuropsychological studies revealed disorders in the cognitive, personal, emotional and behavior status, as well as hyperactivity and diminished attention. Neurological examination revealed disturbances of muscular coordination, muscular hypertension or hypotonia. The patho-biomechanical changes observed were rigidity in the shoulder girdle, shorten muscles of the neck and anterior part of the chest (syndrome of upper aperture), kyphosis, dysfunctions of the pelvis, functional limb asymmetry and postural displacement.

EEG analysis revealed signs of functional immaturity of the cerebral cortex in the children. Manifestations of the weakening of inter-hemispheric interactions were observed in 50% of cases.

According to the color duplex scanning, changes of the brachio-cephalic arteries were divided into three groups:

1) hemodynamically significant (S-or C-shaped crimp of internal carotid arteries);

2) S-or C- shaped hemodynamically significant (misalignment of the vertebral arteries in one or two sides);

3) a combination of pathological tortuosity of the internal carotid and vertebral arteries.

Signs of hypoxia and intracranial venous hypertension occurred in 65% of cases.

The scientifically-based comprehensive neuro-rehabilitation scheme was worked out during this pilot project in order to correct the myotonic syndrome in the neck, cranio-vertebral region, and to improve the cerebral metabolism and liquor dynamics. We used biodynamic poly-receptor techniques, neuro-motor and respiratory gymnastics, aromatherapy and neuroprotectors, because we performed our treatment in school.

Conclusions. Integrated clinical neurological, neuropsychological and instrumental studies of bioelectric activity, metabolic processes of the brain and the state of the brachiocephalic arteries, allowed us to refine pathogenetic mechanisms of the consequences of birth trauma in children, myotonic neurovascular and mental disorders included.

Comprehensive neuro-rehabilitation of the children with mental problems improved their clinical and emotional background, memory and cognitive functions. EEG and NEC examination marked the trends in recovery of inter-hemispheric connections and in normalization of the bioelectrical activity in the brain.

O-3
Clinical features and outcome measures during 1 year enzyme replacement therapy in late onset GSD II patients

C. Angelini[1], C. Semplicini[1], E. Pegoraro[1], M. Filosto[2], G. Marrosu[3] R. Piras[3], T. Mongini[4], L. Vercelli[4], P. Tonin[5], S. Servidei[6], R. Di Giacopo[6], G. Crescimanno[7], S. Ravaglia[8], A. Toscano[9], O. Musumeci[9], G. Siciliano[10], G. Ricci[10], Di Iorio[11], F. Cipullo[11], M. Moggio[12], G. Comi[12], V. Lucchini[12], L. Morandi[13]

[1] University of Padova, Department of Neurosciences, Padova, Italy; [2] Hospital of Brescia, Italy; [3] University of Cagliari, Italy; [4] University of Torino, Centre for Neuromuscular Diseases, Department of Neurosciences, Torino, Italy; [5] University of Verona; [6] Catholic University of Rome, Italy; [7] University of Palermo, Italy; [8] University of Pavia, Italy; [9] Department of Neurosciences, Psichiatry and Anesthesiology, University of Messina, Italy; [10] University of Pisa, Italy; [11] Second University of Napoli; [12] Deparment of Neurological Sciences, University of Milan, Italy; [13] Besta Institute, Milan, Italy

The objective to identify appropriate outcome measures to use in clinical trials or observational studies. Natural history data of patients with the heterogeneous juvenile/adult form of glycogen storage disease type II (GSDII) are useful to evaluate enzyme replacement therapy (ERT).

We evaluated several outcome measures before and during ERT, such as a series of timed and graded functional tests i.e. Gait, Stairs, Gowers, Chair (GSGC) score, the Six-Minute Walk Test (6MWT), Forced Vital Capacity.

During an observational study we monitored a series of 32 patients using these outcome measures at 1 year after ERT and observed a partial but significant improvement. A significant decrease was observed in Gait time and time to raise from the chair and total GSGC score. A gain of function was observed in few cases.

Important, crucial topics seem to be: the use of different functional parameters in determining the efficacy of ERT, since not all juvenile/adult patients respond similarly, and, reliable outcomes of treatment.

O-4
The Italian Network for Laminopathies

G. Lattanzi and the Italian Network for Laminopathies[1]

Institute for Molecular Genetics, IGM-CNR, Bologna, Italy; [1] A. Basso, S. Benedetti, E. Bertini, E. Biagini, G. Boriani, N. Carboni, G. Cenacchi, A. D'Amico, M.R. D'Apice, M. Fontana, A. Gambineri, R. Liguori, L. Mazzanti, E. Mercuri, T. Mongini, L. Morandi, G. Nigro, A. Palladino, R. Pasquali, A. Pini, L. Politano, S. Previtali, C. Rapezzi, G. Ricci, G. Siciliano

Laminopathies are a group of genetic diseases caused by mutations in the nuclear protein lamin A/C or in related proteins. A group of laminopathies targets specific tissues – tissue-specific laminopathies –, other laminopathies affect multiple tissues – systemic laminopathies.

The Italian Network for Laminopathies is a group of Clinical and Research Centers performing clinical and molecular diagnosis or biomedical research in the field of laminopathies. Aims of the Italian Network for laminopathies are: to connect Italian Centers involved in diagnosis and biomedical research of laminopathies; provide information on the clinical features of Laminopathies to family doctors, specialists and patients; provide the contact information of specialists involved in the diagnosis and research of laminopathies; provide updated information on biomedical research in the field of laminopathies; organize an Italian Registry for Laminopathies containing clinical and biological data; establish a bank of biological material; report news on relevant events and meetings; report on funding opportunities in the field of Laminopathies research.

The Italian Network for Laminopathies website provides updated information of the Network and of Laminopathies-related events.

O-5
Novel HLA II associations in myasthenia gravis

R. Massa, M. Andreani[1], C. Terracciano, M. Troiano[1], G.A. Marfia, A. Guagnano[1], E. Pompeo[2], C. Piantadosi[3], G. Testa[1], M. Testi[1]

Department of Neurosciences, "Tor Vergata" University, Rome, Italy; Immunogenetics Laboratory, [1] "IME" Foundation, "Tor Vergata" Policlinic, Rome, Italy; [2] Department of Surgery, "Tor Vergata" University, Rome; Neurology UOC, [3] "S. Giovanni-Addolorata" Hospital, Rome, Italy

Myasthenia gravis (MG) is a heterogeneous disorder encompassing several subtypes. In our patients population, the most numerous and homogeneous group is represented by patients with a late onset, seropositive, non-thymomatous MG (LO-Ab+noTh). We have analyzed the frequency of HLA-A, -B, - DRB1, -DQA1 and -DQB1 alleles in 81 unselected Italian MG patients and in 100 healthy controls. HLA allele frequencies were estimated by direct count and compared in a 2×2 contingency table analysis using the Fisher exact test; p values were corrected for multiple comparisons according to the Bonferroni method (pc). When the entire MG population was considered, no association was found between the occurrence of the disease and the presence of any of the alleles analyzed. However, when the LO-Ab+noTh patients were compared to controls, a positive association of the DRB1*16 and the DQB1*0502 alleles was observed (pc 0,0211 and 0,00768 respectively). On the contrary, the same association was not present in patients with either early-onset, seropositive, non-thymomatous MG, or with thymomatous MG. The association of DRB1*16 and DQB1*0502 with MG has been previously reported in Italian patients with different features, but not in LO-Ab+noTh MG. According to these results, DRB1*16 and DQB1*05:02 might be considered as genetic markers of LO-Ab+noTh MG, while their role as predisposing genetic factors for MG should be clarified by further investigations.