



**2-4
NOVEMBER, 2012
NICOSIA - CYPRUS**

XII NEUROMEDITERRANÉE 2012



FINAL PROGRAM & BOOK OF ABSTRACTS

Venue

*The Cyprus
Institute of
Neurology &
Genetics*



ΕΛΛΗΝΙΚΗ ΕΡΕΥΝΑ - ΕΡΕΥΝΑ

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Welcome

Dear Colleagues, Dear Friends,

On behalf of the organizing committee we cordially invite you to the **XIIth Neuromediterranée Conference** that will take place in **Nicosia, Cyprus, November 2-4, 2012**.

Neuromediterranée has a long tradition of excellent science and networking covering all aspects of neurology, bringing together clinicians and scientists from all countries around the Mediterranean to present the latest advances and discuss key challenges in neurology. For this year a rich scientific program features presentations by world experts on topics such as neurodegenerative disorders, neurological complications of systemic disease, neuropediatrics, neurooncology, brain injury, neurorehabilitation and pain, all areas of great importance for the Mediterranean region and beyond.

Organized by the **Cyprus Institute of Neurology and Genetics**, the **Cyprus Neurological Society**, and the **Neuromediterranée Society**, this year's conference will coincide with the Cyprus Presidency of the European Union. This special occasion emphasizes the bridging role of Cyprus in promoting peace and collaboration between Europe and the Mediterranean region. Cyprus epitomizes the Mediterranean past, present and future, finding itself between three continents and in the crossroads of different religions and civilizations throughout the long and stormy history of the island.

In these times of difficult political and economical challenges in the region and beyond, we strongly believe that cooperation, exchange of information and ideas, and promotion of excellence in medicine and science through international meetings like this will strengthen our collaboration and provide hope for a better future in the region and the world.

Nicosia, the capital of Cyprus offers many historical and cultural attractions. Located in the center of the island it also offers easy access to the coastal cities and the forested mountains. The conference will be hosted by the Cyprus Institute of Neurology and Genetics, the largest neurological center as well as a leading academic and research institution in Cyprus, offering a stimulating environment for a productive meeting.

We look forward to welcoming you in Cyprus

On behalf of the organising committee



Kleopas A. Kleopa



Committees

ORGANIZING COMMITTEE

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- ✓ The Cyprus Institute of Neurology & Genetics and the Cyprus School of Molecular Medicine
- ✓ Cyprus Neurological Society
- ✓ Neuromediterranée Society



THE CYPRUS INSTITUTE OF
NEUROLOGY & GENETICS



CYPRUS SCHOOL
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CYPRUS
NEUROLOGICAL SOCIETY



SCIENTIFIC PROGRAM

FRIDAY, NOV. 2

Session A: NOVEL THERAPEUTICS

Time: 17.00-18.30

Chairperson: K. Kleopa

Fr. A.1

17.00-17.30

Leonidas Stefanis, *University of Athens and Biomedical Research
Foundation of the Academy of Athens, Greece*

**Enhancement of Chaperone-Mediated Autophagy as a therapeutic
strategy in Parkinson's Disease**

Fr. A.2

17.30-18.00

Michael Krams, *Johnson&Johnson, New Brunswick, USA*

CNS drug trials – innovative clinical development strategies

Fr. A.3

18.00-18.30

Arie Stangou, *King's College Hospital, London, UK*

**Advances in the management of the familial and hereditary
amyloidoses**

FRIDAY, NOV. 2

18.30-18.45

OPENING CEREMONY OF THE
NEUROMEDITERRANÉE 2012

George Serratrice

Neuromediterranée Society

Kleopas A. Kleopa

The Cyprus Institute of Neurology and Genetics

George Kaponides

Cyprus Neurological Society

18.45-19.30

KEYNOTE LECTURE

Demetris Michaelides

Professor of Archaeology, University of Cyprus

Archaeological findings of medical nature in Cyprus

19.30-21.30 Cocktail reception

SATURDAY, NOV. 3

Session B: NEURODEGENERATIVE DISORDERS

Time: 9.00-12.30

Chairperson: L. Middleton

Sat. B.1 9.00-9.30

Lefkos Middleton, *Imperial College London, UK*

Alzheimer's and Parkinson's associated dementias. Is there a link?

Sat. B.2 9.30-10.00

Michel Goedert, *Medical Research Council Laboratory of Molecular Biology, Cambridge, UK*

Pathogenesis of the tauopathies

Sat. B.3 10.00-10.30

Amos Korczyn, *Tel Aviv University, Israel*

Is vascular dementia a separate entity?

Coffee break, poster presentations 10.30-11.00

Sat. B.4 11.00-11.30

Maria Grazia Spillantini, *University of Cambridge, UK*

The role of Alpha-synuclein in Parkinson's disease

Sat. B.5 11.30-12.00

Nikos Mazarakis, *Imperial College London, UK*

Gene therapy in Parkinson's disease

Sat. B.6 12.00-12.30

Richard Reynolds, *Imperial College London, UK*

Mechanisms of neurodegeneration in multiple sclerosis

Lunch 12.30-14.00

SATURDAY, NOV. 3

Session C: NEUROLOGICAL COMPLICATIONS OF
SYSTEMIC DISEASE

Time: 14.00-18.00

Chairperson: J.M. Leger

Sat. C.1 14.00-14.30

Jean Pouget, *Paris, France*
Inflammatory myopathies

Sat. C.2 14.30-15.00

Zohar Argov, *Hadassah-Hebrew University Medical Center,
Jerusalem, Israel*
Neuromuscular complications of systemic medications

Sat. C.3 15.00-15.30

Jean-Marc Leger, *Hôpital Pitié-Salpêtrière, Paris, France*
Neuropathy in the context of infection

Coffee break, poster presentations 15.30-16.00

Sat. C.4 16:00-16.30

Guido Cavaletti, *University of Milan-Bicocca, Monza, Italy*
Chemotherapy-induced peripheral neuropathy

Sat. C.5 16.30-17:00

Fadi Abou-Mrad, *Lebanese University, Beirut, Lebanon*
Cardiac manifestations of neurological disease

SELECTED ORAL PRESENTATIONS - Session I

Chairperson: S. Papacostas

Sat. C.6

17.00-17.15

Antonio Federico, *University of Siena, Italy*

Adult-onset parkinsonism and hypermanganesaemia - a novel recessive syndrome caused by SLC30A10 mutation and Kufor-Rakeb (ATP13A2/PARK9) syndrome

Sat. C.7

17.15-17.30

Antonios Kerasnoudis, *University, Bochum, Germany*

The role of neuromuscular ultrasound in the diagnostic of immune mediated neuropathies

Sat. C.8

17.30-17.45

Marios C. Pantzaris, George N. Loukaides, Evangelia E. Ntzani, Ioannis S. Patrikios

¹PALUPA Medical Ltd, ²The Cyprus Institute of Neurology and Genetics,

³University of Ioannina School of Medicine, ⁴European University Cyprus

A Novel Oral Formula (PLP10) for the Treatment of Relapsing Remitting Multiple Sclerosis: A Proof-of-Concept, Randomized, Placebo-controlled, Double-blind Clinical Trial

Sat. C.9

17.45-18.00

K. Kyriacou, R. Papacharalambous, A. Hadjisavvas and T. Kyriakides

Departments of Electron Microscopy and Neuropathology

The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

The contribution of electron microscopy in the diagnosis of a case of childhood vacuolar myopathy

SUNDAY, NOV. 4

Session D: NEUROPEDIATRICS, NEUROMUSCULAR & NEUROONCOLOGY

Time: 9.00-11.00

Chairperson: K. Kleopa

Sun. D.1 9.00-9.30

Athanasios Covanis, Aghia Sophia Children's Hospital, Athens, Greece
Myoclonic syndromes from early infancy to adolescence

Sun. D.2 9.30-10.00

Francois Kamar, Beirut, Lebanon
Current & Future Treatment trends in High Grade Gliomas

Sun. D.3 10.00-10.30

Kleopas A. Kleopa, Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus
Paraneoplastic and non-paraneoplastic disorders of the voltage-gated potassium channel complex

Coffee break, poster presentations 10.30-11.00

SUNDAY, NOV. 4

Session E: BRAIN INJURY, STROKE, PAIN &
REHABILITATION

Time: 11.00-13.30

Chairperson: G. Kaponides

Sun. E.1 11.00-11.20

George Kaponides, *Limassol, Cyprus*

Pharmacological options in rehabilitation of traumatic brain injury

Sun. E.2 11.20-11.40

Savvas Papacostas, *Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus*

Psychiatric Co-morbidity in Epilepsy

Sun. E.3 11.40-12.10

Constantin Potagas, *University of Athens, Greece*

Evolution of aphasia in the rehabilitation from stroke

Sun. E.4 12.10-12.30

Ekaterini Kosma, *Psychiatric Hospital of Athens, Dromokaition, Greece*

Psychopharmacology of chronic Neuropathic Pain

SUNDAY, NOV. 4

SELECTED ORAL PRESENTATIONS – Session II

Chairperson: E. Zamba-Papanicolaou

Sun. E.5

12.30-12.45

Marilena Theodorou, Nektarios Poullos, Christine Kopp, Sabrina

Astner, Anca Ligia Grosu, Michael Molls

Clinic and Policlinic for Radiotherapy and Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Germany

Brain tumors: Radiosurgery and Stereotactic High Precision Radiotherapy

Sun. E.6

12.45-13.00

Carlo Bertoncelli

University Hospital Chu-Lenval, Nice, France

Rehabilitation strategies in Neuropediatrics

Sun. E.7

13.00-13.15

¹Payman Salamati, ²Mohammad Barkhordari, ³Kambiz Sotoudeh,

⁴Zohrehsadat Naji

¹Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences; ²Department of Pediatrics, Tehran University of Medical Sciences; ³Department of Pathology, Tehran University of Medical Sciences; ⁴Research and Sciences Center of Azad University, Iran

Stereotyping Movement in Children

End of the congress, concluding remarks

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is as important as the right treatment*

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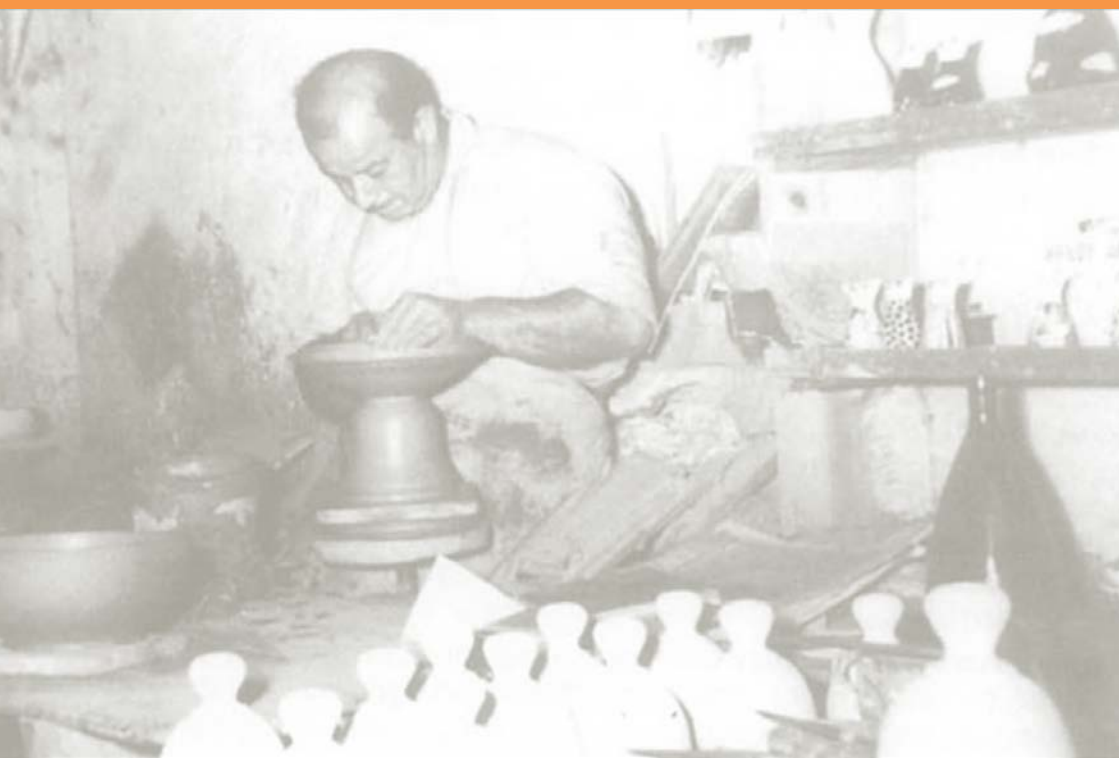
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Invited Abstracts



Sat. B.3**Vascular cognitive impairment****Amos D. Korczyn***Tel Aviv University, Israel*

Abstract - The epidemic proportions of dementia in old age are a cause of great concern for the medical profession and the society at large. It is customary to consider Alzheimer's disease (AD) as the most common cause of dementia, and vascular dementia (VaD) as being the second. This dichotomous view of a primary neurodegenerative disease as opposed to a disorder where extrinsic factors cause brain damage led to separate lines of research in these two entities.

New biomarkers, particularly the introduction of modern neuroimaging and cerebrospinal fluid changes, have, in recent years, helped to identify anatomical and chemical changes of VaD and of AD. However, recently accumulated data suggest that the two disorders have additive effects and probably interact with each other, since older people most commonly harbour both neurodegenerative and vascular changes. It is still unknown to what degree the primary neurodegenerative processes and vascular changes occur independently or interact with each other. Furthermore, epidemiological studies have shown "vascular" risk factors to be associated with AD.

Therefore, a clear distinction between AD and cognitive impairment due to vascular changes cannot be made in most demented people and is furthermore unhelpful. Moreover, in the absence of efficacious treatment for the primary degenerative process, special attention must be given to vascular component even in patients with presumed mixed pathology.

Symptomatic treatment of VaD is similar to that given to AD, although it is less effective than in AD. For prevention of dementia it is important to treat aggressively all relevant factors, in particular risk factors for stroke, even in stroke survivors who do not show evidence of cognitive decline or only mild changes.

Sat. B.6**Mechanisms of neurodegeneration in multiple sclerosis****Richard Reynolds, Roberta Magliozzi, Owain Howell***Centre for Neuroscience, Division of Brain Sciences, Imperial College London*

Abstract - Accumulating neuronal loss and axon damage are thought to be responsible for many aspects of clinical progression in multiple sclerosis (MS), but little is known concerning the mechanisms involved. Recent studies of cortical pathology in secondary progressive MS have shown that the presence of extensive grey matter lesions (GMLs) associates with increased organised and diffuse meningeal inflammation and correlates with a more rapidly progressive disease course. We have investigated the hypothesis that diffusion of pro-inflammatory cytokines from the meninges into the brain parenchyma could be responsible for this pathology. A quantitative analysis of subpial GMLs and normal appearing GM of the motor cortex from MS cases, with and without substantial meningeal infiltrates, revealed a significant gradient of neuronal loss from the pial surface only in cases with organised meningeal infiltrates. Immunohistochemical analysis revealed the presence of tumour necrosis factor (TNF) and interferon-gamma (IFN γ) expressing cells in the meningeal infiltrates and TNF-expressing microglia in active GMLs. Gene expression profiling of the same lesions demonstrated the upregulation of multiple genes and pathways directly regulated by TNF and IFN γ , and in particular genes involved in TNF mediated cell apoptosis/survival signalling. Increased meningeal inflammation gave rise to a shift in the balance of TNF signalling from the TNFR2 and NF κ B anti-apoptotic pathway towards TNFR1 pro-apoptotic signalling, in keeping with the stimulation of TNFR1 gene expression by IFN γ . These results support the hypothesis that an inflammatory milieu in the cerebral meninges could give rise to subpial cortical grey matter pathology, including neuronal loss, in MS.

Sat. C.2**Neuromuscular complications of systemic medications****Zohar Argov**

Kanrich Prof of Neuromuscular Disorders at the Department of Neurology, Hadassah Hebrew-University Medical Center, Jerusalem, Israel

Abstract - Drug induced neuromuscular disorders are not rare in clinical practice. If identified early, these are usually reversible conditions but sometimes are potentially serious and rarely even lethal. The lecture will present the various disorders through clinical cases and dilemmas of their management to enhance the relevance between the theory and the clinical practice. Drug induced myopathies may appear as myalgia only or as chronic weakness (with or without pain). Acute rhabdomyolysis can also be induced by medications. Emphasis will be made on the more commonly used drugs that may cause myopathy, especially the statins. New findings related to the immune pathogenesis of statin myopathy will be discussed. Drug induced impairment of neuromuscular transmission may present itself as unmasking of a known myasthenic condition or aggravating it, but also as an acute episode in the operative and post operative period as well as in the intensive care unit. The more drugs that may aggravate myasthenia and their recognition will be reviewed.

Sat. C.3

Neuropathy in the context of infection

Jean-Marc Leger

National Referral Center for Neuromuscular Diseases / Hôpital de la Salpêtrière and University Paris VI, Paris, France

Abstract - A number of disorders of the peripheral nervous system may be related to an infectious disease. Infection with *Borrelia burgdoferi* (Lyme's disease) is followed by early and rather distinctive neurologic syndrome in about 15% of untreated patients. This consists of a cranial neuropathy, radiculoneuropathy, or a lymphocytic meningitis, often in combination. These syndromes often improve spontaneously over several months, but improve faster with antibiotic therapy. In contrast, the chronic manifestations, mainly a predominantly sensory neuropathy, do not generally resolve spontaneously, and may partially improve with antibiotic therapy. Peripheral neuropathy is a common complication of HIV infection. Four types have been reported : distal symmetric polyneuropathy which mainly occurs in patients with advanced immunosuppression; inflammatory demyelinating polyradiculoneuropathy which is mainly observed in patients who are otherwise asymptomatic of HIV infection ; mononeuropathy and multifocal mononeuropathy, which may occur early in the course as a self-limited inflammatory neuropathy, or as a manifestation of life-threatening systemic CMV infection ; and acute lumbosacral polyradiculopathy which has been reported in late stage of the disease. Other infectious processes associated with peripheral neuropathy include leprosy, hepatitis C virus (HCV) infection and West Nile virus infection. Combination of HCV infection and mixed cryoglobulinemia is frequently associated with either acute multifocal mononeuropathy, or distal polyneuropathy, which may improve with anti-retroviral therapies. West Nile virus infection is responsible for encephalopathy and axonal predominantly motor polyneuropathy.

Sat. C.4**Chemotherapy-induced peripheral neuropathy****Guido Cavaletti***University of Milan-Bicocca, Monza, Italy*

Abstract - Chemotherapy-induced Peripheral Neuropathy (CIPN) is a side-effect that could occur during and after chemotherapy treatment. It is not an infrequent condition. It is second only to haematological toxicities and it is related to widely-used drugs (platinum compounds, taxanes, vinka-alkaloids, proteasome inhibitors).

CIPN generally consists of an axonal long-dependent peripheral neuropathy; its features are mainly sensory, even though some patients could develop a mild distal weakness. Main complaints referred by patients are related to both positive (paresthesia/dysesthesia) both negative (hypoesthesia on different modalities) sensory symptoms, distributed in a stocking/glove fashion. Sensory alterations are usually slightly different, in dependence of the specific kind of drug administered (for example sensory ataxia is more common with platinum compounds).

CIPN, apart from being quite frequent, is highly relevant from a clinical point of view since it affects negatively Quality of Life (QoL) in a population of long-survival patients.

Thus, in recent years many efforts have been employed to better understand its mechanisms and to find a preventive and/or curative treatment.

At the present moment an efficacious treatment has not yet been discovered. A reason for this could be the following: clinical trials performed so far were made even more difficult by the lack of a solid end-point to be selected in clinical trials, since there is not yet a gold standard in CIPN assessment. In particular, it is not yet clear which clinimetric tool(s) could be more useful and the precise role of NCS and QOL questionnaire in this specific setting. Recently, a study has been published aimed to answer this still unmet clinical and scientific need: CI-Perinoms Study. It has demonstrated good validity and reliability findings for a set of selected outcome measures. Subsequent responsiveness study is to be held by the same group, thus possibly solving those pending questions.

Efforts in end-points selection should also be performed in combination with a genomic approach, to discover specific individual risk factors for CIPN. A careful selection of "genomic targets" could be recommended to design these studies: pathways that could be possibly involved in nerve damage should be aimed first.

In the next few years initial answers could be expected to be given, in the hope of discovering a treatment for this potentially curable iatrogenic neuropathy.

Sat. C.5**Cardiac manifestations of neurological disease****Fadi Abou-Mrad**

*Assistant Professor of Neurology & Medical Ethics, Lebanese University
Medical Director, Saint Charles Hospital President, Lebanese Society of
Neurology*

Abstract - The cardiac complications of certain neurologic diseases have been well recognized for over 50 years. They are benign in most circumstances. Serious arrhythmias and myocardial infarctions, may occur. The link to most of these cardiac derangements is a transient or chronic autonomic dysfunction, depending on the specific neurologic disease. Myocardial infarcts, left ventricular dysfunction, and arrhythmias are well-recognized complications of subarachnoid hemorrhage, intracranial bleed, and ischemic strokes. Seizures may present with atonia or sudden death from asystole. Degenerative brain disorders, namely the synucleinopathies, may affect the central control areas or peripheral ganglia of the autonomic nervous system, causing autonomic dysfunction. In addition, cardiac conduction defects and cardiomyopathy are also common in certain neuromuscular disorders such as dystrophies and mitochondrial myopathies.

Sun. D.1**Myoclonic syndromes from early infancy to adolescence****Athanasios Covanis MD, DCH, PhD***Emeritus Director, Neurology Department, The children's hospital "Agia Sophia", Athens, Greece*

Abstract - The past few decades several distinct syndromes have been recognized in families and individuals. Advances in electroclinical correlation during video-EEG, brain imaging, magneto-EEG, family studies, linkage analyses and molecular genetics have contributed very much. The 2010 ILAE Commission on Classification and Terminology classifies electro clinical syndromes according to the age at onset.

Myoclonic seizures in childhood and adolescence whether massive, bilateral, symmetrical or fragmented constitute a heterogeneous group of syndromes with variable clinical and EEG characteristics and prognosis. Several myoclonic syndromes have been identified in childhood and adolescent and some of them are expressed incompletely in infancy and early childhood. The ILAE Task Force on Classification has recognized some of them, while other syndromes are in development and others having myoclonic seizures in their phenotype e.g., Eyelid myoclonia and absences, are accepted as seizure type. For many years the epileptologists have been characterized as "lumpers" and "splitters". It is not surprising that almost all splitters are epileptologists dealing with children.

Myoclonic epilepsy syndromes in infancy, childhood and adolescent, belong either to the group of encephalopathies (Early myoclonic encephalopathy, Dravet syndrome, Myoclonic encephalopathy in nonprogressive disorders, Lennox-Gastaut syndrome) or to the idiopathic group. In the idiopathic group there are syndromes where myoclonic seizures are the only seizure-type or the predominant type and syndromes where both myoclonic and absence seizures predominate in the phenotype. For example in myoclonic epilepsy of infancy/childhood and juvenile myoclonic epilepsy, myoclonic seizures predominate in the phenotype, while in eyelid myoclonia and absences (Jeavons syndrome), facial myoclonia with absences and epilepsy with myoclonic absences (Tassinari syndrome) myoclonic and absence seizures predominate. All these syndromes may not have, or may have to a variable degree, positive response to intermittent photic stimulation.

Early and correct diagnosis based on clinical and EEG characteristics, using correct methodology, will guide us to early and correct treatment which subsequently contributes to a better prognosis. For myoclonic syndromes sodium channel blocker drugs are contra-indicated.

The correct diagnosis will also help us to choose material for genetic studies in identifying specific single gene defects or multiple interrelated defects.

Sun. D.3**Paraneoplastic and non-paraneoplastic disorders of the voltage-gated potassium channel complex****Kleopas A. Kleopa***Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus*

Abstract - A spectrum of increasingly recognized neurological disorders has been associated with autoimmunity to protein components of the voltage-gated potassium channel (VGKC) complex. VGKC antibodies have been reported in association with three main clinical syndromes: neuromyotonia, Morvan's syndrome (MoS) and limbic encephalitis (LE). Neuromyotonia is a syndrome of peripheral nerve hyperexcitability characterized by muscle cramps and stiffness. In MoS, symptoms of neuromyotonia are associated with autonomic and central nervous system dysfunction, with frequent insomnia. Patients with LE typically present with amnesia, confusion, seizures and personality change or psychosis, with discrete hippocampal abnormalities on brain MRI. In addition to these syndromes, VGKC-antibodies have also been identified in some patients with idiopathic epilepsy and late-onset dystonic epilepsy. These disorders share in common a relatively favorable response to immunotherapies if recognized early, although paraneoplastic cases tend to have a worse prognosis.

Recent studies have provided new insights into the antigenic targets of disease causing antibodies and their clinical correlates. Although initially antibodies were thought to bind directly to VGKC, subsequent studies revealed that in most cases they bound to another protein component of the VGKC complex, either Lgi1 or Caspr2, and rarely Tag-1. Most LE patients have antibodies against Lgi1 which is prominently expressed in CNS neurons and axon terminals that play critical roles in excitability, but is not significantly expressed in peripheral nerves. In contrast, NMT patients usually have antibodies against Caspr2, which is an essential component of the VGKC complex in peripheral axons, as well as in central neurons that promote arousal. The majority of MoS patients have both Lgi1 and Caspr2 antibodies, which may explain the combination of PNS and CNS phenotypes.

Searching for an underlying neoplasm is indicated in Caspr2-Ab⁺ cases with MoS and neuromyotonia, although the majority are non-paraneoplastic. Underlying tumors are mostly thymomas and some MoS cases have a history of myasthenia. In contrast, Lgi1 antibodies in LE patients are usually not associated with any underlying malignancy.

Sun. E.3**The evolution of aphasia after stroke****Constantin Potagas***Dept of Neurology, University of Athens, Aeginiteion Hospital,
Athens, Greece*

Abstract - Aphasia occurs in about one third of strokes: in the majority of people in developed countries vascular lesions of left hemisphere in the acute stage lead to important deficits in expression, processing and comprehension of language. In the post-stroke phase, aphasia usually has a spontaneous tendency for more or less complete recovery, and is an example of the ways the brain may adapt to a lesion.

There is much clinical experience in the natural course of aphasia after stroke, though the really documented clinical studies are few. On the other hand, clinical attitudes can also rely on research neurophysiological data confirming that amelioration is the consequence of some kind of reorganization of cerebral activity in the two brain hemispheres; however, the precise mechanisms sustaining this phenomenon still remain unknown and unpredictable. Functional neuroimaging techniques allow us to follow the functional state of the brain during the period of recovery. Some of these results point out to the role of the non-affected right hemisphere in the recovery from aphasia, while, others point out to the role of the perilesional regions of the left hemisphere.

Functional recovery may be observed essentially during the first few months post stroke. However, independent of the evolution of linguistic capacities per se (i.e. scores in the aphasia batteries), it is very important to focus on communicational abilities, which depend mainly on personality traits and are independent of the quality of language processing itself. A number of aspects of aphasia and of the communication deficit may improve even many years after the stroke, if sufficient care and speech therapy is provided. There are some studies and results on the effects of specific and intensive treatment, the effects of some pharmaceutical agents and of the transcranial magnetic stimulation.

It is also known that aphasic deficits and hemiplegia are associated very frequently with depression, leading to major handicap with many secondary consequences. Hence, a major medical issue is avoidance, prevention, and remediation of secondary effects due to wrong strategies (such as care givers attitudes, fear for using compensatory communication strategies, inhibition of utilization of remaining skills) and isolation of the aphasic person.

Sun. E.4

Phychopharmacology of chronic Neuropathic Pain**Ekaterini Kosma***Psychiatric Hospital of Athens, Dromokaition, Greece*

Abstract - Pain is subjective sensory experience that serves a vital function. However pain can be transformed from an adaptive process into a disease state that implicates pathophysiological mechanisms such as peripheral and central sensitization.

This type of pain is called neuropathic, since it develops as a result of a lesion affecting the somatosensory nervous system. Clinically is characterized by throbbing shooting or stabbing pain and exaggerated and prolonged painful response to noxious or even non-noxious stimuli.

Neuropathic pain conditions are often chronic in their course and they range from very well established states such as trigeminal neuralgia and diabetic peripheral neuropathy to less well understood entities such as fibromyalgia or the so called functional somatic syndromes. Independently of the aetiology, neuropathic pain is in most cases intractable and refractory to treatment with common analgesics. On the other hand patients may benefit from a wide variety of psychotropic agents. In addition, chronic neuropathic pain shares many clinical and pathophysiological features with common psychiatric diseases, mainly anxiety and depression and this has been recently one of the main goals of basic research.

All the above have changed entirely our perspective for the management of neuropathic pain in the aspect that medications now target on modulating specific malfunctioning CNS circuits rather on treating causes or symptoms.

Second generation anticonvulsants such as gabapentin and pregabalin bind to the alpha 2 delta subunit of voltage sensitive calcium channels and produce analgesic effect by reducing calcium influx and excessive stimulation of post-synaptic neurons. Other classes of anticonvulsants such as oxcarbamazepine, lamotrigine and topiramate reduce pain by acting on voltage gated sodium channels.

Serotonin and norepinephrine re-uptake inhibitors such as venlafaxine and duloxetine are potent antidepressants and at the same time exert analgesic effect by facilitating neurotransmission in descending inhibitory pathways at the level of the dorsal horns. Evenmore, drugs that are typically used to treat psychosis, such as olanzapine, clozapine and amisulpiride have shown to be effective in selected cases although their analgesic mechanism has not been identified up to now.

Many psychotropic drugs are recommended nowadays as first-line treatment options. However, several limitations regarding pharmacological treatment guidelines should be considered. For example, most of the medications licensed have only been examined in certain neuropathic entities such as diabetic peripheral neuropathy or postherpetic neuralgia. Another limitation is that medications' efficacy as well as adverse effects in randomized clinical trials have only been examined for 12 weeks or less and also there are only very few head-to-head studies that allow comparisons in regard to long term efficacy and adverse events.

Finally it is very common to administer a combination of various drugs in order to achieve a satisfactory pain relief however this practice remains largely empirical, since it has not been confirmed in large randomized studies.

Selected Oral Presentations



Cypriot, Archaic 6th century B.C.
From the temple at Golgoi

Sat. C.6

Adult-onset parkinsonism and hypermanganesaemia - a novel recessive syndrome caused by SLC30A10 mutation and Kufor-Rakeb (ATP13A2/PARK9) syndrome

Antonio Federico

Department of Neurological, Neurosurgical and Behavioural Sciences, University of Siena, Italy

Abstract - Background: In 2012 a new syndrome related to manganese transport impairment has been contemporary described by our group (Quadri, Federico et al. 2012) and by Tuschl et al (2012). Individuals with homozygous frameshift SLC30A10 mutation developed a recessive neurologic syndrome characterized by adult-onset parkinsonism, severe hypermanganesaemia, polycythemia, and chronic hepatic disease. This gene encoded protein belongs to a large family of membrane transporters. It's highly expressed in the brain, including the basal ganglia, and in the human liver, where explained an important role in the manganese homeostasis. In individuals with homozygous loss of function SLC30A10 mutations, the manganese excretion is severely defective, leading to metal accumulation in the liver, the bloodstream, the brain, and other peripheral tissues. This syndrome delineates a primary disease of manganese metabolism and identifies SLC30A10 as a critical regulator of the manganese transport.

Methods: We describe the follow-up after 16 months of chelation therapy, in a 60-years patient born to consanguineous parents with adult-onset parkinsonism, severe hypermanganesaemia, polycythaemia, and chronic hepatic disease, from the original family. Patient received cycles of chelation therapy with disodium calcium edetate five days a month, every two months.

Discussion: After the first infusion cycle at dose of 10 mg/kg twice daily, urinary levels of manganese were considerably increased, but blood manganese levels were still very high (133 mcg/L, n.r. 3.0-8.0). After tenth cycle of therapy the dose was increased to 20 mg/kg: blood manganese levels were within normal range (4.2 mcg/L, n.r. 3.0-8.0) with significant improvement of the extrapyramidal motor symptoms. Chelation therapy were well tolerated and the laboratory investigation showed a normal renal function during all cycles. We applied the Unified Parkinson's Disease Rating Scale (Part III) to follow the longitudinal course of disease: the score was decreased by 22 points than the first evaluation (27 points). T1-weighted brain MRI, that showed at the first observation bilateral, symmetrical hyperintensities at the level of the caudate and lentiform nuclei, thalamus, corticospinal

tract, medial cerebral peduncle, substantia nigra, posterior pons, and bulbar olives, was unchanged.

These data suggest that early diagnosis and treatment cause a remarkable clinical improvement and arrest the disease's progression. We will also report manganese abnormalities in two siblings affected by Kufor Rakeb disease, a disorder related to ATP13A2 dysfunction with parkinsonism discussing the role of manganese in the regulation of basal ganglia functions and its relationship to oxidative stress.

Sat. C.7

The role of neuromuscular ultrasound in the diagnostic of immune mediated neuropathies

Antonios Kerasnoudis

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Abstract - "The immune-mediated neuropathies are a diverse group of syndromes. Their diagnosis is based in classical cases, on the distribution pattern of peripheral nerve impairment and the results of nerve conduction studies (NCS). In some cases though, the clinical presentation may be subtle, so that extended differential diagnostic workup (cerebrospinal-fluid examination, laboratory tests, nerve biopsy) may be needed.

NCS remain nowadays fundamental not only for the diagnosis, but also for the follow-up and measurement of response to immune-treatment in these type of neuropathies. New challenges arise though, on how best to acquire a static and dynamic imaging of the nerves, aiming to provide a complementary and holistic approach to the nerve impairment. As ultrasound technology continues to improve, nerve imaging has become more detailed and allows visualisation of nerve fascicles and small structural changes, which will move nerve imaging closer to the type of detail that can be seen in biopsy material. Neuromuscular ultrasound has been able to detect thickened or swollen roots, peripheral nerves or plexus, findings that are consistent with ongoing inflammation, especially in cases of chronic inflammatory demyelinating polyneuropathy (CIDP). Similar findings have been described also in Guillain-Barré syndrome (GBS), multifocal-motor neuropathy (MMN) and multifocal-acquired demyelinating sensory and motor neuropathy (MADSAM). Although these figures are rewarding to both physicians and patients, it remains unknown, whether ultrasound could be a reliable method for follow-up and measurement of response to immune-treatment.

This review provides a timely-update on the ultrasound findings of different immune-mediated neuropathies, while possible future possibilities of neuromuscular ultrasound are also discussed."

Sat. C.8**A Novel Oral Formula (PLP10) for the Treatment of Relapsing Remitting Multiple Sclerosis: A Proof-of-Concept, Randomized, Placebo-controlled, Double-blind Clinical Trial****Marios C. Pantzaris^{1,2}, George N. Loukaides^{1,2}, Evangelia E. Ntzani³ & Ioannis S. Patrikios^{1,4}**¹PALUPA Medical Ltd, ²The Cyprus Institute of Neurology and Genetics,³University of Ioannina School of Medicine, ⁴European University Cyprus

Abstract - Rationale: Available multiple sclerosis (MS) treatments are products of reductionism, partially effective with no (re)myelinating/neuroprotective abilities associated with significant side-effects. We aimed to assess whether our novel interventions, formulated based on systems medicine (SM), comprising specific polyunsaturated fatty acids (PUFA) and vitamins reduce disease activity in patients with relapsing remitting (RR)MS. **Methods:** We contacted a 30-month randomized, double-blind, placebo-controlled, proof-of-concept clinical study at the CING. Of a total of 80 patients, 20 were randomly assigned to receive intervention A (DHA/ EPA (3:1 w/w) omega-3, LA/ GLA (2:1 w/w) omega-6 FA, omega-3/omega-6 (1:1 w/w), other specific PUFA, monounsaturated FA, minor quantity of specific saturated FA, vitamin A and vitamin E), 20 to receive γ -tocopherol, intervention C, 20 to receive the combination of A and C, intervention B (PLP10) and 20 to receive placebo, as an oral solution, once daily. The primary end point was the annual relapse rate (ARR) and the secondary end point was the time to disability progression. ISRCTN87818535.

Results: PLP10 reduced the ARR (primary end-point) by 58% (95% CI 0.10 to 0.79, $p=0.016$) and significantly reduced the risk of sustained progression of disability (secondary end-point) by 86% over the 2-year period (Hr, 0.11; 95% CI 0.01-0.97, $p=0.047$) vs. placebo. More patients in the PLP10 (72%) vs. placebo group (20%) were free from new or enlarging T2-weighted lesions on brain MRI over the 2-year study. No adverse events were reported. Interventions A and C showed no significant efficacy.

Conclusion: PLP10 treatment significantly reduced the ARR, and the risk of sustained disability progression without any adverse or significant side effects. This is the first clinical study of SM approach formula holding strong promise as an effective treatment for RRMS.

Sat. C.9**The contribution of electron microscopy in the diagnosis of a case of childhood vacuolar myopathy****K. Kyriacou, R. Papacharalambous, A. Hadjisavvas and T. Kyriakides***Departments of Electron Microscopy and Neuropathology**The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus*

Abstract - Vacuolar myopathies comprise a heterogeneous group of disorders which share as their main histopathological feature the presence of vacuoles. Electron microscopy provides important information on the characteristics and contents of the vacuoles, and is crucial for the diagnosis of lysosomal myopathies. Several entities are included and in this presentation we report on a case, which may present a new type of autophagic vacuolar myopathy with unique sarcolemmal features. The case is a six and a half year old girl, referred because of difficulty walking and a tendency to fall easily. Fetal movements had been normal and family history was negative for a neuromuscular disease. The patient managed to walk at the age of two but was always a slow walker with a tendency to fall and having in particular difficulties with climbing stairs. On examination she had a myopathic face, diffuse hypotrophic musculature and she was hypotonic. Nerve conduction study was normal but with a myopathic EMG. A muscle biopsy showed the presence of vacuoles which stained positive staining for spectrin, dystrophin, laminin and dystroglycans. In addition positive staining was seen for acetylcholinesterase, C5b9 and LAMP-2 antibodies. The vacuoles were evident with H+E staining and contained basophilic material; they were also positive for acid phosphatase and non-specific esterase. By electron microscopy the vacuolar membranes had basal lamina on the luminal side of the membrane which confirmed that vacuolar membranes had sarcolemmal features. Electron microscopy also showed the presence of electron dense myeloid type material within the subsarcolemmal vacuoles and there was reduplication of the basal lamina.

Sun. E.5**Brain tumors: Radiosurgery and Stereotactic High Precision Radiotherapy**

Marilena Theodorou, Nektarios Poullos, Christine Kopp, Sabrina Astner, Anca Ligia Grosu, Michael Molls

Clinic and Policlinic for Radiotherapy and Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Germany

Abstract - "Stereotactic Radiation and Radiosurgery are special techniques to deliver precisely directed, high dose radiation that tightly conforms to an intracranial target to create a desired radiobiologic response while minimizing radiation dose to surrounding normal tissue. For an exact tumor definition we use the Fusion of CT, MRI and PET-scan in special treatment planning system. By this way the safe margin is minimized so that the side effects are low and at the same time the dose for the tumor is high. According to the national and international studies the local tumor control is more than 90 %.

With these techniques we can radiate tumors in complicated anatomically location that they are inoperable. The Radiosurgery delivers the high dose in a single fraction while the Stereotactic radiation delivers the high dose in fractionated schedule. The indications for these special techniques are the brain metastasis, brain tumor such as glioma recurrent, acousticneurinoma, meningioma, chordoma, glomus tumor, hypophysis tumor, craniopharyngioma, medulloblastoma, ependymoma.

We present our experience from Munich for Radiosurgery and Stereotactic high Precision Radiation for Brain Tumors so that our published Researches."

Sun. E.6

Rehabilitation strategies in Neuropediatrics**Carlo Bertoncelli***University Hospital Chu-Lenval, Nice (France)*

Abstract - "Focused physiotherapy may cover important role on the whole of rehabilitation strategies dedicated to children with neurological diseases. In France, Neuropediatric Hospital Unit is usually called EEAPs (Etablissement pour Enfants et Adolescent Polyhandicapés: Institute for children and adolescent with multiple disabilities).

EEAP of the University Hospital Lenval of Nice takes care of children with several neurological and psychological associated pathologies. Their clinical picture contains an enormous variety of deficiencies: neuro-developmental disorders, cerebral palsy, epilepsy, nutrition, visual, hearing, communication and intellectual disabilities.

From 2005 to 2012 our EEAP accommodated 72 patients, residents and day hospital.

Our objective was to develop a personal plan of management, including physical, occupational, and speech therapy, recreational and social milieu, as well as family and community resources. We aimed to optimize functional physical therapy intervention.

During these years we structured our rehabilitation strategy based on epidemiology, severity, and comorbidity of neurological deficits and psychopathological factors.

We endeavored to adapt the outcomes of our researches into clinical interventions by:

1. Collecting etiological data of patients
2. Analysing epidemiological information that could help us to preview individual semiology. We have found both neurological and psychopathological factors to be statistically associated to epilepsy

Additionally by:

3. Choosing neurological and psychopathological adapted assessment tools
4. Projecting and programming global and focused rehabilitation tasks
5. Practicing physical therapy based on these data We reviewed the effectiveness of the following physical therapy interventions as:
 - a. Comprehensive physical therapy approaches;
 - b. Upper extremity treatments;
 - c. Postural and Balance training;
 - d. Strength training;
 - e. Cardiovascular fitness/aerobic programmes;
 - f. Constraint-induced therapy
 - g. Sensorimotor therapy (Bobath).

Sun. E.7

Stereotyping Movement in Children

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¹Sina Trauma and Surgery Research Center, Tehran University of Medical Sciences; ²Department of Pediatrics, Tehran University of Medical Sciences; ³Department of Pathology, Tehran University of Medical Sciences; ⁴Research and Sciences Center of Azad University

Abstract - Objective: To study the frequency of stereotyping movements (SM) in children. Methods: Using a multistage sampling method, we selected 300 children from 13 day care centers and primary schools in Urmia (Western Azarbaijan Province) in Iran. Data collection involved parent interviews in the presence of the children.

Results: Three hundred children (167 boys and 133 girls) were included in the study. Nearly 50% (149 out of 300) had one type of SM. The frequency of different types of stereotyping movements was as follows: bruxism 16%, head banging 13%, hair pulling 8%, nails biting 7% and thumb sucking 6%. There were not any significant relationships between sex and various SM varieties- except for head banging, which was more common in boys ($p < 0.001$). There were no significant associations between parents' education or occupation and presence of any type of SM ($p > 0.05$).

Conclusion: The frequency of stereotyping movements is high in children. More comprehensive studies are recommended.



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Posters

Poster 1

Dysregulation of axonal cytoskeleton in a mouse model of X-linked Charcot-Marie-Tooth Disease**Natasa Schiza, Irene Sargiannidou, Kleopas A. Kleopa***The Neuroscience Laboratory, The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus*

Abstract - Mutations affecting the gap junction (GJ) protein connexin32 (Cx32) cause the X-linked Charcot-Marie-Tooth disease (CMT1X). Although Cx32 is expressed by myelinating Schwann cells, patients with CMT1X develop relatively early axonal degeneration, which correlates best with chronic disability. Our recent studies in *Gjb1*-null mice at the age of 2-4 months showed that compared to wild type (WT) littermates, the diameter of myelinated axons was progressively reduced in *Gjb1*-null mice. Furthermore, neurofilaments were progressively dephosphorylated and more densely packed. As a result of these cytoskeletal changes, fast axonal transport was slower in distal axons of mutant compared to WT animals, with reduced accumulation of synaptic vesicle-associated proteins after ligation and increased expression of beta-amyloid precursor protein and tau.

Here we investigated the signaling mechanisms regulating axonal neurofilament phosphorylation focusing on major kinases and phosphatases involved in neurofilament phosphorylation. Interestingly, ERK1/2 kinase, as well as PP2A phosphatase, was localized in non-compact myelin areas, in close proximity to GJs formed by Cx32. Another kinase, Cdk5, was more diffusely localized along the axon. Biochemical analysis showed altered amounts of ERK1/2, PP2A and Cdk5 as well as their upstream activators in *Gjb1*-null nerves. Moreover, the expression of two type alpha ATPase channels was reduced. Finally, assessment of mitochondria in mutant axons showed significantly increased density in *Gjb1*-null axons, which may have implications for energy supply to the axon. These findings clarify for the first time the mechanisms of early axonal pathology that are independent of demyelination in this mouse model of CMT1X. Our results may lead to future therapeutic targets for this and other types of inherited neuropathy.

Funded by Cyprus Telethon

Poster 2

Umbilical cord blood stem cell ability relieve neurologic deficits in rat intracerebral hemorrhage model**Jalali Mehdi, Nikraves Mohammad Reza, Segah Toleslam Masoomeh***Dept. of Anatomy and cell biology, School of medicine, Mashhad, IRAN*

Abstract - Human umbilical cord blood (HUCB) is now considered as a valuable source for stem cell-based therapies. Previous studies showed that intravascular injection of the HUCB significantly improves neurological functional recovery in a model of intracerebral hemorrhage (ICH). To extend these findings, we examined the behavioral recovery and injured volume in the presence of increasing doses of human umbilical cord blood derived mononuclear cells (UC-MCs) after intracerebral hemorrhage in rats.

The experimental ICH was induced by intrastriatal administration of bacterial collagenase IV in adult rats. One day after the surgery, the rats were randomly divided into 4 groups to receive intravenously either BrdU positive human UC-MCs (4 \times 10⁶, 8 \times 10⁶ and 16 \times 10⁶ cells in 1 ml saline, n = 10, respectively) as treated groups or the same amount of saline as lesion group (n = 10). There was also one group (control n = 10) that received only the vehicle solution of collagenase. The animals were evaluated for 14 days with modified limb placing and corner turn tests. The transplanted human UC-MCs were also detected by immunohistochemistry with labeling of BrdU.

Two weeks after infusion, there was a significant recovery in the behavioral performance when 4 \times 10⁶ or more UC-MCs were delivered (P < 0.05-0.001). Injured volume measurements disclosed an inverse relationship between UC-MCs dose and damage reaching significance at the higher UC-MCs doses. Moreover, human UC-MCs were localized by immunohistochemistry only in the injured area.

Intravenously transplanted UC-MCs can accelerate the neurological function recovery of ICH rat and diminish the striatum lesion size by demonstrating a dose relationship between them.

Poster 3

Complement C1Q ablation accelerates amyloid formation in a mouse model of TTRMet30 Amyloidotic Neuropathy

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²Instituto de Biologia Molecular e Cellular (IBMC), Porto, Portugal

Abstract - Penetrance and age of onset of TTRMet30 amyloidotic neuropathy varies significantly among different populations. Penetrance in Sweden, Cyprus and Portugal are 2%, 28% and 80% while age of onset is 52, 46 and 32 years respectively¹. Genetic and epigenetic factors are speculated to play a role. There is good pathological data to implicate the participation of complement in the pathogenic cascades in peripheral nerve tissue ². We have recently demonstrated a correlation within between age of onset and C1Q polymorphisms in the Cypriot cohort of patients with TTRMet30 amyloidotic neuropathy suggesting that this is a genetic modifier ³. The object of the current study was to evaluate the role of complement C1Q in the available mouse model of the disease, the TTRKO/Met30+/+ .

Poster 4

Gene therapy for inherited neuropathy

**Irene Sargiannidou¹, Stavros Bashardes², Jan Richter², Alexia Kagiava¹,
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Abstract - X-linked Charcot Marie-Tooth disease (CMT1X) leads to progressive distal muscle weakness and sensory loss and is one of the commonest forms of inherited neuropathies. The disease is caused by a large number of mutations in the *GJB1* gene encoding the gap junction protein connexin32 (Cx32). Cx32 forms important channels of communication between the layers of the myelin sheath in peripheral nerves and is necessary for the homeostasis and survival of the myelinating cells and the axon. Transgenic disease models generated in our lab as well as clinical-genetic analysis of large number of patients have demonstrated that most CMT1X mutations result in loss of Cx32 function and failure to form gap junctions. Therefore, replacement of the normal gene may be an effective strategy to treat the disease. For this purpose, we have generated a novel 3rd generation lentiviral vector to allow gene delivery to peripheral nerves. In this vector, Cx32 is under the control of the mouse 2', 3'-cyclic nucleotide phosphodiesterase (CNP) promoter, which specifically drives expression in myelinating cells of the Central and Peripheral Nerve System. The expression cassette also includes a green fluorescent protein (EGFP) as a marker. We have successfully produced lentiviral vector particles and delivered them to the CNS and peripheral nerves. Our initial studies show widespread expression of EGFP in Schwann following intraneural injection, as well as in oligodendrocytes following stereotactic brain injection. These results indicate that gene replacement therapy is feasible and may lead to correction of the gap junction loss in myelinating cells of the CNS and PNS.

Funded by the Cyprus Research Promotion Foundation (Grant HEALTH/BIOS/0609/(BIE)/09) and the European Leukodystrophy Association.

Poster 5

Oxaliplatin-induced hyperexcitation of rat sciatic nerve fibers: an intra-axonal study**Kagiava A.^{1,2}, Theophilidis G.²**

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Abstract - Oxaliplatin is an agent that is used extensively in gastrointestinal cancer chemotherapy. The agent's major dose-limiting toxicity is peripheral neuropathy that can manifest as a chronic or an acute syndrome. Oxaliplatin-induced acute neuropathy is caused by an alteration of the biophysical properties of voltage-gated sodium channels. However, sodium channel blockers have not been successful at preventing acute neuropathy in the clinical setting. We report intra-axonal recordings from the isolated rat sciatic nerve preparation under the effect of oxaliplatin. The depolarization phase of single action potentials remains intact with a duration of 0.52 ± 0.02 ms ($n=68$) before and 0.55 ± 0.01 ms ($n=68$) after 1-5 h of exposure to $150 \mu\text{M}$ oxaliplatin (unpaired t-test, $P>0.05$) whereas there is a significant broadening of the repolarization phase (2.16 ± 0.10 ms, $n=68$, before and 5.90 ± 0.32 ms after, $n=68$, unpaired t-test, $P<0.05$). Apart from changes in spike shape, oxaliplatin also had drastic concentration- and time-dependent effects on the firing responses of fibers to short stimuli. In the intra-axonal recordings, three groups of firing patterns were identified. The first group shows bursting (internal frequency 90 - 130 Hz, $n=88$), the second shows a characteristic plateau (at -19.27 ± 2.84 mV, $n=31$, with durations ranging from 45 - 140 ms depending on the exposure time), and the third combines a plateau and a bursting period. Our results implicate the voltage-gated potassium channels as additional oxaliplatin targets, opening up new perspectives for the pharmacological prevention of peripheral neuropathy.

Poster 6

Frequency of anxiety and depression symptoms in patients suffering from chronic pain

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Abstract - Background and aims: Identifying and alleviating any psychiatric comorbidity is considered crucial in the therapeutic approach for chronic pain regardless of patients' pain status. The aim of the present study was to identify the frequency of anxiety and depression symptoms in a patient population suffering from chronic pain.

Methods: A total of 483 patients, 193 men and 290 women with chronic pain symptoms were referred to our Clinic from General Practitioners or other specialities in a period of 4 years. Patients underwent a thorough clinical interview and examination and underwent laboratory and neuroimaging examination when needed. All patients were prompted to complete the Hospital Anxiety and Depression (HADS) questionnaire, and scores over 10 were considered positive for either anxiety or depression symptoms. Patients with a psychiatric history were not included in the sample.

Results: The mean age of patients was 49.3 years for men and 47.6 for women. HADS scores showed that out of 193 men with chronic pain, 38 presented anxiety and/or depression symptoms and out of 290 women, 101 displayed anxiety and/or depression symptoms. The results were also verified by the clinical evaluation of the patients.

Conclusions: A large proportion of patients with chronic pain also suffer from symptoms of anxiety and/or depression and the percentage is even higher for women. Even if these symptoms do not constitute a distinct psychiatric disorder and regardless of patients' pain status, therapeutic approach for chronic pain requires to take these symptoms into account, in order to achieve optimal care.

Poster 7

Major psychiatric disorders identified during interview in patients referred for chronic pain**E.K. Kosma¹, V. Gyftopoulos², L. Revis², A. Stefanova², D. Kontomichou³, E. Ntatsi⁴**¹Dromokaition Psychiatric Hospital of Athens, Pain Clinic, Neurologist;²Dromokaition, Psychiatric Hospital of Athens, Psychiatric Intern;³Psychologist, ⁴Dromokaitio Psychiatric Hospital of Athens, Mental Nurse

Abstract - Background and aims: Psychological suffering takes the form of pain complaints leading to chronic functional impairment if major psychiatric symptoms are undiagnosed. The purpose of this report is to demonstrate the importance of a thorough patient interview prior to any intervention for chronic pain.

Methods: 483 chronic pain cases were referred to our Clinic from General Practitioners or other specialities during 4 years. Patients underwent a thorough patient interview by both a neurologist and a psychologist prior to any investigation and treatment approach. Two patients, as described below, were identified with an undiagnosed psychiatric disorder, and this was considered a treatment priority.

Results: The first was a 58 years-old male who reported severe headache that had emerged after a brain surgery. He believed that a metallic clip was left into his brain and that among others could command him and could direct his movements in space. The patient was referred to a psychiatrist who diagnosed "paranoid schizophrenia" and prescribed neuroleptics. 4 weeks later the patient was free of symptoms. The second patient was a 64 years-old female with a constant severe chronic thoracic pain. She claimed she could "listen to" her pain and she could only be relieved when lying down, so the pain would eventually dissolve. She was diagnosed with "psychotic depression" and after appropriate treatment symptoms were partially remitted.

Conclusions: Medically unexplained chronic pain may sometimes involve major psychiatric disorders. A thorough patient interview before any intervention for chronic pain is considered a priority.

Poster 8

Predicting the progression of cognitive impairment in memory clinics**Andry Giannakou, Chris Metcalfe, Yoav Ben-Shlomo, Margaret Newson, Sarah Cullum***School of Social and Community Medicine, University of Bristol, UK*

Abstract - Neuropsychological tests are routinely undertaken at memory clinics to help diagnose Mild Cognitive Impairment (MCI) and Dementia. For those patients found to have MCI it would be clinically valuable to be able to distinguish patients at high risk of progressing to Dementia. The aim is to develop a prognostic algorithm using neuropsychological test performance, in order to estimate the probability of progressing to dementia in patients with MCI. The cohort providing data of patients who attended the BRACE memory clinic in Bristol, UK comprises 643 MCI patients, 268 of whom were observed to progress to Dementia. To inform our analysis, a systematic search of the published literature and meta-analysis were conducted for an indication of which neuropsychological tests can distinguish those MCI patients at risk of progressing to dementia. This resulted in 38 articles fulfilling the inclusion criteria.

Subsequently the meta-analysis revealed that the most predominant domains associated with progression to dementia were Memory, Learning, and Language. Using the BRACE data, the best subset of neuropsychological tests to predict dementia was found to be comprising the tests of Mini Mental State Examination (MMSE), the Immediate Recall of the Story Test and the total score of Hopkins Verbal Learning Test (HVLT).

Poster 9

First reported cases of oculo-dento-digital dysplasia (ODDD) in Cyprus, caused by a novel GJA1 mutation**G.A. Tanteles^{1*}, A. Hadjisavvas^{1*}, K. Kleopa¹, M. Loizidou¹, K. Kyriacou¹, V. Anastasiadou^{1,2}**¹The Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus; ²Arch. Makarios III Hospital, Nicosia, Cyprus

Abstract - Oculo-dento-digital dysplasia (ODDD) is an autosomal dominant condition which manifests with a characteristic facial gestalt (typically a “pinched” nose with hypoplastic alae nasi and thin nares), microphthalmia, cutaneous syndactyly of the 3rd, 4th and 5th digits (syndactyly, type III), and other skeletal abnormalities. Radiographs usually reveal hyperplasia of the body of the mandible and broadening of the tubular bones. Several authors have noted spasticity and hyperreflexia as well as white matter changes and calcification of the basal ganglia. Loddenkemper et al. (2002) noted that spastic bladder or gait disturbances were the most frequent neurologic presentations starting in the second decade of life. Paznekas et al., (2003) demonstrated mutations in the gap junction alpha 1 (GJA1) gene (encoding Cx43) as the cause of the condition.

We report a mother and a daughter clinically affected with ODDD. Both were heterozygous for a novel three nucleotide deletion in the open reading frame of exon 2 of the GJA1 gene (c.397_399delAAG) resulting in the deletion of the amino acid lysine at codon 133 (p.Lys133Del). This in-frame deletion lies within the intracellular loop of the Cx43 protein. Within the same region, five missense mutations (p.Ile130Thr, p.Lys134Glu, p.Lys134Asn, p.Gly138Ser and p.Gly138Arg) have previously been shown to be pathogenic (Paznekas et al. 2003 and Richardson et al. 2004). In addition, screening of 110 healthy Cypriot controls has proved negative for this deletion. We are therefore proposing that the p.Lys133Del is pathogenic due to possible conformational changes on Cx43. Further functional studies to ascertain pathogenicity are currently underway.

*Equal contribution

Poster 10

An unusual cause of seizures and eye malformations. First report of two Cypriot patients with Mowat-Wilson syndrome**V. Anastasiadou^{1,2}, A.-M. Kotti², E. Spanou-Aristidou¹, T. Delikurt¹ and G. A. Tanteles¹**¹The Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus; ²Arch. Makarios III Hospital, Nicosia, Cyprus

Abstract - Mowat-Wilson syndrome (MWS) is a mental retardation / multiple congenital anomaly syndrome caused by heterozygous mutations or deletions in the ZEB2 gene. It manifests with a characteristic facial gestalt, the presence of moderate to severe mental retardation, epilepsy and multiple congenital anomalies such as Hirschsprung disease, genitourinary anomalies, heart defects, agenesis of the corpus callosum and eye anomalies. Eye structural anomalies are not a common feature of MWS as they are described in only 4 % of the published cases. We report two new MWS patients, both of whom present with structural eye anomalies namely iris/optic nerve colobomata.

Patient 1 was initially examined in infancy and had distinct facial features, bilateral iris colobomata, hypotonia, global developmental delay, and constipation. Brain imaging did not reveal any CNS malformations. Seizures were first reported at the age of 12 years. Mutation analysis revealed a de novo c.652delC ZEB2 mutation thus confirming the clinical diagnosis. Patient 2 was examined at birth because of multiple congenital anomalies (heart anomalies, unilateral iris coloboma and partial aniridia, hypospadias) and distinct facial features. Mild hypotonia and developmental delay without seizures are recorded to date. Mutation analysis showed a de novo c.2769C>G (p.Tyr923X) mutation in exon 8 of the ZEB2 gene.

MWS is a relatively recently delineated condition usually caused by de novo ZEB2 mutations, although rare cases of sibling recurrence have been observed. We report two new cases presenting with ocular malformations (colobomata), suggesting that these anomalies should be included in the spectrum of the MWS.

Poster 11

Neurogenic Vestibular Evoked Potentials: Unique Scalp Waveforms Specific to Bilateral High Intensity Sound Stimulation are Probably Vestibular in Origin**Eleftherios S. Papathanasiou, PhD¹, Marios Pantzaris, MD¹, Maria Lazarou², Savvas S. Papacostas, MD, FAAN¹**¹Clinical Sciences, The Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus, ²Department of Biological Sciences, University of Cyprus, Nicosia, Cyprus

Abstract - Objective: Sound-evoked vestibular responses are a recently discovered phenomenon. It is believed to be due to the fact that the saccule is located close to the stapes footplate. Using the right type of sound, one can elicit eddy currents in the endolymph and stimulate the saccular macula. Our group has previously published the existence of unique neurogenic vestibular waveforms specific to this form of stimulation given unilaterally, but of low amplitude (0.1-0.2 μ V). The purpose of this study is to use bilateral sound stimulation to obtain vestibular specific waveforms of higher amplitude that may be more clinically useful. The rationale for this is that the brain would be expected to respond more meaningfully to stimulation of both saccules, which would normally happen under conditions of vertical acceleration. Materials and

Methods: Ten physiological normal volunteers were examined, and several derivations from the scalp surface were used for recording. Responses were compared between two sound stimulation conditions: (1) 70 dB nHL clicks, known to stimulate the cochlea, and (2) 125 dB pSPL 500Hz tone, known to stimulate both the saccule and the cochlea. Results: Waveforms of high amplitude (0.2-0.4 μ V), specific to the second sound condition were obtained at the following derivations: P3-F7, P4-F8, P3-P4 and P4-F3.

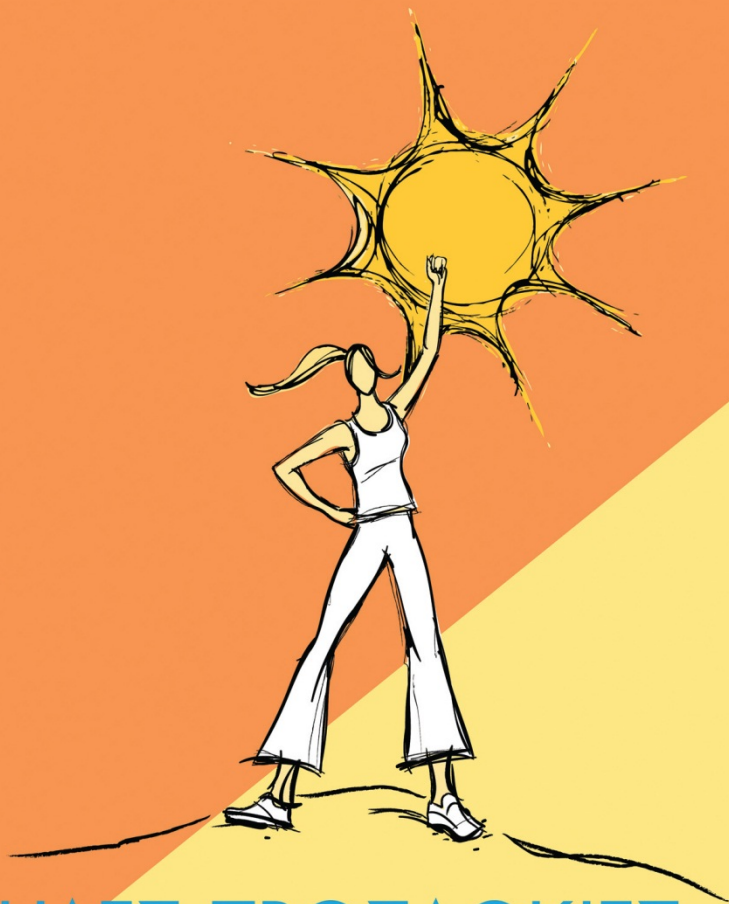
Conclusions: Waveforms that are probably vestibular in origin have been found so far to be preferentially located over the parietal areas. The higher amplitude responses compared to unilateral stimulation reported earlier may make these responses more clinically useful to locate lesions along the vestibular pathway.

Poster 12

Effect of Perindopril on oxidative status in rat hippocampus**Tahereh Mashhoody^a, Fatemeh Zal^b, Masoumeh Emamghoreishi^c, Karim Rastegar^a***Departments of Physiology^a, Biochemistry^b, Pharmacology^c, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran*

Abstract - Oxidative stress and renin- angiotensin system are both involved in the pathophysiology of most of the systemic and central disorders as well as in aging. Angiotensin converting enzyme (ACE) inhibitors, well known for their cardiovascular effects, have also shown antioxidant properties in pathologic conditions. This study aimed to evaluate the effect of ACE inhibition on physiologic oxidative status of the brain. Normal male rats were divided into four groups of 7-9 rats each. Groups were treated orally by perindopril at the doses of 1, 2, 4 mg/kg/day or normal saline as the control for four weeks. At the end of the treatment period the reduced and oxidized glutathione (GSH and GSSG respectively) and malondialdehyd (MDA), the product of lipid peroxidation, were measured in the rats' hippocampus. The GSH and the ratio of GSH to GSSG increased dose dependently and were significantly higher in the group treated with 2 mg perindopril than the control group ($p<0.05$). There was not any significant change in MDA and GSSG. This study demonstrated for the first time that ACE inhibition may promote anti- oxidant defense in the brain of normal healthy subjects.

ΠΟΛΥΑΠΛΗ ΣΚΛΗΡΥΝΣΗ

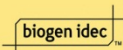


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* Polman CH, et al, *N Engl J Med.* 2006;354:899-910.

Συνταγογραφικές πληροφορίες σε επόμενη σελίδα



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Almeida L, Bialer M and Soares-da-Silva P. Eslicarbazepine Acetate. In: Shorvon SD, Perucca E, Engel J Jr, editors. *The Treatment of Epilepsy*. 3rd ed. Oxford: Wiley-Blackwell. ©2009. p. 485-98.

ZEBINIX® 800 mg, each tablet contains 800 mg of eslicarbazepine acetate and can be divided into equal doses. Therapeutic indications: ZEBINIX® 800 mg is indicated as adjunctive therapy in adults with partial-onset seizures with or without secondary generalisation. **Posology and method of administration:** ZEBINIX® 800 mg must be added to existing anticonvulsant therapy. The recommended starting dose is 400 mg once daily which should be increased to 800 mg once daily after one or two weeks. Based on individual response, the dose may be increased to 1,200 mg once daily. **Contraindications:** Hypersensitivity to the active substance, to other carbamate derivatives (e.g. carbamazepine, oxcarbazepine) or to any of the excipients. Known second or third degree atrioventricular (AV) block. **Special warnings and precautions for use:** Caution should be exercised in the treatment of patients with renal impairment and the dose should be adjusted according to creatinine clearance. In patients with CLCR <30 mL/min use is not recommended due to insufficient data. Eslicarbazepine acetate should be used with caution in patients with mild to moderate hepatic impairment and is not recommended in patients with severe hepatic impairment. **Interaction with other medicinal products:** Eslicarbazepine showed an inducing effect on the metabolism of medicinal products that are mainly eliminated by metabolism through CYP3A4. A study in healthy subjects showed an average decrease of 50% in systemic exposure to simvastatin when co-administered with eslicarbazepine acetate 800 mg once daily, most likely caused by an induction of CYP3A4. An increase of the simvastatin dose may be required when used concomitantly with eslicarbazepine acetate. In a study in healthy subjects there was an average decrease of 36.39% in systemic exposure to Rosuvastatin in healthy subjects when co-administered with eslicarbazepine acetate 1,200 mg once daily. The mechanism for this reduction is unknown, but could be due to interference of transporter activity for rosuvastatin alone or in combination with induction of its metabolism. Since the relationship between exposure and drug activity is unclear, the monitoring of response to therapy (e.g., cholesterol levels) is recommended. Administration of eslicarbazepine acetate 1,200 mg once daily to female subjects using a combined oral contraceptive showed an average decrease of 37% and 42% in systemic exposure to levonorgestrel and ethinylestradiol, respectively, most likely caused by an induction of CYP3A4. Therefore, women of childbearing potential must use adequate contraception during treatment with Zebinix®, and up to the end of the current menstruation cycle after the treatment has been discontinued. In a study in healthy subjects, concomitant administration of eslicarbazepine acetate 800 mg once daily and carbamazepine 400 mg twice daily resulted in an average decrease of 32% in exposure to the active metabolite eslicarbazepine, most likely caused by an induction of glucuronidation. No change in exposure to carbamazepine or its metabolite carbamazepine-epoxide was noted. Based on individual response, the dose of eslicarbazepine acetate may need to be increased if used concomitantly with carbamazepine. **Undesirable effects:** In placebo-controlled studies involving 1,192 adult patients with partial-onset seizures (856 patients treated with eslicarbazepine acetate and 336 treated with placebo), 45.3% of patients treated with eslicarbazepine acetate and 24.4% of patients treated with placebo experienced adverse reactions. Adverse reactions were usually mild to moderate in intensity and occurred predominantly during the first weeks of treatment with eslicarbazepine acetate. Adverse reactions, which occurred at an incidence greater than placebo and numerically present in more than 1 patient are listed by System Organ Class and frequency (very common ≥ 1/10, common ≥ 1/100 to <1/10, uncommon ≥ 1/1,000 to <1/100, rare ≥ 1/10,000 to <1/1,000). **Very common:** Dizziness and somnolence. **Common:** Headache, abnormal coordination, disturbance in attention, tremor, d/plopia, vision blurred, vertigo, nausea, vomiting, diarrhoea, rash, fatigue, gait disturbance. **Uncommon:** Anaemia, hypersensitivity, hypothyroidism, increased appetite, decreased appetite, hyponatraemia, electrolyte imbalance, cachexia, dehydration, obesity, insomnia, apathy, depression, nervousness, agitation, irritability, attention deficit/hyperactivity disorder, confusional state, mood swings, crying, psychomotor retardation, stress, psychotic disorder, memory impairment, balance disorder, amnesia, hypersomnia, sedation, aphasia, dysaesthesia, dystonia, lethargy, parosmia, autonomic nervous system imbalance, cerebellar ataxia, cerebellar syndrome, grand mal convulsion, neuropathy peripheral, sleep phase rhythm disturbance, myasthenia, speech disorder, dysarthria, hypoaesthesia, ageusia, burning sensation, vision disturbance, oscillopsia, binocular eye movement disorder, ocular hyperaemia, saccadic eye movement, eye pain, ear pain, hypacusis, tinnitus, palpitations, bradycardia, sinus bradycardia, hypertension, hypotension, orthostatic hypotension, dysphonia, epistaxis, chest pain, dyspepsia, abdominal pain, dry mouth, abdominal discomfort, abdominal distension, duodenitis, epigastric discomfort, gingival hyperplasia, gingivitis, irritable bowel syndrome, melaena, odynophagia, stomach discomfort, stomatitis, toothache, liver disorder, alopecia, dry skin, hyperhidrosis, erythema, nail disorder, skin disorder, myalgia, back pain, neck pain, nocturia, urinary tract infection, menstruation irregular, asthenia, malaise, chills, oedema peripheral, adverse drug reaction, peripheral coldness, blood pressure decreased, weight decreased, blood pressure diastolic decreased, blood pressure increased, blood pressure systolic decreased, blood sodium decreased, haematocrit decreased, haemoglobin decreased, heart rate increased, transaminases increased, triglycerides increased, tri-iodothyronine (T3) free decreased, thyroxine (T4) free decreased, drug toxicity, fall, joint injury, poisoning, skin injury. **Rare:** thrombocytopenia, leukopenia, pancreatitis. For further information please contact the Marketing Authorization Holder: BIAL-Portela & Cª, S.A. - A.V. da Siderurgia Nacional, 4745-457 S. Mamede do Coronado, Portugal Medicinal product subject to medical prescription. DIDSAM120925

Pregnancy Registry: To provide information regarding the effects of in utero exposure to ZEBINIX®, physicians are advised to enroll pregnant patients taking ZEBINIX® in the International Registry of Antiepileptic Drugs and Pregnancy (EURAP). More information can be found at the website <http://www.eurapinternational.org/>. BIAL-Portela & Cª S.A. Sponsors the EURAP Pregnancy Registry to advance scientific knowledge about safety and outcomes in pregnant women being treated with antiepileptic drugs including eslicarbazepine acetate (ZEBINIX®) and to respond to a requirement of the Committee for Medicinal Products for Human Use (CHMP) to address missing information on safety in pregnancy.

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