THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

TEL AVIV UNIVERSITY

Academia de Științe Medicale din România

UMF UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE IULIU HAȚIEGANU CLUJ-NAPOCA

UPPSALA UNIVERSITET

snr societatea de neurologie din romania

12-15 July 2010

ANA Hotels / Eforie Nord / Romania

5th SSNN Eastern European Neurology Summer School for Young Neurologists

www.ssnn.ro

Final Program and Abstract Book

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Faculty

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General Information

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Registration Desk

All materials and documentation will be available at the registration desk located at SSNN booth.
The staff will be pleased to help you with all enquiries regarding registration, materials and program. Please do not hesitate to contact the staff members if there is anything they can do to make your stay more enjoyable.

Language

The official language is English. Simultaneous translation will not be provided.

Changes in program

The organizers cannot assume liability for any changes in the program due to external or unforeseen circumstances.

Name Badges

Participants are kindly requested to wear their name badge at all times. The badge constiutes admission to the scientific sessions and gala dinners.

Final Program & Abstract Book

The participants documents include the program and abstract book which will be handed out together with the congress bag at the registration counter.

Coffee Breaks

Coffee, tea and mineral water are served morning and afternoon coffee breaks free of charge to all registered participants.

Mobile Phones

Participants are kindly requested to keep their mobile phones turned off while attending the scientific sessions in the meeting rooms.

Currency

The official Romanian currency is RON.

Electricity

Electrical current is 220 volts, 50Hz. Two-prong plugs are standard.

Time

The time in Romania is
Eastern European Time (GMT+2).

CONTACT:

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For updates and details please visit our website www.ssnn.ro

SCIENTIFIC PROGRAM

Monday, 12th July 2010

Coordinators: Ovidiu Băjenaru (Romania), Pieter Vos (The Netherlands)

08:30 - 08:45	**Welcome Address** **Natan Bornstein** (Israel), **Laurenţiu M. Popescu** (Romania) **Dafin F. Mureşanu** (Romania), **Ovidiu Băjenaru** (Romania)	
08:45 - 09:00	**Laurenţiu M. Popescu** (Romania)	Who Were the First Cells? Why Not Neurons?!
09:00 - 09:45	**Ovidiu Băjenaru** (Romania)	Pathogenic Mechanisms in Dystonia - Clinical and Therapeutic Implications
09:45 – 10:30	**Pieter Vos** (The Netherlands)	Traumatic Brain Injury - a Neurological Disorder?
10:30 – 11:15	**Dimitar Maslarov** (Bulgaria)	Head Injuries – Assessment, Investigation and Early Management
11:15 – 11:30	**Coffee Break**	
11:30 – 12:15	**Dafin F. Mureşanu** (Romania)	Spinal Cord Injuries: Clinical Assessment and New Treatment Options
12:15 - 13:00	**Gelu Onose** (Romania)	Integrated Anatomical-Clinical and Patho-Physiological Approach of the Conservative Treatment in the Lumbar Disc Hernia, Including with Radiculopathy - Conceptual and Practical Aspects -
14:00	**Lunch**	
18:00 – 20:00	**Cultural Event**	
20:30	Welcome Reception	

Tuesday, 13th July 2010 - Dementia

Coordinators: Kurt Jellinger (Austria), Bogdan O. Popescu (Romania)

09:00 - 09:45	**Hari Shanker Sharma** (Sweden)	Nanoparticles and the Blood-Brain Barrier and Brain Edema Formation
09:45 – 10:30	**Kurt Jellinger** (Austria)	Is There a Gold Standard for the Pathological Diagnosis of Dementing Disorders: Routes Out of the Swamp?
10:30 – 10:45	**Coffee Break**	
10:45 – 11:30	**Kurt Jellinger** (Austria)	The Enigma of Mixed Dementia
11:30 - 12:15	**Judith Aharon** (Israel)	Frontotemporal Lobar Degeneration
12:15 – 13:00	**Bogdan O. Popescu** (Romania)	Guidelines for Diagnosis and Management of Alzheimer's Disease
13:00	**Lunch**	
18:00 – 20:00	**Case presentations**	
20:30	Gala Dinner	

Wednesday, 14th July 2010 - Stroke

Coordinators: Natan Bornstein (Israel), Dafin F. Mureşanu (Romania)

09:00 - 09:45	**Dafin F. Mureşanu** (Romania)	Neuroprotection in Acute Stroke
09:45 – 10:30	**Natan Bornstein** (Israel)	Secondary Stroke Prevention, Medical and Surgery Approach
10:30 – 10:45	**Coffee Break**	
10:45 – 11:30	**Natan Bornstein** (Israel)	The Heart's Effect on the Brain
11:30 - 12:15	**László Csiba** (Hungary)	Acute Stroke Management
12:30	**Lunch**	
18:00 – 20:00	**Case presentations**	
20:30	Farewell Party	

Thursday, 15th July 2010 – Neurorecovery

Coordinators: Klaus von Wild (Germany), Volker Hömberg (Germany)

09:00 – 09:45	**Klaus von Wild** (Germany)	What Quality of Life Following TBI? Can Encephalotropic Drugs Influence TBI Outcome?
09:45 – 10:30	**Volker Hömberg** (Germany)	Practical Pharmacology in Neurorehabilitation
10:30 – 10:45	**Coffee Break**	
10:45 – 11:30	**Klaus von Wild** (Germany)	Unresponsive Wakefulness Syndrome (UWS) Proposal for a New Terminology of Apallic Syndrome / Vegetative State
11:30 - 12:30	**Final Examination**	
12:30 - 13:30	**Lunch**	
13:30	**Official Closing Ceremony**	

ABSTRACTS

Frontotemporal Lobar Degeneration

Judith Aharon-Peretz
Department of Neurology and the Cognitive Neurology Unit, Rambam Medical Center, Haifa, Israel

Frontotemporal lobar degeneration (FTLD) is a clinically and pathologically heterogeneous syndrome, characterized by progressive decline in behaviour or language associated with degeneration of the frontal and anterior temporal lobes. FTLD has recently been appreciated as a leading cause of dementia in patients presenting before the age of 65 years. Three distinct clinical variants of FTLD have been described: behavioural-variant frontotemporal dementia, characterized by changes in behaviour and personality in association with frontal-predominant cortical degeneration, semantic dementia, a syndrome of progressive loss of knowledge about words and objects associated with anterior temporal neuronal loss and progressive nonfluent aphasia, characterized by effortful language output, loss of grammar and motor speech deficits in the setting of left perisylvian cortical atrophy. The majority of pathologies associated with FTLD clinical syndromes include either tau-positive (FTLD-TAU) or TAR DNA-binding protein 43 (TDP-43)-positive (FTLD-TDP) inclusion bodies. FTLD overlaps clinically and pathologically with the atypical parkinsonian disorders corticobasal degeneration and progressive supranuclear palsy, and with amyotrophic lateral sclerosis. The majority of familial FTLD cases are caused by mutations in the genes encoding microtubule-associated protein tau (leading to FTLD-TAU) or progranulin (leading to FTLD-TDP). The clinical and pathological heterogeneity of FTLD poses a significant diagnostic challenge. The clinical entities and the pathological and genetic heterogeneity of FTLD will be described.

Pathogenic Mechanisms in Dystonia - Clinical and Therapeutic Implications

Ovidiu Băjenaru
University Hospital of Emergency Bucharest, Department of Neurology, „Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Dystonia reffers to one of the most distressing group of neurological disorders, which sometimes are even very invalidating. According to the etiology, there are primary and secondary dystonias. Most of the primary dystonias are genetic neurochemical diseases related to specific abnormalities more or less somatotopically extended (most of them still not completely known exactly) of synaptic activity in the motor circuits related to basal ganglia. These primary abnormalities disturb the normal processing of information related to the control of the motor behaviour in a localized area (focal and segmental dystonias) or in most of the muscle groups of the body (generalized dystonias). These primary synaptic abnormalities are the generators of both clinical motor abnormalities and of abnormal messages to the motor cortex, which are enhanced by the peripheral afferent proprioceptive stimulation due to dystonia itself. The result of these cascade of events is the activation of excessive neuroplasticity mechanisms in specific areas of the brain leading to patological modification of the motor cortical maps and their activity related to the affected region of the body. In most of the cases, also functional abnormalities of the neuromuscular spindles have been shown to be present, adding to and probably enhancing the striato-cortical abnormal processing of the motor activity. The understanding of these complex pathogenetic mechanisms of dystonia offer a rationale support to its management approach, which has to target not only the symptomatic peripheral decrease of dystonia, but also the abnormal neuroplasticity in the affected brain regions.

The Heart's Effect on the Brain

Natan M. Bornstein
Head of Stroke Unit
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Sackler Faculty of Medicine, Tel-Aviv University, Israel

Approximately 20%-25% of all ischemic strokes are attributed to emboli from the heart cavities namely, cardioembolic strokes. cardioembolic stroke.

Atrial Fibrillation
Atrial fibrillation is the most frequently found arrhythmia with a prevalence of 0.4 – 0.7% in the general population. The prevalence of AF is 0.5% in the group aged 50 to 59 years, it rises to approximately 6% in population older than 65 years, and up to 10% in people older than 75 years. About 20% of all ischemic strokes are attributed to cardioembolism, and AF related stroke comprises approximately 45% of all cardioembolic strokes.

Risk for stroke. Atrial fibrillation is a well-established independent risk factor for stroke, leading to 5.6-fold increase of risk according to data from Framingham study. About 16% to 25% of ischemic strokes are associated with AF, the percentage being higher in patients with large supratentorial infarcts (59%).
The randomized clinical trials of AF confirmed an overall annual stroke incidence of about 5% in the general population of patients with AF not treated with anticoagulation. Risk for recurrent stroke in AF patients without antithrombotic treatment is 12% per year, which is strikingly high comparing with rate of 5% annually after the first year for AF-free patients after first stroke or TIA. An ischemic stroke will occur during lifetime of about 35% non-anticoagulated AF patients.
The attributable risk of stroke from AF is rising from 1.5% in 50-59-year-old age group to 15% in the 70s-old age group. Atrial fibrillation is present in over one third of individuals aged 80-89 years with acute ischemic stroke and is considered to be a leading cause of stroke in the elderly. Increased stroke severity, disability and mortality in AF patients have been documented.
Recommendations. According to Class I evidence from previous trials, adjusted-dose warfarin reduces risk of stroke in AF patients by about 70%. Though aspirin has some efficacy in reducing stroke risk in AF patients for about 20%, it is clearly less efficacious than warfarin. For patients with AF aged 75 or younger who are at high risk for stroke and are considered to be safe candidates for anticoagulation, treatment with warfarin is recommended with target INR of 2.5 (range 2.0-3.0). Warfarin dose in elderly AF patients (more than 75 years) is optional, since warfarin may be used with lower INR target of 2.0 (target range 1.6 to 2.5) in order to decrease risk of hemorrhage; however, there are experts who disregard age and accept higher INR target of 2.5 (target range 2.0-3.0), considering it appropriate and safe. For patients with AF considered to be unable to receive anticoagulation therapy or to be at low risk of stroke, aspirin 325 mg/day is recommended. In a group of AF patients with moderate risk of stroke, decision between warfarin and aspirin should be made considering individual patient's bleeding risk and preferences.Decision-analysis models have

been developed and can be used in making clinical decision on anticoagulation treatment.

Implementation of treatment in clinical practice. Although benefit from warfarin treatment in AF patients is clear, not all appropriate candidates for anticoagulation actually receive this treatment. Anticoagulation is underused in high-risk elderly patients, especially women, often is used in low risk patients, and frequently used in an inadequate dosage, with a peak of INR in a zone lower than recommended (2.0-2.4), indicating that “the doctors were playing safe”. Both physicians and patients influence this problem, risk-versus-benefit evaluation of anticoagulation use being the essential physician-related factor.
Recently new oral direct thrombin inhibitor, Dabigatran., was proven to be similarly effective in reducing embolic events and strokes in NVAF patients with lower rate of major hemorrhage [NEJM 2009; 361:1139-51]. Several other anti-factor Xa drugs are in phase III clinical trials and the results are awaited in the near future. These newly developed drugs might subsitude warfarin as the treatment for stroke prevention in patients with NVAF.

Secondary Stroke Prevention, Medical and Surgery Approach

Natan M. Bornstein
Head of Stroke Unit
Dept. of Neurology, Tel-Aviv Medical Center
Sackler Faculty of Medicine, Tel-Aviv University, Israel

Patients with TIA or ischemic stroke carry a risk of recurrent stroke between 5 and 20% per year. In patients with TIA or ischemic stroke of noncardiac origin antiplatelet drugs are able to decrease the risk of stroke by 11-15% and the risk of stroke, MI and vascular death by 15-22%. Aspirin is the most widely used drug. It is affordable and effective. Low doses of 50-325 mg aspirin are as effective as high doses and cause less gastrointestinal side effects. Severe bleeding complications are dose-dependent. The combination of aspirin with slow release dipyridamole is superior to aspirin alone for stroke prevention (ESPS-2 and ESPRIT1). Both studies have shown approximately 20%-24% relative risk reduction (RRR) of stroke and death. Clopidgrel is superior to aspirin in patients at high risk of recurrence by about 8.7% RRR (CAPRIE2). The combination of aspirin plus clopidogrel is not more effective than clopidogrel alone but carries a higher bleeding risk (MATCH3 and CHARISMA4). None of the antiplatelet agents is able to significantly reduce mortality. The recent results of the PRoFESS5,6 will be presented..

References

1. *Lancet 2006;367:1665-73*
2. *Lancet 1996;348:1392-1339*
3. *Lancet 2004;364:331-337*
4. *N Eng J Med 2006;354(16):1744-6*
5. *Cerebrovasc Dis 2007;23:368-380*
6. *N Engl J Med 2008;359:1238-51*

Acute Stroke Management

László Csiba
Department of Neurology, Debrecen University, Hungary

The iv-thrombolysis is widely used and effective recanalisation intervention in acute stroke therapy. The recanalisation rate depends on the location of thrombus:TICA:6%, M1-MCA:30%, M2-MCA:44%, tandem MCA- ICA: 27%. Because of the weakness of iv.-t-PA therapy new interventions have been tested. The intraarterial lysis results in absolute difference of 15% in good clinical outcomes at 3 month over placebo (up to 6 h from symptom onset in patients with proximal middle cerebral artery occlusions). Ultrasonic insonation (by routine 2MHz transcranial Doppler) during iv. thrombolysis achieves a recanalization rate of 38% vs. 13% $p < 0.05$. Combination of ultrasound insonation and gaseous microspheres may result in further improvement of systemic or ia. tPA therapy. The SENTIS and BRAINSGATE trials are also new interventions by increasing the blood flow into the ischemic area using non-pharmacological devices. Other intraarterial mechanical devices are also used (MERCI, MULTI-MERCI, Penumbra)
The following recanalisation rates and clinical improvement (mRankin 0-2) were published by different interventions: IV tPA<3 h:50% and 37%, Merci<8 h: 57% and 36%, Penumbra<8 h:82% and 20%, bridging therapy with IV tPA<3 h + i.a. t-PA:64% and 38%, t-PA+ Sonothrombolysis with Transcranial Doppler<3 h:83% and 51%, respectively. Combinations of a fibrinolytic +either anticoagulant or antiplatelet agent offer potential to maintain the patency, but more studies are needed. Finally, there is a need for a drug with robust neuroprotectant effect usable on „battle-field" without previous CT.The present data indicate that no single approach can be applied in all acute ischemic strokes. Instead, individualized decision is necessary and either pharmacological/non-pharmacological intervention or their combination could be applied.

Practical Pharmacology in Neurorehabilitation

Volker Hömberg
St. Mauritius Therapieklinik, Meerbusch, Germany

Beside the use of training techniques and other behaviouel interventions neurological rehabilitation can be augmented significantly by the use of pharmacological agents: Beside the necessary pharmacological treatments for risk factors such as hypertension and hyperlipidemia and secondary prevention, drugs can also be used to facilitate brain recovery. On the other hand certain drugs have to be avoided because they are known to impair brain repair mechanism.

This lecture will address the following issues:

1. It is of critical importance to avoid so called “detrimental” drugs defined from animal experimental as well as from clinical catamnestic studies to interfere with brain plasticity.

2. The use of particular drugs will be discussed which can be used for neuro-protection and brain repair.
Among the neuroprotective drugs only two (oerebrobysin, acetylcholine) out of hundreds have been proven to be of some value. This is similarly true for the use of drugs tried affecting monaminergic pathways such as amphetamines, dopamine or amantadine. Such drugs can be used to e.g. improve consciousness in MCS or VS or can help to improve behaviour.

3. One of the best evidence-proven concepts is the use of antidepressive agents in patients after stroke with signs of depression. In these patients mood, rehabilitative outcome and life expectancy are improved by antidepressive therapy.

Is There a Gold Standard for the Pathological Diagnosis of Dementing Disorders: Routes Out of the Swamp?

Kurt A. Jellinger
Institute of Clinical Neurobiology, Vienna, Austria

Dementia defined as deterioration in several cognitive domains is not only caused by neuronal cell death/loss, but predominantly by dysfunction and loss of synapses and by cholinergic neuronal and axonal abnormalities.There are several consensus criteria for both the clinical and neuropathological diagnosis of different types of dementias. The clinical diagnostic accuracy using revised research criteria and newly developed biomarkers (MRI, PET, CSF analysis, genetic markers) ranges from 65 to 96% (for Alzheimer disease) with a diagnostic specificity versus other dementias of 23-88%. Neuropathological assessment of dementing disorders using immunohistochemistry, molecular biologic and genetic methods can achieve a diagnosis/classification, based on homogeneous definitions, harmonized inter-laboratory methods and standards for the assessment of nervous system lesions, in almost 99%, without, however, being able to clarify the causes/etiology of most of these disorders. Further prospective and concerted clinico-pathological studies using revised methological and validated protocols and uniform techniques are required to establish the nature, distribution pattern and grades of lesions and thus to overcome the limitations of the current diagnostic framework. Data fusion may allow their uniform application and correlation with clinical data in order to approach a diagnostic “gold standard”, and to create generally accepted criteria for differentiating cognitive disorders from healthy brain aging. Detection of disease-specific pathologies will be indispensable to determinate the efficacy of new therapy options.

The Enigma of Mixed Dementia

Kurt A. Jellinger
Institute of Clinical Neurobiology, Vienna, Austria

Mixed dementia (MD) refers to a combination of definite Alzheimer disease (AD) and vascular encephalopathy, but the distinction between both disorders is controversial. For the diagnosis of MD the clinical/neuroimaging criteria of possible AD plus cerebrovascular disease (CVD) as separate entities are used, but causal relations between vascular brain lesions and dementia are unclear. We proposed the combination of autopsy-proven AD with multiple vascular or ischemic lesions with about 30–50 ml of infarcted/damaged brain tissue. The population-based prevalence of MD is unknown. In retrospective and prospective autopsy studies, it ranges from 2 to 58% with reasonable means of 6–12%. In a consecutive autopsy series of 1700 demented elderly subjects (mean age 84.3±5.4 yrs, 90% over age 70), 950 of which with clinically probable AD, in Vienna, Austria, 45.6 to 56% showed "pure" AD, 7% atypical AD, 20-25% AD plus cerebrovascular lesions, and 9% AD plus Lewy body pathology; MD was diagnosed in 5.2 and 3.2%, and "pure" vascular dementia (VaD) in 13 and 3.0%, respectively, while 7/4% were other dementing disorders, and 1% showed no specific pathology. Like the MRC-CFAS and other studies, this indicates frequent coexistence of AD with multiple cerebrovascular lesions in cognitively impaired patients. In both AD and VaD, vascular lesions frequently involved subcortical regions (basal ganglia, thalamus, hippocampus, and white matter) or were multiple microinfarcts, whereas in MD, large/hemispheral infarcts and multiple microinfarcts were more frequent, suggesting different pathogenic mechanisms. In early/mild AD, critically located small vascular lesions may induce/promote cognitive decline, but in full-blown AD they appear of minor importance. Discussion of the major pathogenic factors inducing AD, VaD and MD suggests synergistic relations between these disorders. However, currently available morphological criteria for AD and VaD are of limited value for the diagnosis of MD and generally accepted and validated histopathological criteria for the diagnosis of VaD and MD are currently not available. Therefore, more distinct and critically evaluated clinico-pathological criteria are warranted.

Head Injuries – Assessment, Investigation and Early Management

Dimitar Maslarov
Neurology Clinic, 1st MHAT - Sofia, Bulgaria
Department of Urgent Neurosurgery, Pirogov Hospital, Sofia, Bulgaria

"Head injury" is defined as any trauma to the head, other than superficial injuries to the face. clinically important brain or cervical spine injury is defined as any acute condition that has been identified by imaging or by assessment of risk factors.

All patients presenting to an emergency department with a head injury should be assessed by a trained member of staff within a maximum of 15 minutes of arrival at hospital. Part of this assessment should establish whether they are high risk or low risk for clinically important brain injury and/or cervical spine injury.
Where a request for urgent CT imaging of the head (that is, within 1 hour) has also been received, the cervical spine imaging should be carried out simultaneously. The main focus of emergency department assessment for patients who have sustained a head injury should be the risk of clinically important brain injuries and injuries to the cervical spine and the consequent need for imaging. Due attention should also be paid to co-existing injuries and to other concerns the clinician may have (for example, non-accidental injury, possible non-traumatic aetiology such as seizure).
Early imaging, rather than admission and observation for neurological deterioration, will reduce the time to detection of life-threatening complications and is associated with better outcomes.

Spinal Cord Injuries: Clinical Assessment and New Treatment Options

Dafin F. Mureşanu
Department of Neurology, Faculty of Health Sciences, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania

Spinal cord injury (SCI) is an insult to the spinal cord resulting in a change, either temporary or permanent, in its normal motor, sensory, or autonomic function.

The subject of this teaching course focus on the diagnosis and the therapy of SCI and also covers the pathophysiological mechanisms involved in SCI and the relationship between these mechanisms and therapy .

The mechanisms of the primary injury themselves are not yet completely elucidated. The secondary injury process leads to disastrous consequences: neuronal necrosis, neuronal apoptosis, scar and cyst formation, demyelination, disruption of neural pathways (disconnection).

Aside from conventional therapy, new therapies like anti-NOGO antibodies: 11C7 and 7B12, MAG antagonists, sialidase , rolipram, dibutyril cAMP (db-cAMP), inhibitors of RHO signaling, Neuromodulators of EDA (endogenous defense activity) are studied in order to reduce the sequels and improve the quality of life.

Neuroprotection in Acute Stroke

Dafin F. Mureşanu
Department of Neurology, Faculty of Health Sciences, University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, Romania

Neurologists are now confronted with a barrage of new information regarding the intimate processes taking place in both normal and pathological brains.

In order to determine the correct therapeutic approaches for neurological disorders, we need to understand the basic biological and pathophysiological processes and the interrelationships between the two.

In particular, concepts like neurotrophicity, neuroprotection, neuroplasticity, neurogenesis and anoikis, as well as their clinical utility, may be daunting. Even more specifically, there are many points in the pathophysiological cascade between vessel occlusion and irreversible cell death where pharmacological intervention might be beneficial. It is becoming clear that concepts of single mechanism neuroprotective molecules are utopian. Comprehensive research of multimodal drugs and combination therapy, followed by appropriate clinical use, should be encouraged.

Integrated Anatomical-Clinical and Patho-Physiological Approach of the Conservative Treatment in The Lumbar Disc Hernia, Including With Radiculopathy - Conceptual and Practical Aspects

Gelu Onose
The Physical & Rehabilitation Medicine Clinic Division of the Teaching Emergency Hospital "Bagdasar-Arseni", Bucharest, Romania

Lecture abstract/ syllabus

1. Introductive aspects
- Scope of the lecture
- Low back pain, including most frequent lumbar disk hernia related pathology: general considerations, including historical and succinct actual epidemiological data
- Medical and social importance of the subject matter

2. Minimal, basic notions of functional spine column - and (distal) cord - structure/ biomechanics and some related patho-physiological comments
- Synoptic overview on spinal nerves' distribution territories and roles (including fig. 1)
- Mielomeres and spinal nerves roots in low lumbar spine: topographic relations and observations (including fig. 2)
- The vertebral column unit
- Biomechanics synthetic data

3. Main pathological pathways in lumbar disc hernia
- Phylogenesis of the spine/ human orthostatic posture – biomechanical implications (including fig.3)
- Human orthostatic posture – normal and deviations (including figg. 4,5)
- Axial orthostatic dynamic balance and muscles involved (including figg. 6-10)
- Pressure distribution on inter-vertebral disks (including figg. 11, 12)
- Morphological phases of the degenerative disk-vertebral disease (including fig. 13)
- Anatomical conditions of inner spine channel space crisis and related spinal nerve root mechanical compression, after lumbar disk hernia (including figg. 14, 15)
- Conceptual/ schematic and Imagistic identification & quantification of lumbar disk hernia and respectively, of the spine channel inner space consequent crisis - "Canal-Hernia mass Ratio" (including figg. 16, 17)
- Mechanisms of pain and spinal nerve root sufferance in lumbar disk hernia (including figg. 18-20)
- Clinical and imagistic evidence of the "usual" evolution in lumbar disk hernia (including fig. 21)
- Morphological/ clinical common pattern and particularities, of evolution & prognosis in lumbar disc hernia (including table 1)
- Synopsis of the degenerative discal-vertebral disease and its - including long-term - evolution and consequences (including fig. 22)

4. Clinical and functional assessment of the degenerative vertebral disk disease (inc. table 3)
- Vertebral static and dynamic syndromes
- Dural syndrome

- Radicular neural syndrome
- Myo-fascial syndrome
- Psycho-emotional syndrome

5. Targets of the conservative therapy in radiculopathies subsequent to spinal, vertebral disk degenerative pathology

- Key patho-physiological targets
- Connected, simptomatic targets

6. Pharmacological therapy in disc hernias with radiculopathy

- Non-steroid anti-inflammatory drugs
- Analgesics
- Muscle relaxants
- Tranquilizers
- α-blockers (adrenergic α-antagonists)
- Neurotrophics
- Antioxidants
- Topical medication
- The role of corticoid therapy (including fig. 23)

7. Physical therapy in disc hernias with radiculopathies

- Interferential medium frequency
- Low frequency currents
- LASER applications
- US applications
- Thermotherapy/ cryotherapy
- Massage
- Kinesitherapy/ hydrokinesitherapy (including fig. 24)
- Bed rest
- Spinal tractions
- Williams' back exercises
- McKenzie' back exercises
- Orthotic support
- Patient's education and lifestyle adjustments
- Spa cure

8. Algorithmic approach to acute lumbosacral radiculopathy – without cauda equine (including fig. 25)

9. Summary of the conservative therapeutic approach in disc hernias with radiculapathies (main phases of the pharmacological and physical treatment sequences)

10. Selected references:

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f. Takada E, Takahashi M, Shimada K. Natural history of lumbar disc hernia with radicular leg pain: Spontaneous MRI changes of the herniated mass and correlation with clinical outcome. J Orthop Surg (Hong Kong). 9(1): 1-7, 2001

Guidelines for Diagnosis and Management of Alzheimer's Disease

Bogdan O. Popescu
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Elaboration of guidelines for diagnosis and management for frequent diseases is based on the best existing evidence and it serves for standardization of quality medical assessment and care. Alzheimer's disease is the most frequent form of dementia which affects between 5 and 10% of population over the age of 65 and up to 50% over the age of 85 (1). There is a consensus in all current guidelines that AD should be detected and treated early. Persons with Mild Cognitive Impairment (MCI) should be monitored due to their high risk of conversion to dementia. The clinical criteria for diagnosis of AD are defined in DSM IV and by NINCDS-ADRDA and are reliable. However, it has been suggested that based on the current criteria AD in diagnosed at an advanced stage of neurodegeneration and therefore new criteria have been proposed (2). Main tools for early AD detection are biomarkers, such as neuroimagery studies and CSF analysis. Unfortunately there is no treatment yet to stop or cure the disease and the only evidence-based therapies allow a temporary alleviation of symptoms, after which a decline follows in clinical evolution and quality of life of patients and their families. Many new clinical studies, including vaccination are on their way, and better translational concepts from bench to bed are currently evaluated.

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Nanoparticles and the Blood-Brain Barrier and Brain Edema Formation

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Nanoscale materials and their possible effects on the biological system have attracted great attention of neuroscientists to unravel their effects on the human health system [1-3]. Thus, a possibility exits that nanoscale materials comprising “microfine particles” that are normally present in the environment, or “engineered nanomaterials from metals” emanating from some industrial sources at certain work places could affect our central nervous system (CNS) [4-6]. Based on these studies, a new discipline “Nanoneuroscience” has emerged [2,3,7-9]. The new discipline is aimed to deal with the effects of nanoparticles on the CNS related to their both beneficial and harmful effects [2-5,7-9].

The need of the hour is to focus on research related to nanoparticles on the CNS toxicity in vivo situations [4,8]. It appears that our brain function is severely compromised following exposure to these microfine particles. We need to find out whether presence of carbon nanoparticles in the environment due to motor vehicle exhausts, or silica dust in desert environment could influence our reactions to stress or CNS injuries [1,8-10]. However, the potential neurotoxic effects caused by nano-drug delivery should be examined first in great details.

There are evidences that nanoparticles derived from metals could induce profound neurotoxicity probably by inducing breakdown of the blood-brain barrier (BBB) [8,9] and exacerbate the adverse effects of hyperthermia induced bran injury. This indicates that nanoparticles exposure alters the physiological response of the organisms following CNS injury or stress. This may result in aggravation of cellular and molecular reactions within the CNS. Thus, new investigations are needed to further expand our knowledge in the field of nanoneurosciences, nanoneuropharmacology, nanoneuroprotection and nanoneurotoxicity. In conclusion, the effects of nanoparticles on our CNS health can’t be ignored now.

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Traumatic Brain Injury a Neurological Disorder?

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Traumatic brain injury is a heterogeneous disease that may affect people of all ages. Severity may range from mild with a low frequency (1 per 100) of life threatening intracranial hematoma that needs immediate neurosurgical operation and very low mortality (1 per 1000) to severe with a high likelihood of life threatening intracranial hematoma (up to 1 per 3) and a 40% case fatality rate and a 50-60% disability rate in survivors. TBI is heterogeneous in definitions, pathology, age of onset and in the presence of additional injury to other body regions.

Traumatic Brain Injury (TBI) encompasses the functional disturbances and structural damage of the brain caused by direct impact, by external acceleration, deceleration and/or rotation forces to the head.

Pathophysiologically, TBI is characterized by diffuse damage of grey matter and white matter tracts in the brain, and by contusion, laceration and intracerebral or extracerebral haemorrhage signifying focal and/or diffuse damage (primary damage). Secondary brain injury consists of the damage that occurs in the hours-dayas post injury. Both intracranial and systemic insults (e.g. hypoxia and/or hypotension) may exacerbate secondary damage.

The incidence of TBI is high, in the international literature varying between 100 and 300 per 100,000, with the highest incidence occurring in men, aged 15 to 24 years. The average age of patients with TBI is 30-40 years1, 2. Recent data indicate an increase in average age and a larger contribution of elderly patients with TBI. Approximately 90–95% of all TBIs are considered mild. Intracranial complications of mild traumatic brain injury (MTBI) are infrequent but potentially life-threatening, and may require neurosurgical intervention in a minority of cases (0.2–3.1%). Because of the importance to exclude the small chance of a life-threatening complication in large numbers of individual patients much research has been dedicated to the prediction of these complications.

In the presentation the diagnosis, treatment options and consequences of traumatic brain injury will be discussed. In particular we will emphasize currently acknowledged predictors of outcome including the clinical and biochemical markers of brain damage3-5.

A second topic will be how to read the CT scan with respect to relevant intracranial lesions in mild, moderate and severe TBI.

Thirdly, we will discuss traumatic axonal damage (diffuse axonal injury (DAI)) that usually results from shearing stresses on brain parenchyma, which stretch and injure axons (and or myelin) and bloodvessels, causing oedema and axoplasmic leakage. DAI is microscopic in nature and difficult or impossible to detect with CT. DAI is a white matter disorder, consisting of myelin dysfunction/ demyelination, axonal dysfunction/ injury or both. DAI causes immediate and often prolonged unconsciousness and accounts for 35% of the mortality from head injury.

Currently no accurate method is available for diagnosing and assessing the distribution and severity of diffuse axonal injury. This presentation will also focus on the clinical aspects of DAI, the diag-

nosis of DAI using MRI techniques inlcuding diffusion tensor imaging(DTI), susceptibility weighted imaging (SWI). In addition although no efficacy of any (drug) treatment has been proven untill now, some of the available evidence and the possible treatment mechanisms will be discussed.
Untill recently TBI was a neglected research topic, with few documented randomized controlled trials(less than 20), receiving little public and pharmaceutical attention and government funding.6-8 This has been alluded to the pathological heterogeneity of TBI resulting in a scarcity of successful evidence based strategies to restore the normal physiological state of the injured brain and in a complete lack of randomized controlled trials of targeted drug interventions with a positive effect on mortality and long term outcome. But a positive change emerges because of: 1) Increased awareness of the fact that TBI is a disease (and not merely an incident) that may lead to chronic disability and reduced quality of life years and enormous societal costs. 2) The appearance of systematic reviews and guidelines stating that TBI may benefit from an evidence based interdisciplinary approach to improve early conventional management and rehabilitation.8-10 3) The use of new MRI techniques like DWI, SWI & DTI in the acute stages of TBI demonstrating the pathological heterogeneity of TBI which may open ways for new drug intervention studies.11, 12 4) Finally it is increasingly recognized that outcome may be influenced by other factors than injury alone and that the patients previous history or pre-injury characteristics may modify the response of injured individuals. TBI can be classified according to aetiology, the clinical condition and patho-anatomical abnormalities.

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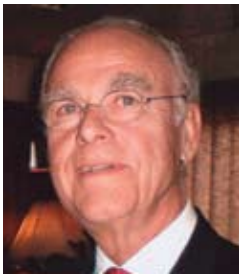

Unresponsive Wakefulness Syndrome (UWS) Proposal for a New Terminology of Apallic Syndrome / Vegetative State

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Objective: As a result of modern emergency intensive care treatment, diagnostic neuroimaging, and sophisticated nursing many individuals who would have died in the past do increasingly survive from severe brain damage. This, however, is at the expense of severest impairments of higher brain functioning and disabilities causing specific behavioural signs and symptoms that are known as an Apallic Syndrome (AS), a term still used in Central and East Europe and Asia, and as a Vegetative Sate (VS) in the English literature.
Method and Patients: Full state AS/VS could be present either as a remission defect or an irreversible end stage. For Europe the prevalence of AS/ VS in hospital cases is reported to be 0.5–2 /100.000 population/year. One quarter to one-third is caused by traumatic brain damage. Roughly 70% are non-traumatic brain lesions (e.g. due to intracranial haemorrhages, tumours, cerebral hypoxemia following cardiac arrest (with an increasing frequency!) and chronic neurological diseases (e.g. Mb.Alzheimer, Parkinsons D.)
Results: Full stage AS / VS is clinically defined in three domains (a) anatomy, (b) behaviour, and (c) consciousness (self-awareness). The term apallic syndrome was coined by Kretschmer to describe patients who are awake but unresponsive secondary to severe brain damage. AS is the clinical manifestation of a functional multi modular disconnection syndrome characterized by signs and symptoms of a pathological neurobehavioral syndrome
Apallic cannot be explained by or taken for a conditio sine qua non of an anatomically completed and permanent disconnection of neocortical structures and higher cerebral functioning as previously suspected by Kretschmer, when he coined the term “apallic” “Vegetative” State, first introduced as persistent VS by Jennett and Plum must not be permanent persistent . The name “vegetative ” was chosen to refer to the preserved vegetative (autonomous) nervous functioning.. The purpose of this contribution is to recommend a new nomenclature for an old pathological behavioural syndrome: Unresponsive Wakefulness Syndrome (UWS) to replace AS/VS as decided in Rome on 18.9.09.
Conclusion: UWS will enable clinicians and scientists to assess and describe objectively all its different stages regarding neuro-physiology,-pathology,-psychology, prognosis, and ethics.

*European Workshop of international Task Force on the Vegetative State
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What Quality of Life Following TBI?
Can Encephalotropic Drugs Influence TBI Outcome ?

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Objective: Restoration of impaired higher cortical functioning following TBI are focussed at 1. the Physical domain: Sensory-motor functions of brain- ,spinal cord- peripheral nerve lesions and 2. the mental- cognitive, behavioural domain: nneurobehavioral functions –social interaction.

Methods: Neurorehabilitation is primarily based on the diagnosing, prevention, and treatment of post-lesion complications secondary to acute /chronic impairments of the CNS and PNS. This is to define specific strategies in respect to various (neurological) deficits that (might) decrease the individual's functional ability. Early NN-rehabilitative interventions aim at the preservation of higher cortical functioning as to quicken restoration of impaired sensory motor, mental-cognitive, neurobehavioral impairments and to avoid secondary / tertiary damage. The patients and his family's needs, wishes, and all cultural and economic aspects have to be considered.
QOLIBRI is been shown to be a reliable assessment tool for QoL after TBI by measuring the TBI individuals personal experience. Encephalotropic drugs are known to effect impaired higher cortical functioning and to support brain plasticity and restoration regarding both motor skills and mental cognitive, behavioural performance.Anticholinesterase therapy has been interpreted by Luria and others as particular amenable to the interpretation of diachisis. Thus recovery might be due to „de-inhibition" of neurons, the activity of which had been depressed by TBI.

Results: Neurorehabilitation is an ongoing chain of restorative interventions within an holistic approach . It aims at social re-entry and a good HRQoL in the long run. TBI individuals live within a social context. Early assessment of impaired higher cortical functioning (social cognition) is imperative in acute brain damage and post-acute care as to guide brain protection and restoration. For clinical studies on quality management after TBI and the impact of specific treatment modalities on HRQOL and social re-entry , e.g. ENNR and encephalotropic drugs at present QOLIBRI seems to be the only reliable assessment tool. QOLIBRI showed an added –value over SF-36 by measuring the individual's subjective experience via a consensual & parallel cross-cultural approach. After the first year behavioural and psychiatric problems start dominating the individuals final outcome & social reentry. Main predictors for HRQOL after TBI are depression, help needed ,health complaints, anxiety, disability

Discussion: Impairment of higher cortical functioning refers to loss of structures, functions, and social contact. Rehabilitation after brain damage is targeted to reconstruct and to humanize the Most observers agree that mental cognitive, behavioural disabilities are both more persistent and constitute more of a handicap than focal neurological signs. In the acute stage after TBI neurolo-

gists and neurosurgeons have to direct their treatment programmes toward utilizing in an optimal manner those higher nervous functions which are uninvolved and/ or the substitution of others that are still preserved as to protect and to foster brain plasticity and recovery of CNS.

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