







# Seminars Traumatic Brain Injuries

Department of Neurosciences
University of Medicine
and Pharmacy "Iuliu Hatieganu"
Cluj-Napoca | Romania

FEBRUARY 28, 2012
"Multimedia" Auditorium / UMF "Iuliu Hatieganu"
CLUJ-NAPOCA | ROMANIA

FEBRUARY 29, 2012 "Marinescu" Auditorium / UMF "Iuliu Hatieganu" CLUJ-NAPOCA | ROMANIA

### Welcome Address

It is a pleasure to welcome you to the 1st Seminar of the Department of Neurosciences, "Traumatic Brain Injuries", February 28-29th, 2012. The seminar is hosted by the Department of Neurosciences, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca.

This seminar aims to establish itself as a highly useful framework that will enable local specialists to benefit from the expertise of our invited speakers who are part of associated international faculty of our Department of Neurosciences. Our scope is to flourish over years and set up an educational network tool aiming to meet our junior and senior specialists' needs.

In contrast to large international conferences, the intention behind these seminars is to create an informal and intimate setting, which hopefully will stimulate open discussions. As organizers, we would therefore be deeply grateful if you participate and share your time with us these days.

We are looking forward to your active participation in this educational event!

With consideration,

Prof. Dr. Dafin F. Mureşanu, Chairman Department of Neurosciences

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### Organizers



"Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Romania www.umfcluj.ro



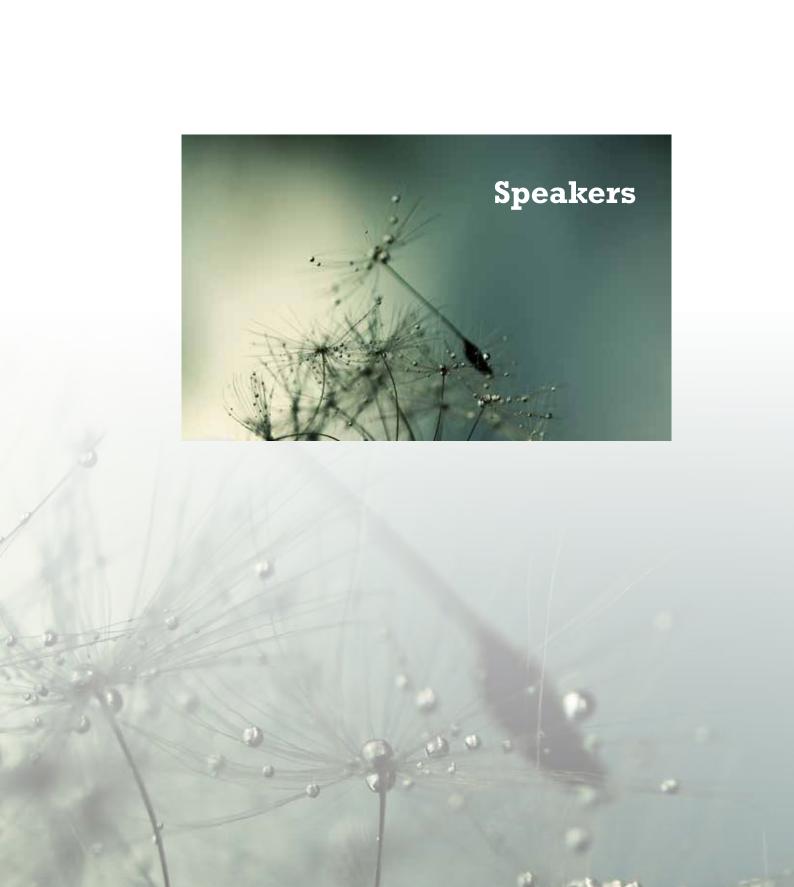
Faculty of Medicine Department of Neurosciences University of Medicine and Pharmacy Cluj-Napoca, Romania



The Society for the Study of Neuroprotection and Neuroplasticity www.ssnn.ro



International School of Neurology



### Speakers

Born, 1952, he specialized in Veterinary Medicine between 1971 and 1974 at the University in Munich, then changed to the University in Cologne in 1974 and specialized in Human Medicine from 1974 to 1980. In 1976 to 1979, he additionally studied biometric methods for pharmacology and clinical research at the Institute for Data Analysis and Study Planning in Munich.

While studying human medicine, he completed research work on pattern recognition in the visual brain and developed a pharmacodynamic Neuron Simulation Model at the Institute for Medical Documentation and Statistics of the University at Cologne.

From 1985 to 1995, he was member of the Ultrahigh Dexamethasone Head Injury Study Group and leading biometrician of the German GUDHIS Study.

Since 1982 he holds advanced training courses on biometry for professionals in clinical research and university establishments. His work also involves human engineering of biometric software and GCP-compliant tutorials for biometric appraisal of clinical studies.

Since 1995 he cooperates closely with the Institute for Data Analysis and Study Planning as Senior Consultant for Biometry & Clinical Research. He planned and evaluated about 150 randomized clinical studies worldwide and is member of various international advisory boards including participation as biometric expert in regulatory authority panels and in FDA, EMEA, and BfArM hearings.



JOHANNES C. VESTER /GERMANY

Pieter Vos is neurologist at the Institute of Neurology at Radboud University Nijmegen Medical Centre, The Netherlands. His research activities are connected with traumatic brain injury, traumatic spinal cord injury and other acute neurological disorders. Focus of the research activities consist of studies aiming to unravel the clinical, biochemical and genetic determinants of neuroplasticity and recovery after mild, moderate and severe traumatic brain injury. Pieter Vos is founder of the Dutch working group on Neurortraumatology. Current international activities are chairman of the scientist panel on neurotraumatology and head of the task force mild traumatic brain injury, both residing under the European Federation of Neurological Societies.



PIETER E. VOS /THE NETHERLANDS

### Speakers

Prof. Dr. Ioan Ștefan Florian is Head of the Department of Neurosurgery and President of the Senate of the University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Romania. He has a rich scientific activity, being the author and co-author of 13 books and manuscripts dealing with neurosurgery field (treatment options in pituitary adenomas, in intracerebral hemorrhage) as well as a high experience in the neurosurgical treatment of brain tumors, having over 4000 surgeries of adult and pediatric aged patients.

Research line in neurosurgery-oncology includes the evaluation of the therapeutical effect of Temozolomide and antiangiogenetic factors in glioblastoma multiforme, the evaluation of the therapeutical effect of the Calpaine inhibitors and angiogenetic factors in spinal cord injuries.

Rich organizing activity aiming the continuous medical education of neurosurgerons, from which the annual CME Course for resident doctors since 2003, two neuro-oncology conferences (National Conference of Neuro-oncology with International Participation in 2007, 2008), the annual German Romanian Neurosurgery Courses (2009, 2010, 2011 and the forthcoming course in May 2012), promoter and organizer of the 1st Regional Congress of the Danube-Carpathian Region in the period of 24th -27th May 2011, at Cluj-Napoca, Romania, and of the 2nd Regional Congress of the Danube-Carpathian Region in May 2012.



ȘTEFAN FLORIAN /ROMANIA

Mureşanu Fior Dafin, MD, PhD, MBA, is Professor of Neurology, Chairman of the Neurosciences Department, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, member of the Academy of Medical Sciences, Romania. He is also President of the Society for the Study of Neuroprotection and Neuroplasticity. In these roles, he acts as coordinator in international educational programs of European Master type (European Master in Stroke Medicine, University of Krems), organizer and co-organizer of European and international schools and courses (Eastern European Neurology Summer School for Young Neurologists - www.ssnn.ro, European Stroke Organisation Summer School, Danubian Neurological Society Teaching Course). His activity includes his involvement in many clinical studies and research projects, his membership in the executive board of many national and international societies, participations as invited speaker in national and international congresses, and a significant portfolio of scientific articles, contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Muresanu has been honoured with the Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy of Medical Sciences "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.



DAFIN F. MUREŞANU /ROMANIA





### Scientific Program

#### February 28<sup>th</sup>, 2012

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	"Multimedia" Auditorium / UMF "Iuliu Hatieganu" 8 Victor Babeş Street
09:00 - 09:45	How to Manage the Mild TBI Patient in the Acute and Chronic Phase / Pieter E. Vos (The Netherlands)
09:45 - 10:30	How to Read the CT and the Prognostic Importance of the TCDB Score in Traumatic Brain Injury / Pieter E. Vos (The Netherlands)
10:30 - 11:00	Coffee Break
11:00 - 11:45	Novel MRI Methods for Assessment of Traumatic Brain Injury / Pieter E. Vos (The Netherlands)
11:45 - 12:30	Spinal cord injuries: clinical assessment and new treatment options / Dafin F. Mureşanu (Romania)
12:30 - 14:30	Session Break
14:30 - 15:15	The Role of Surgery in Severe Traumatic Brain Injury / Ștefan Florian (Romania)
15:15 - 16:00	End-Of Life Decisions in Traumatic Brain Injury / Pieter E. Vos (The Netherlands)
19:00	Get Together Party   Department of Neurosciences / Opera Plaza

## Scientific Program

#### February 29<sup>th</sup>, 2012

"Marinescu" Auditorium / UMF "Iuliu Hatieganu"	,
23 Gh. Marinescu Street	

09:00 - 10:30	Hypothesis Testing and Statistical Significance:	
	The Basic Concept of a Statistical Test	
	/ Johannes C. Vester (Germany)	

10:30 - 11:00	Coffee Break
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11:00 - 12:30	P-Values, Effect Sizes and Confidence Intervals: Definition and
	Handling in Superiority and Non-Inferiority Trials
	/ Johannes C. Vester (Germany)

10:00 14:00	Caccian Drank
12:30 - 14:30	Session Break

14:30 - 16:00	Definition and Interpretation of Common Effect Sizes for Binary,
	Ordinal and Continuous Data: Rate Difference, Odds Ratio, Mean,
	Median, Mann-Whitney
	/ Johannes C. Vester (Germany)

16:00 - 16:30	Coffee Break
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16:30 - 18:00	Proper Interpretation of Study Results: Examples from Recent TBI Trials
	/ Johannes C. Vester (Germany)



The primary goal of the statistical lectures is to provide non-statisticians with an basic understanding of the interconnections and relationships which are important in practice and the ability to implement and apply this basic knowledge in the proper interpretation of study results.



JOHANNES C. VESTER /GERMANY

The lectures will adress the following issues:

1. Hypothesis testing and statistical significance: the basic concept of a statistical test. One-sided and two-sided tests. Definition and interpretation of P-values. Level of significance. Correct and false interpretation of significance through examples from the literature.

- 2. Effect sizes and confidence intervals: Basic principles and interpretation. Relationship with significance tests. Definition and handling in superiority and non-inferiority trials. Why confidence intervals rather than P-values?
- 3. Definition and interpretation of common effect sizes for binary, ordinal and continuous data: rate difference, rate ratio, odds ratio, mean, median, Mann-Whitney. Examples from clinical research.
- 4. Proper interpretation of study results: examples from recent TBI trials. Pros and cons of dichotomization. Univariate vs. multidimensional approach. Current recommendations. What can we learn from "failed" studies.



#### HOW TO MANAGE THE MILD TBI PATIENT IN THE ACUTE AND CHRONIC PHASE

Mild Traumatic brain injury(MTBI) is in the acute phase characterized by a low but significant risk (1%) for life threatening intracranial hematoma (epidural, subdural) and a low case fatality rate (0,1%). To accurately identify patients with an increased risk for intracranial hematoma, by means of CT, formal decision rules exist. We will overview the various decision rules and discuss aspects of acute management in MTBI.

Every MTBI patients suffers from post traumaticcomplaints, that subside in most patietns within 3 months. A minority of the MTBI patients suffers from chronic post traumatic complaints. We will discuss the potential causes of the post concussion syndromeafter MTBI and review patient management issues in the chronic phase.

Keywords :mild head injury; outcome; post concussion syndrome; CT;mild traumatic brain injury; prognostic factor; decision rule



PIETER E. VOS /THE NETHERLANDS

#### HOW TO READ THE CT AND THE PROGNOSTIC IMPORTANCE OF THE TCDB SCORE IN TRAUMATIC BRAIN INJURY

Traumatic brain injury(TBI) is characterized by high rates of case fatality (15-20% in moderate TBI and 40% in severe TBI) and disability in survivors (30-40% in moderate and 50-60% in severe TBI). Accurate determination of the initial severity of the primary brain damage is imperative in establishing a prognosis and to weigh risks and benefits of specific treatment options. In additiontoclinicalinjurycharacteristicslike the Glasgow Coma Scale score andpupillaryreactions, findings on brainComputedTomography(CT) are important indicators of injuryseverityandoutcome. Qualitativeandquantitave assessment of CT characteristics is thereforeessential in obtainingan accurate picture of TBI victims. In thislecture I willdiscuss CT andformal CT classification systems of TBI.

Keywords: severe head injury; outcome; Glasgow Outcome Scale; CT; severe traumatic brain injury; prognostic factor;

#### NOVEL MRI METHODS FOR ASSESSMENT OF TRAUMATIC BRAIN INJURY

A head CT scan is performedroutinely in the acute phase of moderate and severe TBI, and in a large proportion of mild TBI patients. CT enablesquickidentification of traumaticcranialandintracranialabnormalitiesrequiringimmediateneurosurgicalintervention or extensive monitoring. CT characteristics, like the basalcisterns, midline shift, presence of subarachnoidhemorrhage are associated without comeafter moderate to severe TBI, andmaybeusedtopredictoutcome. The site, numberand volume of lesions as seen on T1, T2-weighted, andFluidAttenuatedInversion Recovery (FLAIR) MR sequences have been related to outcome after moderate and severe TBI demonstrating a modest associationwithglobaloutcome but weakassociation with specific cognitive tests. CT and conventional MRI are insensitivetodetect diffuse axonalinjury. In contrast Susceptibility Weighted Imaging has a high sensitivityforhemosiderinand small punctatehemorrhagiclesionsas aresult of extravasation of bloodfromdamaged small bloodvesselsthataccompanytraumaticaxonaldamage.Toqualitativelyandquantitaivelyassesstraumaticwhite matter lesions in the brain, Diffusion Tensor Imagingdemonstratedgrossdifferencesbetween TBI patientsandcontrolsanda relationbetweenabnormal DTI signal in specificanatomicalbrainregionsandspecificcognitive tests.

Keywords: head injury; outcome; CT; MRI; traumatic brain injury; prognostic factor; susceptibility weighted imaging; diffusion weighted imaging.

#### END-OF LIFE DECISIONS IN TRAUMATIC BRAIN INJURY

Traumatic brain injury(TBI) may affect all ages but involves predominantly young persons. End-of-life decisions in moderate severe TBI do occur in the acute phasewhen-further treatment becomes futile. In a more chronic phases witching to palliative care in vegetative state or minimal conscious state patients are issues raising ethical questions. Decisions should only be taken when absolute certaintity has been achieved on the prognosis of individual patients. This topic will discuss the accuracy and limits of current existing models for determining outcome after TBI.

Keywords: severe head injury; outcome; Glasgow Outcome Scale; CT; severe traumatic brain injury; prognostic factor; palliative care; end-of-life decisions

#### THE ROLE OF SURGERY IN SEVERE TRAUMATIC BRAIN INJURY

Traumatic brain injury is a leading cause of mortality and morbidity worldwide.

In Romania this represents the fourth cause of mortality according to the statistics issued by the Ministry of Health.

Neurosurgery as a specialty is deeply involved in all types of traumatic brain injuries in the respect of conservative treatment and/or surgery as well. Regarding the surgery of these kind of lesions only form 2006, with the appearance and acceptance of the guidelines elaborated by Brain Trauma Foundation and published in Neurosurgery in March 2006 issues, a unitary vision was created regarding the case management from the point of view of the surgery and of the most recommended surgical approaches as well.

The lecture presents these aspects based on the recommendation of Brain Trauma Foundation together with my personal experience in the most frequently met lesions of TBI, namely epidural hematomas, acute subdural hematomas, traumatic parenchimal lesions and depressed scalp fractures.

Keywords: TBI, epidural hematomas, subdural hematomas, contusion, intracerebral hemorrhage, diffuse axonal brain injury,



ȘTEFAN FLORIAN /ROMANIA



#### SPINAL CORD INJURIES: CLINICAL ASSESSMENT AND NEW TREATMENT OPTIONS

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.



DAFIN F. MUREŞANU /ROMANIA



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