



**UMF**  
IULIU HATIEGANU  
UNIVERSITY OF  
MEDICINE AND PHARMACY  
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Danube-University  
Krems



THE SOCIETY FOR THE STUDY OF  
NEUROPROTECTION AND  
NEUROPLASTICITY



FACULTY of MEDICINE  
DEPARTMENT of  
NEUROSCIENCES



International  
School of Neurology

# Seminars

## Advances in Diagnosis and Treatment of Cerebrovascular Disorders

Department of Neurosciences  
University of Medicine and  
Pharmacy "Iuliu Hatieganu"  
Cluj-Napoca | Romania  
in cooperation with  
Department of Clinical Neurosciences  
Danube University Krems  
Austria

**FEBRUARY 13, 2014**  
**"Multimedia" Auditorium / UMF "Iuliu Hatieganu"**  
**CLUJ-NAPOCA | ROMANIA**

# Welcome Address

It is a pleasure to welcome you to the 7th edition Seminars of the Neurosciences Department, February 13<sup>th</sup>, 2014. The seminars are hosted by the Department of Neurosciences, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hațieganu" Cluj-Napoca in cooperation with Department of Clinical Neurosciences, Danube University Krems, Austria.

These seminars aim to establish a highly useful framework enabling local specialists to benefit from the expertise of our invited speakers who are part of associated international faculty of our Department of Neurosciences. Our goal is to flourish over years and set up an educational network tool meeting our junior and senior specialists' needs.

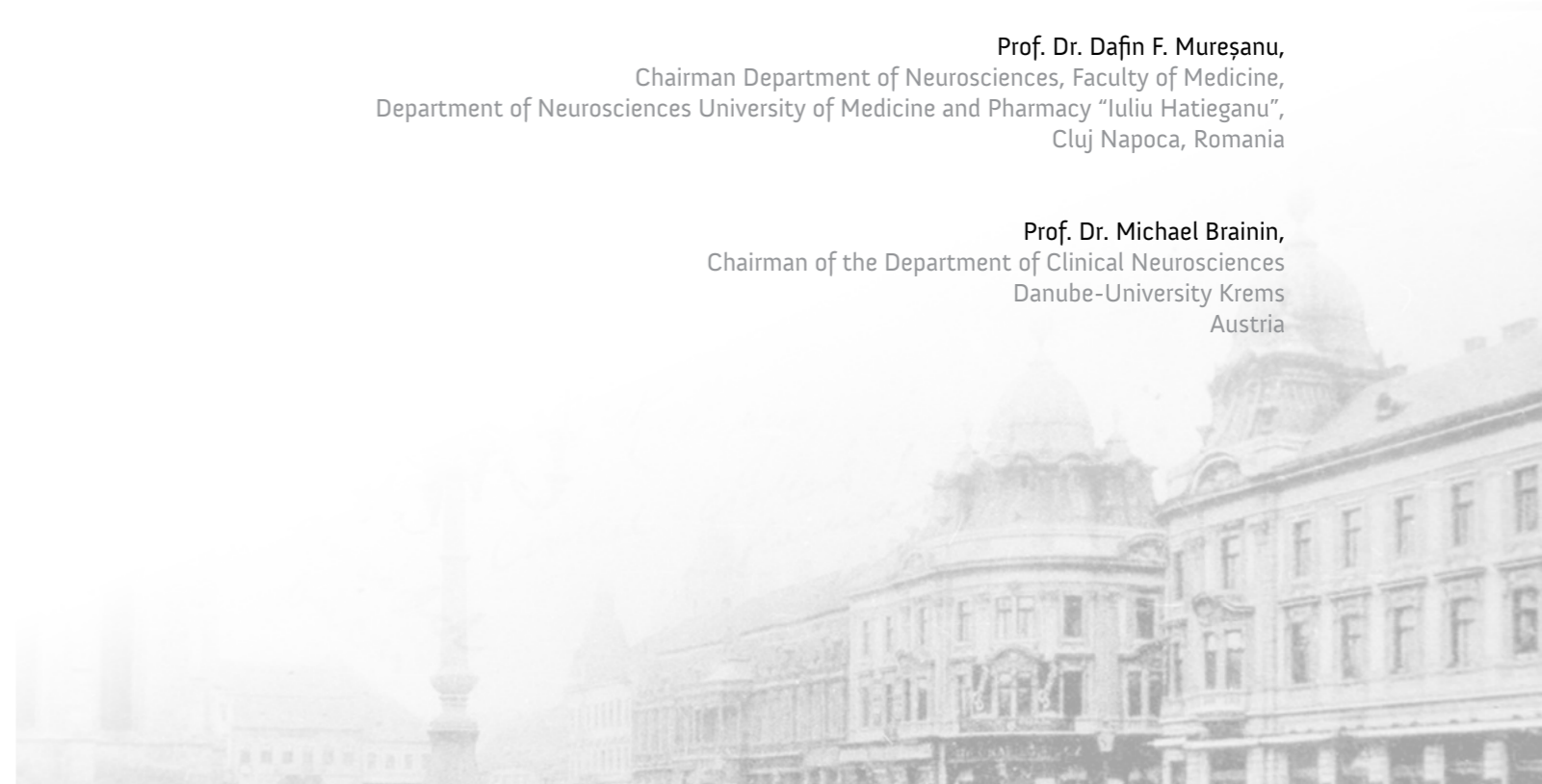
In contrast to large international conferences, the intention behind these seminars is to create an informal and intimate setting, which hopefully will stimulate open discussions. As organizers, we would therefore be deeply grateful if you participate and share your time with us.

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

With consideration,

**Prof. Dr. DaŃin F. Mureșanu,**  
Chairman Department of Neurosciences, Faculty of Medicine,  
Department of Neurosciences University of Medicine and Pharmacy "Iuliu Hațieganu",  
Cluj Napoca, Romania

**Prof. Dr. Michael Brainin,**  
Chairman of the Department of Clinical Neurosciences  
Danube-University Krems  
Austria



# Organizers



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Cluj-Napoca, Romania



**International  
School of Neurology**

International School of Neurology



# Speakers

Michael Brainin is Professor of Clinical Neurology, chairman of the Department of Clinical Neurosciences at the Danube-University Krems, and head of the Department of Neurology at the University Teaching Hospital Landeskrankenhaus Tulln in Austria.

He currently is President of the European Stroke Organisation and Executive Board Member (Treasurer) of the World Stroke Organisation. He chairs the Scientific Committee of the European Federation of Neurological Societies and is member of the programme committee for the first congresses of the European Academy of Neurology to be held in 2014 and 2015.

He is chairman of the WSO Education Committee for which he has co-directed teaching programmes in many world regions, such as in China, Vietnam and South Africa. He chairs the World Stroke Academy, an innovative and global web-based teaching website of the WSO. He directs several postgraduate teaching programmes at his university among them an MSc Programme for Neurorehabilitation and the WSO supported ESO European Master's Programme for Stroke Medicine (co-chair Prof. WD Heiss) which currently has attracted students from 17 countries.

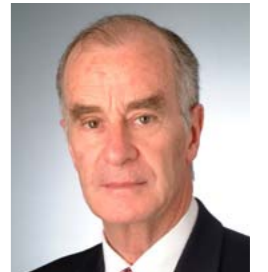
He is actively conducting several clinical trials including on stroke recovery and has published more than 150 peer-reviewed articles. He is Associate Editor of the European Journal of Neurology and has editorial functions for 'Stroke' (Field Editor: Brain recovery and Neurorehabilitation, and the 'International Journal of Stroke' (Field Editor: Education). He is active on the editorial boards of 'Neuroepidemiology', 'European Medical Journal' and 'Cerebrovascular Diseases'. He is Co-editor of 'Stroke News'. He is regular reviewer for funding agencies including the Canadian Stroke Network, the European Science Foundation, and the European Commission Public Health section. He was elected Fellow of the European Stroke Organisation and International Fellow of the American Heart Association. He is honorary member of several scientific societies, among them the French Neurological Society, the Hungarian Stroke Society and the Indian Stroke Society. He was awarded a honorary doctor's degree in Hanoi university in Vietnam and a honorary professorship at Zhengzhou University in China.

He has been invited to more than 900 clinical lectures mostly to international conferences, where in many instances also acted as chairperson and/or programme or editorial committee member.



**MICHAEL  
BRAININ**  
/AUSTRIA

Wolf-Dieter Heiss, born 31.12.1939 in Zell am See, Austria, graduated in medicine from the University of Vienna, Austria, in 1965. He achieved his training in neurology, neurophysiology, psychiatry and nuclear medicine at the University hospital in Vienna and spent research fellowships at the MIT, Cambridge, USA, the Physiological Institute in Stockholm, Sweden, the Department of Physiology of SUNY, Buffalo, NY and the Department of Neurology of the University of Minnesota, Minneapolis, USA. 1976 he was appointed associate professor at the Department of Neurology of the University of Vienna. In 1978 he became director of the Center for Cerebrovascular Research of the Max Planck Institute for Brain Research and of the Department of Neurology of the City Hospital Cologne-Merheim, Germany. 1981 he was appointed as director at the Max Planck Institute for Neurological Research. 1985 – 2005 he was professor of neurology and chairman of the Department of Neurology of the University of Cologne and director of the Department of General Neurology at the MPI in Cologne. He was president of the International Stroke Society 1992-96, was on the board of directors of the Society for Cerebral Blood Flow and Metabolism, deputy editor of the Journal of Cerebral Blood Flow and Metabolism and at present is associate editor of the Journal of Nuclear Medicine and section editor of Stroke. He was chairman of the program committee of the European Federation of Neurological Societies (EFNS) 1998 - 2001 and was president of the EFNS 2001 – 2005. Since 2005 he is Visiting Professor at the Danube University in Krems, Austria, and since 2009 Adjunct Professor at the McGill University in Montreal, Canada.



**WOLF-DIETER  
HEISS**  
/GERMANY

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.ssn.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.



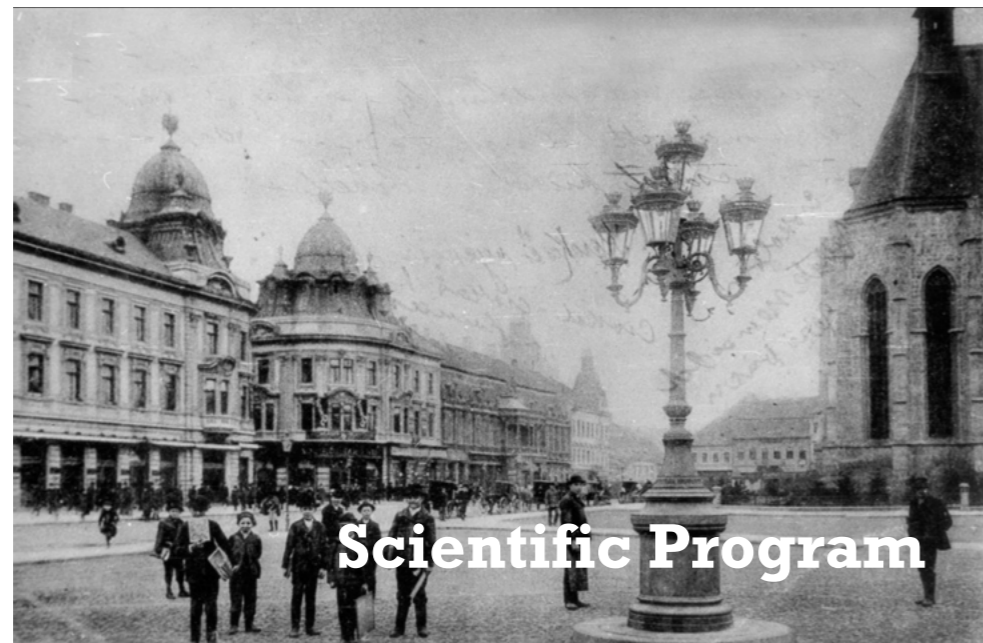
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MUREŞANU**  
/ROMANIA

# Scientific Program

February 13<sup>th</sup>, 2014

“Multimedia” Auditorium / UMF “Iuliu Hațieganu”  
8 Victor Babeș Street

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09:00 - 10:00	Imaging the Penumbra: The Pathophysiologic Basis for Therapy of Ischemic Stroke (Part I) / Wolf-Dieter Heiss (Germany)
10:00 - 11:00	Imaging the Penumbra: The Pathophysiologic Basis for Therapy of Ischemic Stroke (Part II) / Wolf-Dieter Heiss (Germany)
11:00 - 11:30	Coffee Break
11:30 - 12:30	Evidence-Based Principles of Acute Stroke Treatment (Part I) / Michael Brainin (Austria)
12:30 - 13:30	Evidence-Based Principles of Acute Stroke Treatment (Part II) / Michael Brainin (Austria)
13:30 - 14:30	Lunch
14:30 - 15:30	Towards a Roadmap in Brain Protection and Recovery – How to Bridge Acute to Long Term Neurorehabilitation/Neurorecovery Treatment (Part I) / Dařin F. Mureșanu (Romania)
15:30 - 16:30	Towards a Roadmap in Brain Protection and Recovery – How to Bridge Acute to Long Term Neurorehabilitation/Neurorecovery Treatment (Part II) / Dařin F. Mureșanu (Romania)
20.30	Dinner

# Abstracts



## EVIDENCE-BASED PRINCIPLES OF ACUTE STROKE TREATMENT

The basis of acute stroke care is rapid recognition of symptoms, notification of medical systems for rapid transport, the admission to a stroke unit and availability of thrombolysis and performance of protective measures and monitoring by trained specialized personnel.

Measures to improve prehospital management and to shorten the door-to-needle time should also be monitored. Reduction of 10 minutes already show significant changes in outcome.

Recent data show that thrombolysis can be safely extended to elderly patients and that intravascular approaches including thrombectomy can be performed in selected cases. Investigating the likely cause of the stroke enables to focus on early prevention, the use of transesophageal echocardiography, Holter monitoring and neurosonological methods prove to be of importance.

Monitoring includes observation of cardiac and pulmonary functioning and to prevent aspiration. Specialized care also includes measures to prevent and treat urinary tract infection, fever, pain, deep vein thrombosis, cardiac failure, GI bleeds, and incontinence. Early use of anti-thrombotics or anti-coagulants should be considered according to indications, as well as carotid thrombectomy or stenting.

Early mobilization is an effective measure contributing to improved outcome as is the use of SSRI antidepressants to improve motor rehabilitation. Also new techniques can be used in rehabilitation and these include robotics, computer games and virtual reality as well as mirror-therapy and enhanced use of stimulation techniques such as rTMS. Late effects also have to be monitored and these include depression, cognitive decline, risk of falls, pain and spasticity.



MICHAEL  
BRAININ  
/AUSTRIA

# Abstracts

# Abstracts

## IMAGING THE PENUMBRA: THE PATHOPHYSIOLOGIC BASIS FOR THERAPY OF ISCHEMIC STROKE

The concept of the ischemic penumbra was formulated 30 years ago based on experiments in animal models showing functional impairment and electrophysiological disturbances with decreasing flow to the brain below defined values (the threshold for function) and irreversible tissue damage with blood supply further decreased (the threshold for infarction). The perfusion range between these thresholds was termed "penumbra", and restitution of flow above the functional threshold was able to reverse the deficits without permanent damage. However, in further experiments the dependency of the development of irreversible lesions on the interaction of severity and duration of critically reduced blood flow was established, proving that the lower the flow the shorter the time for efficient reperfusion. Therefore, infarction develops from the core of ischemia to the areas of less severe hypoperfusion. The propagation of irreversible tissue damage is characterised by a complex cascade of interconnected electrophysiological, molecular, metabolic and perfusional disturbances. Waves of depolarisations, the peri-infarct spreading depression like depolarisations, inducing activation of ion pumps and liberation of excitatory transmitters have dramatic consequences as drastically increased metabolic demand cannot be satisfied in regions with critically reduced blood supply.

The translation of experimental concept as the basis for efficient treatment of stroke requires non-invasive methods by which regional flow and energy metabolism can be repeatedly investigated to demonstrate penumbra tissue which can benefit from therapeutic interventions. Positron emission tomography (PET) allows the quantification of regional cerebral blood flow, the regional metabolic rate for oxygen and the regional oxygen extraction fraction. By these variables a clear definition of irreversible tissue damage and of critically perfused but potentially salvageable tissue (i.e. the penumbra) can be achieved in animal models and stroke patients. Additionally, further tracers can be used for early detection of irreversible tissue damage, e.g. by the central benzodiazepine receptor ligand flumazenil. However, PET is a research tool and its complex logistics limit clinical routine applications. As a widely applicable clinical tool perfusion/diffusion weighted magnetic resonance imaging (PW/DW-MRI) is used, and the "mismatch" between the PW- and the DW-abnormalities served as an indicator



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of the penumbra. However, comparative studies of PW/DW-MRI and PET pointed to an overestimation of the core of irreversible infarction as well as of the penumbra by MRI modalities. Some of these discrepancies can be explained by unselective application of relative perfusion thresholds, which might be improved by more complex analytical procedures.

In several studies it was demonstrated that a large portion of the final infarct is irreversibly affected in the first few hours in many patients. A considerable tissue volume is viable but critically hypoperfused; a smaller portion of the final infarct is sufficiently perfused and in this area secondary and delayed biochemical and molecular mechanisms contribute to the damage. Based on this concept the improvement of perfusion within the time window of opportunity must be the primary goal in treatment of ischemic stroke, and neuroprotective and other strategies can only play a supportive and additive role. That this is the case can be seen from the results of many controlled therapeutic trials, in which up to now only thrombolytic therapy with a 4.5 h time window for systemic and a 6 h time window for intraarterial application proved its efficacy, whereas all trials with neuroprotective, anti-inflammatory or anti-apoptotic strategies failed. A drug with multimodal action might be more successful in stroke treatment in addition to reperfusion or after the time window for recanalization procedures has elapsed. A drug like Cerebrolysin which was effective in reducing mortality and improving outcome in severely affected cases in a large controlled trial therefore might have a place in comprehensive treatment strategies of ischemic stroke, which combine acute efforts to reduce infarct size with restorative activities to promote repair and improve final functional outcome. Since the direct treatment strategies are limited the acute management of stroke victims is of utmost importance. It is still to be investigated if the combination of reperfusion and neuroprotective therapy can improve the outcome after ischemic stroke.

# Abstracts

## TOWARDS A ROADMAP IN BRAIN PROTECTION AND RECOVERY – HOW TO BRIDGE ACUTE TO LONG TERM NEUROREHABILITATION/NEURORECOVERY TREATMENT

This presentation briefly reviews some of the mechanisms involved in the pathogenesis of neurological diseases, i.e. damage mechanisms, and their interactions and overlap with protection and reparatory processes (i.e., endogenous defense activities). A relationship between damage mechanism (DM) and endogenous defense activity (EDA) regarding therapy principles will also be described.

Currently, it is difficult to find the correct therapeutic approach for brain protection and recovery, especially because we do not fully understand all of the endogenous neurobiological processes, the complete nature of the pathophysiological mechanisms and the links between these two categories. Moreover, we continue to use a simplistic and reductionist approach in this respect.

Endogenous neurobiological processes, such as neurotrophicity, neuroprotection, neuroplasticity and neurogenesis, are central to protection and recovery and represent the background of EDA.

The biological reality of the nervous system is far more complex. In fact, there is an endogenous holistic process of neuroprotection and neurorecovery that should be approached therapeutically in an integrated way.

The current tendency to exclusively frame drug activity in terms of single mechanisms and single focus effect might distract from other paradigms with greater explanatory power and hinder the development of more effective treatment strategies. A change of concept is required in pharmacological brain protection and recovery. This presentation will also highlight some prospective considerations including an integrated pharmacological approach, focusing on drugs with multimodal activity and pleiotropic neuroprotective effect which are biological drugs, rather than single mechanism drugs, which usually are chemical drugs.

The development of the concept of brain protection and recovery in stroke will be also highlighted. Relevant clinical trials in the field will be commented as well.



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