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"IULIU HATIEGANU" UNIVERSITY
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DOCTORAL SCHOOL NEUROSCIENCE

PROGRAM

2020-2021 | SECTION 2

9 MARCH, 2021
VIRTUAL MEETING

PhD NEUROSCIENCE PROGRAM COORDINATOR

Dafin F. Mureşanu

President of the European Federation of NeuroRehabilitation Societies (EFNR)

Chairman of EAN Communication and Liaison Committee

Co-Chair EAN Scientific Panel Neurotraumatology

Past President of the Romanian Society of Neurology

Professor of Neurology, Chairman Department of Neurosciences "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

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2020-2021

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COURSE PROGRAM

COURSE PROGRAM

9 MARCH, 2021

VIRTUAL MEETING

12:00 – 12:10	Welcome Address
12:10 – 12:40	New vistas in stroke Dafin F. Mureșanu/ Romania
12:40 – 13:25	Efficacy of stroke units Michael Brainin /Austria
13:25 – 14:10	Functional anatomy of the brain Michael Brainin /Austria
14:10 - 14:55	Post-stroke cognitive decline: intervention trials for prevention and treatment Michael Brainin /Austria
14:55 - 15:00	Concluding remarks

INTERNATIONAL GUEST LECTURER

DAFIN F. MUREȘANU
ROMANIA

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, President of the European Federation of Neurorehabilitation Societies (EFNR), Chairman Communication Committee of the European Academy of Neurology (EAN), Past President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), Chairman "RoNeuro" Institute for Neurological Research and Diagnostic, Corresponding Member of the Romanian Academy, Member of the Academy of Medical Sciences, Romania and secretary of its Cluj Branch. He is member of 17 scientific international societies (being Member of the American Neurological Association (ANA) - Fellow of ANA (FANA) since 2012) and 10 national ones, being part of the executive board of most of these societies. Professor Dafin F. Muresanu is also a specialist in Leadership and Management of Research and Health Care Systems (specialization in "Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998"; "MBA – Master of Business Administration - Health Care Systems Management, The Danube University - Krems, Austria, 2003"). He has performed valuable scientific research in high interest fields such as: neurobiology of central nervous system (CNS) lesion mechanisms; neurobiology of neuroprotection and neuroregeneration of CNS; the role of the Blood-brain barrier (BBB) in CNS diseases; developing comorbidities in animal models to be used in testing therapeutic paradigms; nanoparticles neurotoxicity upon CNS; the role of nanoparticles in enhancing the transportation of pharmacological therapeutic agents through the BBB; cerebral vascular diseases; neurodegenerative pathology; traumatic brain injury; neurorehabilitation of the central and peripheral nervous system; clarifying and thoroughgoing study on the classic concepts of Neurotrophicity, Neuroprotection, Neuroplasticity and Neurogenesis by bringing up the Endogenous Defense Activity (EDA) concept, as a continuous nonlinear process, that integrates the four aforementioned concepts, in a biological inseparable manner.

Professor Dafin F. Muresanu is coordinator in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of many educational projects: European and international schools and courses (International School of Neurology, European Stroke Organisation Summer School, Danubian Neurological Society Teaching Courses, Seminars - Department of Neurosciences, European Teaching Courses on Neurorehabilitation) and scientific events: congresses, conferences, symposia (International Congresses of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), International Association of Neurorestoratology (IANR) & Global College for Neuroprotection and Neuroregeneration (GCNN) Conferences, Vascular Dementia Congresses (VaD), World Congresses on Controversies in Neurology (CONy), Danube Society Neurology Congresses, World Academy for Multidisciplinary Neurotraumatolgy (AMN) Congresses, Congresses of European Society for Clinical Neuropharmacology, European Congresses of Neurorehabilitation). His activity includes involvement in many national and international clinical studies and research projects, over 500 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (231 papers indexed on Web of Science-ISI, H-index: 23) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dafin F. Muresanu has been honoured with: „Dimitrie Cantemir" Medal of the Academy of The Republic of Moldova in 2018, Ana Aslan Award 2018 - "Performance in the study of active aging and neuroscience", for the contribution to the development of Romanian medicine, National Order "Faithful Service" awarded by the President of Romania in 2017; "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, Faculty of Medicine, the "Iuliu Hatieganu Great Award 2016" for the best educational project in the last five years; the Academy of Romanian Scientists, "Carol Davila Award for Medical Sciences / 2011", for the contribution to the Neurosurgery book "Tratat de Neurochirurgie" (vol.2), Editura Medicala, Bucuresti, 2011; the Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.

MICHAEL BRAININ
AUSTRIA

Professor and Chair, Department of Clinical Neurosciences and Preventive Medicine Danube University Krems, Austria.

He was co-founder of the national stroke unit network and founding president of the Austrian Stroke Society 2003-2006.

He was President of the European Stroke Organisation (2012-2014).
Currently he is the President of the World Stroke Organisation (2018-2020).
He is co-chair of the ESO-WSO 2020 Congress to be held in Vienna, Austria.

Dr. Brainin has led the WSO Education Committee 2008-2017 and was editor of the World Stroke Acedemy, a web-based learning platform for the WSO. He chairs the European Master's Program in Stroke Medicine since 2007. He has published more than 200 peer-reviewed papers, edited three textbooks on stroke, and has given more than 1.000 invited lectures. His scopus h-index is 46 and scopus citations are >15.000.

He is Senior Editorial Consultant for ‚Stroke', Associate Editor of the European Journal of Neurology and member of the editorial boards of Neuroepidemiology, International Journal of Stroke, The European Stroke Journal and The Journal of Neurological Sciences. He received several awards, honorary doctorates and honorary memberships from scientific societies.

ABSTRACTS

NEW VISTAS IN STROKE

DAFIN F. MUREȘANU
Chairman Department of Neurosciences University of Medicine and Pharmacy 'Iuliu Hatieganu', Cluj-Napoca, Romania

EFFICACY OF STROKE UNITS

MICHAEL BRAININ
Clinical Neurology Danube University Krems, Austria

Organised stroke unit care is a form of care provided in hospital by nurses, doctors and therapists who specialise in looking after stroke patients and work as a co-ordinated team. An updated systematic review has confirmed significant reductions in death (3% absolute reduction), dependency (5% increase in independent survivors) and the need for institutional care (2% reduction) for patients treated in a stroke unit, compared with those treated in general wards. All types of patients, irrespective of gender, age, stroke subtype and stroke severity, appear to benefit from treatment in stroke units. These results have been confirmed in large observational studies of routine practice. Stroke units may also improve patients' quality of life, and improvements in outcome may persist for several years. Of available therapies in the acute phase of stroke (antiplatelet therapy, intravenous thrombolysis, stroke unit care), stroke unit care has the overall largest benefit because this principle of care may potentially be applied to all patients with acute stroke.

The core components of stroke unit care include

- Rapid medical assessment and diagnosis, and early assessment of nursing and therapy needs
- early management, consisting of early mobilization, prevention of complications, and treatment of hypoxia, hyperglycaemia, pyrexia and dehydration
- ongoing rehabilitation, involving coordinated multidisciplinary team care, and early assessment of needs after discharge.

Making an early diagnosis of stroke is crucial because a time-dependent deterioration occurs that is caused by oxygen depletion in the neural tissue that shows ongoing compromise of blood-flow. Without intervention this compromised area of the brain will develop into an infarct and cannot be rescued. This critical time, which enables us to perform recanalisation and reperfusion therapy is called therapeutic time window. If one quantifies the time factor of ischemia it has been estimated that up to two million neurons will be lost per minute which amounts to more than 30.000 neurons per second. Thus, it is important to recognize stroke as an emergency. Persons with stroke should be hospitalized and treated as soon as possible. In many countries there is a recommended chain of recovery which includes firstly the recognition of stroke, then the reaction towards stroke, then the response, the reveal and the treatment.

In some regions of the world these transport systems are well developed and the ambulance personnel regularly receives special training. Once the patient arrives in the emergency department it should be clear that an urgent triage and a priority code should be assigned to a stroke patient. Priority includes the setting up of an IV line, measuring blood glucose, performing routine biochemistry including blood count and performing standard ECG. Trained medical personal should perform an accurate clinical diagnosis and exclude mimics. Under ideal circumstances, the stroke team should be notified before the arrival of the patient and urgent clarification of the diagnosis preferably by usage of brain imaging as soon as possible should be thought for.

Thrombolytic therapy should be used by personnel trained in its use in a centre equipped to investigate and monitor patients appropriately. Currently thrombolysis is only approved for treatment within 4.5 hours of symptom onset. Thrombolysis requires admission of stroke to hospital and it cannot easily be given in small local hospitals. More recently, endovascular thrombectomy has become standard treatment for large thromboses in the M1 or 2 segment of the ACM which usually causes severe strokes with NIHSS values of 15 or more. This therapy can only be applied within 6 hours of onset and must be performed in specialized comprehensive stroke centers.

In the acute phase, aspirin is associated with a very significant reduction in acute ischemic strokes, as well as deaths (of any cause) and the combined end-point of death and further strokes. There is no significant access of intracerebral hemorrhages. Subgroup analyses showed that aspirin was beneficial in all types of ischemic strokes irrespective of age and gender. For every 1000 patients treated aspirin treatment avoids 9 deaths or stroke in the acute phase, 12 death and dependency, and an extra 10 patients make a complete recovery. Consequently, prompt treatment with aspirin should be considered for almost all patients presenting with suspected acute ischemic stroke.

Strategies to prevent further strokes should be initiated already when the patient is under early treatment for a first stroke. All patients with stroke (ischemic, hemorrhagic, and stroke of unknown cause) will benefit from modification of life style changes, in particular cessation of smoking, and blood pressure reduction with a diuretic and an ACE-inhibitor. Blood pressure reduction should not be started until after the acute phase.

Patients with ischemic stroke benefit from long-term use of antiplatelet therapy as well as from a statin if total cholesterol is >3.5 mmol/liter.

The structure and process quality of stroke units include that there is a seamless and constant observation of vital parameters including blood pressure, heart rate, temperature, breathing and other parameters. This adds to the direct observation of the patient by trained personnel to notice early changes in the state of consciousness, to recognize epileptic fits and extracerebral causes of clinical deterioration.

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FUNCTIONAL ANATOMY OF THE BRAIN

MICHAEL BRAININ
Clinical Neurology Danube University Krems, Austria

Localization of function within the brain was the starting point for clinical neurology. Only with Brodman the cartography of the cerebral cortex based on clinical observation and experiments had a lasting effect and was accepted as the basis of localization of function of the cortex. Controversies among great minds of neurology took place and had to wait for pathological confirmation which often took years. The dichotomy of localization and function was united in a model by Luria who laid the foundations of modern neuroplasticity. Neuroimaging enabled neurologists and neurosurgeons to localize function much more easily and speculations about functional models could be put to a test. Tailarach and his school in Marseille founded stereotactic localisation and laid this down in his famous atlas which allowed the exact location pinpointed in the depth of the hemispheres and enabled comparability among humans. Later on, based on modern imaging, brain atlases were developed to guide the clinician and researcher on the transversal, coronary, or sagittal cuts of CT and MRI images. Among the most notable ones was the CT/MRI Atlas of Hanna and Antonio Damasio developed as a guide for vessel anatomy and cortical Brodman areas, This is especially helpful for analysis of small groups of patients who have similar lesions or similar clinical deficits and can used in a semiquantitative way. Finally, Marsel Mesulam from Boston proposed a functional model of the human cortex which allows interpretation of function in health and disease alike. This combined usefulness allows the interpretation of cortical syndromes as disconnection disturbances and explains most neuropsychological syndromes on the basis of disconnected localisation of function, either intra- or interhemispheric. New methods of imaging such as fibre tract imaging or functional MRI confirm these models and visualize such disconnections. Several examples will be given, including the neuroanatomical basis of problem solving, the working mind of a calculating prodigy, or the neural basis of frontal lobe dysfunctions.

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POST-STROKE COGNITIVE DECLINE: INTERVENTION TRIALS FOR PREVENTION AND TREATMENT

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Previous randomized trials aiming at promoting recovery after stroke such as with levodopa, natural biologicals (Cerebrolysin) or SSRI's have been successful in showing improvement of motor recovery. But currently no established treatment exists for the preservation or restoration of cognitive status following stroke. Given the high frequency of delayed onset of cognitive deterioration following stroke it is surprising that large studies have yet to be performed. Single or combined drug interventions tested up to now were based on secondary outcome analyses and included antihypertensive drugs which showed only a modest effect on cognition in general and no consistent effect was shown for lipid lowering drugs. Combination of antiplatelet drugs have been tested in the SPS3 trial but showed no effect on cognitive outcomes. Life-style interventions include studies of a Mediterranean diet with extra virgin olive oil and nuts but while stroke occurrence can be reduced, no data on post-stroke cognition exist. The same applies for physical exercise programs which show good effects on physical fitness.

Ongoing registered stroke testing either drug and/or lifestyle interventions all are planned either for small sample sizes and /or a complex endpoint or combination of endpoints that are not likely to produce practice-changing results.
Multi-domain intervention studies are much more likely to be effective on cognition because they perform multiple risk factor management with lifestyle adaptation including diet changes with increase of drug compliance and adherence. Intensifying these interventions and to monitor them is crucial. The first comprehensive multi-domain intervention trial (ASPIS) has recently been terminated. The primary endpoint was a significant change of the z-score of 5 neuropsychologically assessed cognitive domains. While the overall result was neutral, a signal for change of dysexecutive function was seen and follow-up studies might have to consider this finding.

In the future, there is a need for including cognitive outcome measurements in all trials targeting the brain, to consider larger sample sizes, to harmonize assessment strategies, to focus on a high risk population, and to include biomarkers and imaging data for confirmatory analyses. Overall, it is crucial to aim for intervention intensities that create significant group differences.

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