FOUNDATION OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

International School of Neurology

UMF IULIU HAȚIEGANU UNIVERSITY OF MEDICINE AND PHARMACY CLUJ-NAPOCA

RoNEURO Institute for Neurological Research and Diagnostic

FUNDATIA JURNALULUI Journal of Medicine and Life

Seminars

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

7 JULY, 2021

VIRTUAL MEETING

Welcome Address

It is a pleasure to welcome you to the 77th edition Seminars - 7 July, 2021. The seminar is hosted by the Department of Neurosciences, Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy, 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 Cluj-Napoca, Romania and RoNeuro Science network. Our scope is to flourish over years and set up an educational vector aiming to meet our junior and senior specialists' needs.

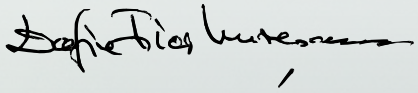
In contrast to large international conferences, the intention behind these seminars is to create an informal and intimate setting, which hopefully will stimulate open discussions.

Due to the uncertainties about the continuing impact of the COVID-19 pandemic, our events will be held in the virtual space, for the time being. 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. Dafin F. Muresanu,
Chairman Department of Neurosciences, Faculty of Medicine,
"Iuliu Hatieganu" University of Medicine and Pharmacy,
Cluj-Napoca, Romania



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

Organizers

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Academia de Științe Medicale din România

ACADEMIA ROMANA

UNIVERSITAS MEDICINAE ET PHARMACIAE "CAROLUS DAVILA" BUCURESTIS
DOCENDO DISCITUR
A.D. 1857


SPEAKERS

SPEAKERS

Dafin F. Muresanu
/Romania

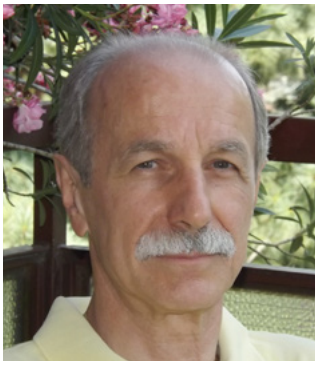
Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca, President of the European Federation of Neurorehabilitation Societies (EFNR), Chairman Communication Committee of the European 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 (239 papers indexed on Web of Science-ISI, H-index: 24) 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

SPEAKERS

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.

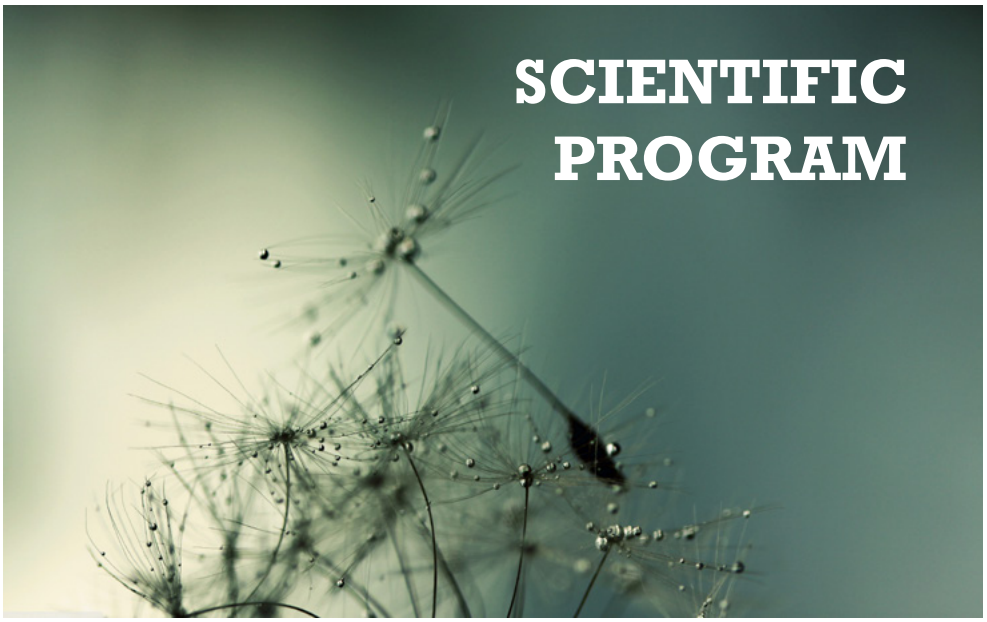
SPEAKERS



Ettore Beghi
/Italy

Head of the Laboratory of Neurological Disorders (since 1996) at the "Mario Negri" Institute, Milano. Former Research Fellow at the Department of Medical Statistics and Epidemiology, Mayo Clinic, Rochester, MN (1982-83). Associate Editor of EPILEPSIA OPEN. Member of the Editorial Board of 5 journals (Neuroepidemiology, Epilepsia, Clinical Neurology & Neurosurgery, Clinical Drug Investigation, ALS & Frontotemporal Dementia) and referee of more than 20 journals. Past or current member (or chair) of the following scientific societies/groups: Mayo Alumni Association, Italian Neurological Society, Italian League against Epilepsy, Italian Neuroepidemiology Section of the INS, Neuroepidemiology Section, AAN, Commission "Epilepsy, Risks, and Insurance" of the IBE, Commission "Antiepileptic Drugs" of the ILAE, Cochrane Epilepsy Group, Commission on the Burden of Epilepsy of the ILAE, International Subcommittee of the AAN, Course Director at the American Academy of Neurology, European ALS registry, Italian Epilepsy Study Group, Epilepsy and Quality of Life Study group, Italian Drug Agency (AIFA)(consultant), European Medicines Agency (consultant), Fellow of the AAN (FAAN), President of the Italian League against Epilepsy (LICE), Co-Chair ILAE Commission on the Epidemiology of Epilepsy, Member of the ILAE Task Forces on .Epilepsy and Driving and Epilepsy in the Elderly.

Author of more than 400 indexed scientific publications in the field of epilepsy (epidemiology, prognosis, treatment), peripheral neuropathy (epidemiology, prognosis, treatment), amyotrophic lateral sclerosis (ALS) (epidemiology, prognosis, treatment), myasthenia gravis (MG) (epidemiology, prognosis), Parkinson's disease (epidemiology), headache (epidemiology), and stroke (epidemiology).


SCIENTIFIC
PROGRAM

Scientific program

7 JULY, 2021

VIRTUAL MEETING

12:00 – 12:30	Controlled clinical trials: methodology, types, phases Ettore Beghi / Italy


ABSTRACTS

Abstracts

CONTROLLED CLINICAL TRIALS: METHODOLOGY, TYPES, PHASES

ETTORE BEGHI
/ITALY

The randomized clinical trial (RCT) represents the best model to assess the efficacy, tolerability and safety of any treatment for all clinical conditions, including neurological disorders. The structure of the trial reflects the need to disentangle the effects of an experimental treatment (to be compared to one or more control treatments) from variables with prognostic significance, which may act as confounders and to control the expectations of the patients and the caring physicians. To perform this task, a number of restrictions are in place to make the experimental and the control group highly comparable and to show statistically significant differences between the experimental groups and the controls in a relatively limited timeframe. These strengths are, at the same time, limitations of the RCT and affect the external validity, ie the applicability of the results in clinical practice.

The major steps in the planning and conduction of an RCT include the definition of the study population, the random assignment of treatments, the choice of the measures of treatment effects, the duration of the experiment, the assessment of the tolerability and safety of the treatment, and the choice of alternative design models. In doing this, a constant reference will be made to the peculiarities (and diversities) of neurological disorders. Other aspects of the RCT protocol (that will not be addressed here) include administration, funding, quality control, and the infrastructure. These sources can be addressed by those interested in regulatory matters.

The major steps in planning and conducting an RCT include study population, diagnosis, randomization process, blinding procedures, end-points, clinical & statistical issues, duration of the experiment, adverse treatment effects and internal & esternal validity. The study population must be homogeneous in terms of disease characteristics and outcome in order to disentangle the effects of treatment from the «natural history» of the disease. In most [neurological] diseases the diagnosis is strongly dependent on clinical judgment. The inclusion of patients with erroneous diagnosis tends to dilute treatment effects. Bias may be greater in multicenter trials. Clinical assessment and diagnostic tests may have poor validity and reliability.

The randomization is the procedure aimed at removing systematic errors, producing balanced comparisons and quantifying errors attributable to chance. It exerts an active control on the procedures adopted by the investigator to assign a treatment. An «impartial» assignment does not always correspond to a «balanced» assignment of treatments (unequal distribution of prognostic factors in the treatment arms). Placebo is justified by the observation that even ineffective treatments may be

Abstracts

followed by improvements due to chance fluctuations (regression to the mean) or the expectancy of a therapeutic benefit. Placebo is most appropriate in studies in self-limiting diseases, mild clinical condition, diseases deprived of effective treatments. Placebo is not indicated at the presence of effective treatments for ethical reasons. Blindness is the procedure adopted to increase the objectivity of an observation, preventing the expectations of both patient and investigator. Blindness may refer only to the patient (single), both patient and investigator (double), and may also include the assessor of the outcome (triple). Particularly important for treatments requiring self-assessment and for "soft" end-points. The end-points are measure units of treatment efficacy They must be, where possible, the result of observations that are accurate (reflecting the truth) e reproducible (confirmed by different investigators). Accurate and reproducible observations imply the use of «hard» rather than «soft» end-points. Primary end-points are the measure used to confirm or disprove treatment efficacy; sample size is calculated on the primary end-points. Secondary end-points are additional measures that complement primary end-points; results based on secondary end-points can be only used to generate hypotheses for subsequent studies. The statistical analysis implies the assessment of the efficacy of an intervention is based on the comparison of the frequency of occurrence of significant events in patients given the experimental and the control treatment. The comparison is based on a probabilistic analysis, that is the fundament of the statistical analysis.

An investigational treatment is effective when a significant difference is found against a comparator in the impact on pre-specified end-points measuring the outcome of the disease. The larger the sample the higher the probability to find a statistically significant difference. An investigational treatment is effective when a significant difference is found against a comparator in the impact on pre-specified end-points measuring the outcome of the disease. The larger the sample the higher the probability to find a statistically significant difference. For practical and economic reasons, the randomized trial must have limited duration. A limited duration is dictated by the need to preserve compliance, reduce drop-outs, and contain costs. Symptoms/signs should recur at a frequency sufficient for the event to be captured during the course of the experiment. Patients with more severe disease varieties are most frequently enrolled. Safety/tolerability is a pre-requisite of any investigational treatment. Newer drugs brought to the market products with less adverse effects and interactions. This does not prevent the occurrence of rare adverse events, which can be detected only when the drug is given to a number of patients greater than those exposed in the experimental phase.

Abstracts

The phases of an RCT are the following: Phase I: clinical pharmacology & toxicology; Phase II: preliminary assessment of efficacy and safety/tolerability of treatment, dose ranging, pharmacokinetics & pharmacodynamics; Phase III: pivotal study to assess treatment efficacy and safety/tolerability; Phase IV: Post-marketing surveillance.
RCTs can be of two major types: "Explanatory", ie they measure treatment effects adjusting for confounding from other prognostic indicators (Elevated internal validity); "Pragmatic": measure treatment effects in populations and settings replicating clinical practice (Elevated external validity).

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