24 OCTOBER, 2020



16TH CONGRESS OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY



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



NATAN M. BORNSTEIN

Director of Neurological Division, Shaare Zedek Medical Center

Vice President of the World Stroke Organization (WSO)

Chairman of the Israeli Neurological Association

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SCIENTIFIC PROGRAM



SCIENTIFIC PROGRAM

FRIDAY, SATURDAY 24[™], 2020

09:50 WELCOME ADDRESS

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SESSION 1 CHAIRPERS	DNS: Dafin F. Mureșanu (Romania), Michael Brainin (Austria) Natan M. Bornstein (Israel)
10:00 - 10:30) Global, national & regional burden of neurological disorders Ettore Beghi (Italy)
10:30- 11:00	Preventing the global burden of stroke and dementia Michael Brainin (Austria)
11:00 - 11:30	Post-stroke cognitive decline-current concepts and treatment approaches Natan Bornstein (Israel)
11:30 - 12:00) Brain lesion and recovery after stroke Stroke and microcirculation Dafin F. Mureșanu (Romania)

12:00 - 12:30 SESSION BREAK

SESSION 2

CHAIRPERSONS: Michael Brainin (Austria), Volker Hömberg (Germany)

- 12:30 13:00 Pharmacology in postacute neurorehab: Lessons from Cars and Captain trials Volker Hömberg (Germany)
- 13:00 13:30 The meta-analysis of CAPTAIN Trials Johannes Vester (Austria)
- 14:00 14:30 Epilepsy and seizures after TBI Alla Guekht (Russia)
- 14:30 15:00 Cerebrolysin enhances the therapeutic efficacy and safety of thrombectomy and thrombolysis with tPA for treatment of ischemic stroke Michael Chopp (USA)

15:00 - 15:30 **SESSION BREAK**

SESSION 3

CHAIRPERSONS: Antonio Federico (Italy), Amos Korczyn (Israel)

- 15:30 16:00 Update of Clinical and pathogenetic aspects of inherited small vessel diseases Antonio Federico (Italy)
- 16:00 16:30 Modelling cost-effectiveness for post-stroke interventions using Markov chains and probabilistic sensitivity analysis Ștefan Strilciuc (Romania)

16:30 - 17:00 Outcome measures on TBI – benefits of a registry Peter Lackner (Austria)

17:00 - 17:30 **SESSION BREAK**

SESSION 4

CHAIRPERSONS: Max Hilz (Germany), Hari Shanker Sharma (Sweden)

- 17:30 18:00 The problem with Alzheimer's disease Amos Korczyn (Israel)
- 18:00 18:30 Diabetic autonomic neuropathy Max Hilz (Germany)
- 18:30 19:00 Brain injury exacerbates neuropathology of sleep deprivation.
 Superior neuroprotection by co-administration of TiO2-nanowired with alpha-MSH and neurotrophic factors
 Hari Shanker Sharma (Sweden)

19:00 - 19:10 CONCLUDING REMARKS

ABSTRACTS



GLOBAL, NATIONAL & REGIONAL BURDEN OF NEUROLOGICAL DISORDERS

ETTORE BEGHI

Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milano, Italy

The Global Burden of Disease (GBD) is the most exhaustive initiative measuring levels and geographic and temporal trends of diseases and injuries worldwide. The GBD is coordinated by the Institute for Health Metrics and Evaluation (IHME, University of Washington). This collaboration involves more than 3,000 investigators from 205 countries. The data, collected and analyzed by the GBD collaborators, capture premature mortality and disability for more than 300 diseases, by sex and age and socio-economic status from 1990 to 2016, with comparisons with time and within countries. 20

The GBD collaborators perform a systematic review of epidemiological studies on all clinical conditions. Included are representative, population-based surveys and reporting of prevalence, incidence and mortality. The population health is measured using the Disability-Adjusted Life Years (DALYs), a summary metric representing health gap. DALYs measure the state of a population's health compared to a normative goal. DALYs are the sum of two components: Years of Life Lost (YLLs) due to premature mortality, and Years Lived with Disability (YLDs). DALYs are an absolute measure of health loss; they count how many years of healthy life are lost due to death and non-fatal illness or impairment. They reflect the number of individuals who are ill or die in each age-sex group and location. Population size and composition influences the number of DALYs in a population. The GBD diseaseand-injury-cause list is a hierarchical list of diseases and injuries. The available data are presented in the world population, WHO super-regions, countries, and for some countries – at sub-regional levels. Data are also disaggregated by age, sex, and socio-economic status. Disease definition is mostly based on the ICD-10 codes.

Globally, in 2016, neurological disorders were the leading cause of DALYs (276 million) and the second leading cause of deaths (9.0 million). Between 1990 and 2016, the absolute number of deaths and DALYs from all neurological disorders increased whereas their age-standardised rates decreased. The four largest contributors of neurological DALYs were stroke (42.2%), migraine (16.3%), dementias (10.4%), and meningitis (7.9%). For all neurological disorders, age-standardised DALY rates predominated in males while migraine, multiple sclerosis, and tension-type headache were most common and caused most burden in females.

In 2017, the total number of DALYs attributable to neurological disorders in the European Union was 21,046,899 and the total number of deaths was 1,116,037. DALYs and deaths in WHO-Europe were 41,322,498 and 1,974,840. In the European Union, neurological disorders ranked third after cardiovascular diseases and cancers. Stroke, dementias and headache were the three commonest causes of DALYs in the European Union. Stroke was the leading cause of DALYs also in WHO-Europe. From 1990 to 2017 there was a significant increase of all-age burden of neurodegenerative diseases despite a significant decrease in the rates of stroke and infections. The burden of neurological disorders in Europe was higher in men than in women, peaked in the 80-84 age group, and varied significantly with WHO-European region and country. All-age DALYs, deaths and prevalence of neurological disorders in all countries except for Azerbaijan, Turkmenistan and Uzbekistan. Decrease was mostly attributed to the reduction of premature mortality despite of an overall increase in the number of DALYs.

POST-STROKE COGNITIVE DECLINE-CURRENT CONCEPTS AND TREATMENT APPROACHES

NATAN BORNSTEIN

Director of the Brain Division, Shaare-Zedek Medical Center, Jerusalem, Israel

Stroke is a major cause of long-term physical, cognitive, emotional and behavioral disability. There is poor recognition of the emotional burden after stroke. Depression is abnormal and considered as "emotional distress". Post -stroke Depression (PSD) is the most frequent non-cognitive neuropsychiatric complication affecting up to a third of all ischemic stroke patients. PSD is associated with increased mortality, poorer functional recovery and lower quality of life. Despite its great clinical relevance the relationship between stroke, depression and cognitive impairment remains relatively unexplained and the awareness of . The potential mechanisms of PSD are either neuroanatomical caused by lesions in the frontal areas, or directly affecting neural circuits involving mood regulation, or as a result of psychological adjustment required by the disease. There is controversy regarding the appropriateness of diagnosing depression in the setting of an acute stroke. Geriatric Depression Scale (GDS) is the most widely used.

Regarding treatment there is insufficient randomized evidence to support the routine use of antidepressants for the prevention of depression or to improve recovery from stroke.

The approaches to management should be multidisciplinary including nurses and allied health staff.

PREVENTION OF STROKE AND DEMENTIA

MICHAEL BRAININ

President Elect, World Stroke Organisation Professor of Neurology, Chair and Director, Department of Clinical Neurosciences and Preventive Medicine, Danube University Krems, Austria

Currently, 14 million stroke occur every year and 80 million people are living with the consequences of stroke. While vascular brain lesions contributing to the appearance of dementia are guite frequent, at least one third of all dementias are a direct consequence of stroke. The World Stroke Organisation has published a Declaration of Prevention of Stroke and Dementia (Lancet Neurology 2020) which focuses on major changes of prevention: It is argued that in order to reduce incidence rates of both stroke and dementia, population-based prevention measures must become effective. Mostly only individual high-risk prevention is established as medical practice, whereas the very more frequent stroke numbers caused by low and medium-risk persons are hardly ever the focus of attention. It is postulated that heat maps showing differing risks by colour in a population or showing risk attributes such as 'low risk' and 'medium risk' should be abandoned in favor of a continuum of risk. The attribute 'low risk' gives false assurance that there is no risk. Population-based prevention also includes the need for bolder activities by governments focusing on increased sugar, tobacco and alcohol taxation (STAX). Moreover, the project 'Cut Stroke in Half' is estimated to prevent 50% of strokes and 30% of dementias occurring in a population. Initial experiences are already ongoing and encouraging. With use of community health workers, e-health measures and polypill applications these population-wide prevention effects can be seen and become effective for the reaching the sustainable developmental goals to reduce excess mortality by NCDs by 2030.

Keywords: stroke, dementia, prevention, population-based

NEUROTROPHIC FACTORS MAY ENHANCE THE THERAPEUTIC EFFICACY AND SAFETY OF THROMBECTOMY AND THROMBOLYSIS WITH tPA

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MICHAEL CHOPP

ZHENG GANG ZHANG, CHAO LI, HUA TENG

Henry Ford Hospital, Department of Neurology, Detroit, MI, USA Oakland University, Department of Physics, Rochester, MI, USA

In this presentation I will provide a compelling argument supported by experimental data that

Cerebrolysin, should be employed as a vascular therapy and as an adjunctive therapy to mechanical thrombectomy (MT) and thrombolysis with tPA for the treatment of ischemic stroke. Although MT and tPA provide opportunity for cerebral tissue reperfusion, the majority of stroke patients fail to achieve full tissue perfusion; the ischemic lesion evolves and expands in time, with many stroke patients experiencing disability. Thus, there is a potent need to augment these acute recanalization stroke treatments with Cerebrolysin.

Reasons for the failure of acute stroke therapies to fully restore function will be provided, I will also pre-sent novel mechanistic insight of how Cerebrolysin has a protective as well as a restorative therapeutic impact on brain vasculature post stroke and as a co-therapy with MT and tPA.

I show how Cerebrolysin reduces the permeability of human cerebral endothelial cells, reduces proin-flammatory, procoagulant and prothrombotic vascular mediators and enhances tight junction proteins, which in concert, thereby augment the integrity and function of the blood brain barrier and the cerebro-vasculature. New and potentially transformative data will be presented on the role of exosomes in me-diating Cerebrolysin therapeutic impact on cerebral vascular cells and thereby in mediating therapeutic efficacy of Cerebrolysin in combination with MT and tPA for acute ischemic stroke.

GENETIC SMALL VESSEL DISEASES: UPDATES IN CADASIL AND RELATED CONDITIONS

ANTONIO FEDERICO

Department of Medicine, Surgery and Neurosciences, Medical School, University of Siena, Siena, Italy

Past Chairman of the Scientific Committee and Past Member of the Board of the European Academy of Neurology

Chairmen of EAN Task Force for Rare Neurologic Diseases

Genetic ischemic cerebral subcortical small vessel diseases (SSVD) are rare, usually autosomal dominant conditions related to impairment of proteins mainly involved in small vessel functions. Symptoms are characterized by combinations of migraine with aura, ischemic events (transient ischemic attacks, lacunar strokes) and progressively worsening ischemic lesion load in brain imaging, vascular cognitive impairment (usually of the frontal-subcortical type) with behavioral-psychiatric symptoms and bilateral pyramidal and pseudobulbar signs leading to severe disability and premature death. In some patients, microbleeds and hemorrhagic strokes may be evident. A large clinical heterogeneity is usually present.

Between the different forms the most frequent is CADASIL, due to mutations of the NOTCH3 gene, followed by COL4A1/A2-related disease, autosomal dominant forms of HTRA1-related disease and leucoencephalopathies with calcifications and cysts. CARASIL, with an autosomal recessive HTRA1 mutation, is less frequent. A new form has been recently described, named CARASAL.

Here we will report our experience with these patients describing recent data on their pathogenesis and some guideline on the diagnosis and therapeutic options.

DIABETIC AUTONOMIC NEUROPATHY

MAX J. HILZ

Department of Neurology, University of Erlangen-Nuremberg, Erlangen, Germany Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Diabetic autonomic neuropathy is the most frequent neuropathy in western countries presenting with a variety of clinical features. Diabetic autonomic neuropathy may occur with and without somatic neuropathy. At the onset of diabetic autonomic neuropathy, resting heart rate is often already increased, while heart rate variability is usually reduced at rest or during challenge manoeuvers such as metronomic breathing, the Valsalva maneuver, or active standing. Apart from the Valsalva maneuver, all challenge maneuvers can be easily performed as bedside tests. The typical criteria required to confirm the diagnosis of diabetic autonomic neuropathy will be presented in adequate detail to understand and apply the procedures assessing cardiovascular autonomic dysfunction due to diabetes mellitus. Orthostatic hypotension is one of the most common manifestations of diabetic autonomic neuropathy. Patients complain of postural dizziness, blurred vision, neck pain or syncope. Hypohidrosis or anhidrosis, particularly in a glove- and stocking-like distribution, frequently manifests in early stages of diabetic autonomic neuropathy and may be accompanied by compensatory hyperhidrosis of proximal body sites. Among other autonomic problems are gastrointestinal dysmotility with esophageal atony and dysphagia, gastroparesis with nausea, vomiting, meteorism, loss of appetite, bacterial overgrowth of the gastrointestinal tract, gastritis and gastric ulcers. 60% of the diabetic patients suffer from diarrhea frequently alternating with constipation. 37-50% of the diabetic patients have bladder dysfunction with delayed and slowed micturition, increased micturition intervals or increased residual volume. These patients are predisposed to ascending urinary tract infections that may accelerate renal failure. Erectile dysfunction occurs in 30-75% of male diabetics. Recurrent or chronic foot ulcers with chronic osteomyelitis frequently result in amputations. Other signs of diabetic autonomic neuropathy include pupillary dysfunction, unawareness of hypoglycemia, respiratory disturbances including sleep apnea. Early diagnosis is essential to prevent further progression and pursue a stringent treatment regimen.

PHARMACOLOGY IN POSTACUTE NEUROREHAB: LESSONS FROM CARS AND CAPTAIN TRIALS

VOLKER HÖMBERG

EFNR Vice President WFNR Secretary General Head of Neurology SRH_GBW Bad Wimpfen and Neurology Coordinator for the SRH group of hospitals and clinics, Germany

Within the last 10 years the number of survivors after stroke and traumatic brain injury (TBI) has dramatically increased due to advances in acute medical care.

Nevertheless the question remains if we have really made progress to influence impairment by restorative strategies rather than just improving function and consecutively participation by compensatory strategies.

Are we really able to influence impairment?

First published in 2008 (Prabhakaran et al 2008) described an interesting phenomenon: The spontaneous impairment recovery after stroke at day 90 after the ictus (with or without treatment) for upper extremity was usually 70% of the maximum possible difference between initial score and the maximum possible. There were outliers from this rule attributable to severe pathology in the primary descending motor tracts especially the corticospinal tract. In the meantime this "proportional recovery rule was also demonstratesd to apply for impairments in non-motor domains as neglect and language abilities.

If this 70% proportional spontaneous recovery is a universal rule and cannot be influenced , this of course would mean that impairment oriented rehab is not possible. The challenge is to change the slope (i.e.from 70% to 80% or more) or to make outliers inliers .

This enigma increases the need for better pharmacological options to improve impairment the subacute stage e.g. after stroke:

So far larger RCT showed evidence for impairment reduction for only 2 substances: Antidepressants were shown to be effective in the FLAME trial with fluoxetine (Chollet et al 2011) This could however not be corroborated in subsequent trials with larger sample size using SSRIs as citalopram (TALOS trial) and fluoxetine again (FOCUS trial). Much larger effects could be shown fort he multimodal drug cerebrolysin , a mix of neurotrophic factors: The CARS trial (Muresanu et al 2016) documented for the first time after decades of frustrane attempts to achieve some sort of neuroprotective and/or neurorestorative effects that a mutimodal drug can improve impairment after stroke. This was further corroborated in a consecutive trial (Guekt et al 2017) and further corroborated by a metaanalysis of stroke related trials with cerebrolysin (Bornstein et al 2018).

The CAPTAIN trials looking at cerebrolysin effects in TBI fort he first time used a new statistical approach to encompass a broader ensemble of endpoints not just a single measure (e.g. Glasgow outcome scale) Results from the Captain 1 and Captain 2 trials showed significant superiority of Cerebrolysin over placebo when administered in the immediate postacute phase after TBI in mild to severely affected patients.

These trial certainly need further corroboration but the available data definitely open a new window for pharmacological interventions using a multimodal substance in combination with rehabilitative treatment.

THE PROBLEM WITH ALZHEIMER'S DISEASE

AMOS KORCZYN

The Sieratzki Chair of Neurology, Sackler School of Medicine Tel-Aviv University, Ramat-Aviv, Israel

Patients who suffer from senile dementia frequently harbor mixed pathology, which includes deposits of beta-amyloid and NFT. It still unknown whether the existence of these deposits is causatively related to the cognitive decline and attempts to eliminate them has not resulted in clinical benefits. The fight to reduce or delay the onset of senile dementia should target risk factors, and this should be started at young age.

OUTCOME MEASURES ON TBI / BENEFITS OF A REGISTRY

LACKNER PETER

Department of Neurology, Otto-Wagner-Spital, Vienna, Austria

Due to the complexity of traumatic brain injury (TBI), outcome prediction for individual patients is a big challenge. To compensate for patient heterogeneity, large cohorts are needed. So far, only few solid outcome predictors have been derived from big clinical studies. Alternatively, outcome prediction models using data from national registries can be applied. A crucial point is the selection of the optimal scores for motor and non-motor, functional outcome evaluation. In addition, complexity of a registry and usability are inversely correlated. Hence, finding the right balance between these factors is one of the most difficult tasks when designing a powerful registry. This talk will focus on the possibilities and limitations of registry data analyses. In addition different approaches for identifying optimal outcome parameter sets and balancing complexity and usability will be discussed.

STROKE AND MICROCIRCULATION - IS THERE A CHANCE FOR AN ADD-ON THERAPY TO IMPROVE POST-STROKE REPERFUSION AND HEMORRHAGIC TRANSFORMATION?

DAFIN F. MUREŞANU

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

Revascularization interventions have significantly improved the outcome of patients with acute ischemic stroke. Fibrinolytic agents (rtPA) are highly effective within a narrow therapeutic window but have shown limitations in large proximal arterial occlusions and are associated with serious adverse effects, particularly when administered beyond their intended timeframe. International treatment guidelines recommend thrombolytic therapy as the first line of treatment for acute ischemic stroke, followed by endovascular thrombectomy in eligible patients. This approach dissolves clots by plasminogen activation or mechanically removes them to re-establish blood flow in the brain. Effective cerebral revascularization is considered essential for preventing additional infarction of functionally inactive but viable brain tissue in the ischemic penumbra.

After the success of drugs and endovascular procedures in outcome-based clinical trials for acute ischemic stroke, the race to treat as many patients as possible began

in conjunction with the resolved of precision medicine to tailor interventions up to the individual level. To evaluate outcomes of thrombolytic or endovascular therapies, recanalization, and reperfusion, although frequently used interchangeably, are not equivalents. The objective of recanalization is to reopen an occluded vessel, while reperfusion refers to the restoration of blood flow in a formerly occluded vascular territory, particularly at the level of cerebral microcirculation.

A plethora of evidence has recently proven that reperfusion is a much better indicator for post-stroke imaging (infarct volume, infarct growth, salvaged penumbra) and clinical outcomes (NIHSS). Recanalization is neither a prerequisite for reperfusion nor does it always lead to the latter. Full recanalization after rtPA or thrombectomy often fails to induce clinically significant reperfusion, due to a myriad of complex factors related to microvascular circulation, such as distal micro-emboli or extensive endothelial damage.

The potential to improve overall reperfusion requires a multimodal approach aimed at preventing additional vascular damage and enhancing cerebral microcirculation. The key challenge in the current pharmacological environment is safety. Cerebral microcirculation is extremely difficult to regulate, as chemically induced vasodilation that would allow reperfusion, would also significantly increase the risk of serious adverse events in combination with rtPA.

Cerebrolysin, an agent with pleiotropic pharmacodynamic properties, has been proven safe in combination with alteplase (Lang, 2013), registering significantly more patients with favorable response in neurological outcome measures (NIHSS) as compared to placebo in this exploratory study.

The avenues of combination, concomitant and add-on treatment in ischemic stroke are very much worth pursuing not only in the context neurorehabilitation but especially in very early, acute phases of the disease.

BRAIN INJURY EXACERBATES NEUROPATHOLOGY OF SLEEP DEPRIVATION. SUPERIOR NEUROPROTECTION BY CO-ADMINISTRATION OF TIO2-NANOWIRED WITH ALPHA-MSH AND CEREBROLYSIN

HARI SHANKER SHARMA^{1,3,4,8}

DAFIN FIOR MURESANU³, JOSÉ VICENTE LAFUENTE⁴, ASYA OZKIZILCIK⁵, RYAN TIAN⁶, ALA NOZARI⁷, IGOR MANZHULO⁸, RANJANA PATNAIK⁹, ARUNA SHARMA^{1,3,4,8}

1. Int. Expt. CNS Injury & Repair (IECNSIR), Surgical Sciences, Anesthesiol. & Intensive Care Med., Uppsala Univ., Uppsala, Sweden;

2. Dept. Clin. Neurosciences, Univ Med. Pharm. & 3"RoNeuro" Inst. Neurol. Res. & Diag., Cluj-Napoca, Romania;

4. Dept. Neurosciences, Univ. of Basque Country, Bilbao, Spain;

5. Biomed. Engin., Univ. of Arkansas, Fayetteville, AR; 6Chem. & Biochem., Univ. of Arkansas, Fayatteville, AR, USA;

7. Anesthesia and Critical Care, Massachusetts Gen. Hosp., Boston, MA, USA;

8. Nat Scientific Cent of Marine Biology, Far Eastern Branch, Russian Acad of Sci,

Vladivostok, Russia & Sch. of Biomed, Far Eastern Fed. Univ., Vladivostok, Russia;

9. Sch. of Biomed. Engin., Indian Inst. of Technology, Banaras Hindu Univ., Varanasi, India;

Sleep deprivation (SD) is common in military personnel engaged in combat operations. Our previous reports show that 12 h SD alone induces brain pathology and continued until 72 h in a progressive manner. However, these military personnel with SD are also prone to traumatic brain injury (TBI). Thus, a possibility exists that TBI could further exacerbate SD induced brain pathology. Several lines of evidences suggest that both in TBI and in SD a decrease in alpha-melanocyte stimulating hormone (MSH) and brain derived neurotrophic factor (BDNF) levels occur in plasma as well as in the brain. This could be one of the leading causes of brain pathology in SD or in TBI. Thus, exogenous supplement of alpha-MSH and/ or BDNF could induce neuroprotection in SD or TBI. In present investigation effect of concussive head injury (CHI) in SD induced brain pathology and effects of alpha-MSH and neurotrophic factors treatment leading to neuroprotection in a rat model was examined. SD was induced in rats using the inverted flowerpot methods surrounded by water level 1 cm below the platform (6.5 cm in diameter) that allow free movement but continuously sleep leads to fell down in water disturbing the sleep process. SD was induced in healthy rats as well as in rats that were subjected to CHI by dropping a weight of 114.6 g over the skull causing an impact of 0.224 N on the brain without skull fracture. Rats subjected to 48 h SD in CHI (24 h after insult) exhibited greater brain pathology e.g., higher leakage of Evans blue albumin and radioiodine ([131]-I) by 3-to 4 fold as compared to naïve rats subjected to identical SD. Neuronal, glial and axonal damages using histopathological techniques were also exacerbated by several fold in CHI after SD. Plasma alphaMSH and BDNF level shows significant reduction (alpha-MSH 8.34 ± 0.23 vs. Control 20.34 \pm 0.12 pg/ml; BDNF 8.23 \pm 0.11 vs. control 22.34 \pm 0.21 pg/ml) in SD group after CHI as compared to SD group alone (alpha-MSH 15.13 \pm 0.12 pg/ml; BDNF 14.23 \pm 0.08 pg/ml). Intravenous administration of alpha-MSH (100 μ g/kg) together with cerebrolysin (a balanced composition of several neurotrophic factors and active peptide fragments 5 ml/kg) significantly induced neuroprotection in CHI or SD groups alone. However, TiO2 nanowired delivery of alpha-MSH and cerebrolysin is needed to induce neuroprotection in SD rats after CHI. The levels of alpha-MSH and BDNF were also retired by this treatment in SD rats after CHI (alpha MSH 22.34 \pm 0.12 pg/ml; BDNF 23.34 \pm 0.17 pg/ml). Taken together our results are the first to point out that TiO2 nanowired administration of alpha-MSH and cerebrolysin induces superior neuroprotective effects following SD in CHI, not reported earlier.

*Acknowledgements:

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MODELLING COST-EFFECTIVENESS FOR POST-STROKE INTERVENTIONS USING MARKOV CHAINS AND PROBABILISTIC SENSITIVITY ANALYSIS

STEFAN STRILCIUC

Department of Neurosciences, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania RoNeuro Institute for Neurological Research and Diagnostic, Cluj-Napoca, Romania

In the last decade, significant breakthroughs in fundamental, clinical, and behavioural research have pushed forward real innovation in medicines, medical devices and procedures, as well as targeted population-based interventions for improving health. Despite this progress, most healthcare systems cannot afford translation of these innovations into current practice.

This issue is now becoming increasingly relevant, given the economic turmoil occurring worldwide due to the novel coronavirus. Patients are suffering from a severe disruption in chronic disease care, including delays in diagnosis and treatment and interruption of clinical studies. Countries with weaker health infrastructure are disproportionately exposed to this vulnerability. Romania is a reference case for this phenomenon. Its emergence as a high-income country (gross national income of USD 12.630 in 2019) is insufficiently reflected in access and quality to healthcare due to historically low health expenditure (5% vs 9.8% European Union average) and Semashko-style infrastructure. A recent report by the Romanian Health Observatory shows startling decreases in inpatient admission (up to 80%) of chronic patients, to the extent that researchers now hypothesize the indirect societal impact of disruptions due to the pandemic might exceed the one directly attributed to COVID-19 morbidity and mortality.

Despite its pretentious title, this presentation aims to promote an accessible framework to evaluate the cost-effectiveness of interventions after stroke. The talk uses the Markov model of Briggs and Sculpher and probabilistic sensitivity analysis, based on international and local estimates of economic burden and intervention effectiveness in acute ischemic stroke.

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- Alec Miners London School of Hygiene and Tropical Medicine

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THE META-ANALYSIS OF CAPTAIN TRIALS

JOHANNES VESTER

Senior Consultant Biometry and Clinical Research idv - Data Analysis and Study Planning, Germany

Leading interdisciplinary research groups recently highlighted the multidimensional nature of TBI, such as, e.g., the International Mission on Prognosis and Clinical Trial Design in TBI (IMPACT), stating that "outcome after TBI is by definition multidimensional" or the US Traumatic Brain Injury Clinical Trials Network Group, pointing out that "multiple measures are necessary to address the breadth of potential deficits and recovery following TBI".

An evaluation of neuroprotection intervention studies conducted in the last 30 years has determined that methodological design flaws are among the major reasons why pharmacological agents fail to demonstrate efficacy. Almost all the inconclusive studies used a single outcome measure approach. This classic approach in clinical TBI trials cannot capture all clinical relevant functional information in survivors of any kind of TBI. Even survivors of mild to moderate TBI may experience lifelong disturbances in the physical, behavioral, emotional, cognitive (memory, attention, reasoning, communication and planning), motor, sensory, perception and social domains of life that may affect specific or global functioning.

Multidimensional analysis opens a completely new direction for clinical and statistical thinking and is perhaps much closer to the complicated reality of outcome after traumatic brain injury than the previous "one-criterion paradigm" which ruled clinical research on neuroprotective treatments for the last decades. It is thus fortunate that new data analysis procedures are available that are appropriate for this important new multidimensional approach. Currently, one of the most promising TBI clinical trial approaches, with cutting edge state of the art methodology, is the series of CAPTAIN trials - the first true multidimensional approach in TBI history based on full outcome scales. The objective of the CAPTAIN I and CAPTAIN II trials was to measure the effect of Cerebrolysin as adjunctive treatment for standard care in eligible individuals after moderate-severe TBI. Both performance and emotional state outcome measures were applied in these trials. Outcome domains such as depression are needed to complement functional independence measures and to capture the multifaceted process of neurorecovery after TBI. The pre-planned meta-analysis of the CAPTAIN trials, based on the multivariate outcome ensembles, confirmed the safety and efficacy of Cerebrolysin in patients who have suffered moderate to severe TBI, opening a new horizon for neurorecovery in this field. In addition, substantial reduction of the burden of depression was shown with final normalization of the HADS despression score in 70.5% of the Cerebrolysin patients as compared to 39.5% of the placebo patients.

CURRICULUM VITAE





ETTORE BEGHI

Head of the Laboratory of Neurological Disorders (since 1996) at the Institute Mario Neuri IRCCS, Milano. Associate Editor of EPILEPSIA. Former Research Fellow at the Department of Medical Statistics and Epidemiology. Mayo Clinic. Rochester, MN (1982-83). Member of the Editorial Board of the journals Neuroepidemiology, Epilepsia Open, 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 (INS), Italian League against Epilepsy (LICE), Neuroepidemiology Section of the INS, Neuroepidemiology Section of the American Academy of Neurology (AAN), Commission on the Epidemiology of Epilepsy of the International League Against Epilepsy (ILAE), Commission "Epilepsy, Risks, and Insurance" of the International Bureau of Epilepsy (IBE), ILAE Commission "Antiepileptic Drugs", Cochrane Epilepsy Group, ILAE Commission on the Burden of Epilepsy, International Subcommittee of the AAN, Course Director at the AAN, 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) and European Academy of Neurology (EAN), Co-Chair of the Epidemiology Panel of the EAN, Past President of the LICE, member of the ILAE Task Forces on the Global Cost of Epilepsy, Epilepsy and Driving and Epilepsy in the Elderly.

Author of more about 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).



NATAN BORNSTEIN ISRAEL

EDUCATION

1970-73 University of Sienna, Medicine, Sienna, Italy 1973-79 Technion Medical School, Hifa, Medicine, MD, 1979 Date of receiving specialization certificate: 11 September, 1984 Title of Doctoral dissertation: Dextran 40 in acute ischemic stroke Name of Supervisor: Dr. Jacob Vardi

FURTHER EDUCATION

1978-83 Tel-Aviv University, Sackler Faculty of Medicine, neurology
(residence), Israeli Board certified in Neurology, 1983
1979-83 Tel-Aviv University, Sackler Faculty of Medicine, Post graduate
studies in Neurology
1984-87 Sunnybrook Medical Center, University of Toronto, M.R.C stroke,
Fellowship

ACADEMIC AND PROFESSIONAL EXPERIENCE

1982-1995	Tel-Aviv University, Neurology, instructor
1991-present	European stroke Conference (ESC), Executive committee
1995-1999	Tel-Aviv University, Neurology, Senior lecturer
1995	Eliprodil CVD 715 clinical trial, Steering Committee
1995-1997	International Stroke Study (IST), Steering Committee
1995-1999	American Academy of Neurology, Member of the International Affairs Committee
1996	Asymptomatic Carotid Stenosis and Risk of Stroke(ACSRS), Advisory Committee
1996-present	The Mediterranean Stroke Society (MSS), President
1996-2002	EFNS, Management Committee
1997-2009	Israeli Neurological Association, Secretary
1999-present	Tel-Aviv University, Neurology, Associated Professor
2001- present	European Society Neurosonology and Cerebral Hemodynamics
	(ESNCH) Executive committee
2005-present	Neurosonolgy Research Group, Executive committee
2006-present	European Master in Stroke Medicine, Member of faculty
2006-2008	NEST II clinical Trial, Steering Committee
2006-present	SENTIS clinical Trial, Steering Committee
2006-present	CASTA Trial, Steering Committee

2006-present	Brainsgate clinical Trial, Steering Committee
2008- present	World Stroke Association (WSO), Vice president
2009-present	Israeli Neurological Association, Chairman
2009-present	European Stroke Organization (ESO), Member on the board of
	directors
2010-	NEST III clinical Trial, Steering Committee

PROFESSIONAL ACHIEVEMENTS- EDITORIAL BOARD

1991-present	Neurological Research Journal, Guest Editor
1991-present	STROKE, Member of the editorial board
1998-present	European Journal of Neurology, Member of the editorial board
1999-present	Journal of Cerebrovascular disease, Member of the editorial board
2000-present	Journal of Annals of Medical Science, Consulting Editor
2001-present	Journal of Neurological Science (Turkish), Member of the editorial board
2001-present	Acta Clinica Croatica, Member of the editorial Counsil
2003-present	Italian Heart Journal, International Scientific Board
2003-present	Journal of Neurological Sciences, Guest Editor
2004-present	Turkish Journal of Neurology, International Advisory Board
2005-present	Archives of Medical Sciences (AMS) , Member of the Editorial Board
2006-present	Journal of Cardiovascular Medicine, International Scientific Board
2006-present	International Journal of Stroke, Editorial Board
2006-present	Acta Neurologica Scandinavica, Editorial Board

- 2009-present American Journal of Neuroprotection& Neurogeneration (AJNN) Member of the Editorial Board
- 2010 Meinder of the Eurofian Board
- 2010 Neurosonology, International Editorial Board
- 2010 Frontiers in Stroke, Review Editor

PROFESSIONAL ACHIEVEMENTS- REVIEWER

- 1998-present Diabetes and its complications, Ad Hoc reviewer
- 1999-present Journal of Neuroimaging, Reviewer
- 1999-present Journal of Neurology, Ad Hoc reviewer
- 2000-present Neurology, Ad Hoc reviewer
- 2003-present Israeli Medical Association Journal (IMAJ), Reviewer
- 2003-present Acta Neurologica Scandinavica, Ad Hoc reviewer
- 2006-present Journal of Neurology, Neurosurgery & Psychiatry, Reviewer
- 2010- European Neurology, Ad Hoc reviewer

MEMBERSHIP IN PROFESSIONAL SOCIETIES

- 1977-present Israeli Medical Association
- 1983-present The Israeli Neurological Association
- 1985-present Stroke Council of the American Heart Association (Fellow)
- 1986-present American Academy of Neurology
- 1986-present Neurosonology Research Group of the World Federation of Neurology

1987-present	Stroke Research Group of the World Federation of Neurology
1990-2008	International Stroke Society
1995-2008	European Stroke Council
1995-present	Mediterranean Stroke Society (MSS)
1998-present	European Neurosonology Society
2005-present	World Stroke Organization (WSO)
2008-present	Fellow of the European Stroke organization (FESO)

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MICHAEL BRAININ AUSTRIA

Professor and Chair, Department of Clinical Neurosciences and Preventive Medicine Danube University Krems, Austria (2000-) and Emeritus Chair and Professor of the Clinic for Neurology at the University Hospital Tulln, Austria (1994-2016). He has acted as Associate Professor of the Karl Landsteiner University of Health Sciences in Krems and is Adjunct Professor at the Medical Faculty of the University Cluj, Romania.

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

He was chairman of the Scientific Committee of the European Federation of Neurological Societies and Board Member of the European Academy of Neurology.

He acted as 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 was President of the 6th World Stroke Congress in Vienna, has led the WSO Education Committee 2008-2017 and was editor of the World Stroke Academy, a web-based learning platform for the WSO. He chairs the European Master's Program in Stroke Medicine since 2007, which is held biannually and currently is visited by medical doctor participants from 23 countries around the world.

He has acted as PI or co-PI in numerous stroke-related drug and intervention trials, has published 220 pub-med listed papers, edited three textbooks on stroke, and has given more

than 1.000 invited lectures. His scopus h-index is 48 and scopus citations are >19.000.

He is Senior Editorial Consultant for "Stroke", acted as Associate Editor of the European Journal of Neurology (2007-2019) and currently is member of the editorial boards of Neuroepidemiology, International Journal of Stroke, The European Stroke Journal and The Journal of Neurological Sciences. He received numerous awards, among them the Marinescu Medal from the Romanian Society of Neurology, and the 2017 Life-time Achievement 'Würdigungspreis' of the Region of Lower Austria. He holds several honorary doctorates, fellowships and honorary memberships from scientific societies including the French Neurological Society, the Hungarian Stroke Society, the Brazil Stroke Society and the Stroke Society of Korea.



MICHAEL CHOPP USA

Michael Chopp, PhD, joined the Henry Ford Health System in Detroit in 1983. He was appointed Vice Chairman for Research of the Department of Neurology in 1991, Scientific Director of the Henry Ford Neuroscience Institute in 1999, and is the Zoltan J. Kovacs Chair in Neuroscience Research. Dr. Chopp is also Distinguished Professor of Physics at Oakland University in Rochester, MI.

He received his MS and doctorate degrees in Mathematical and Solid State Physics from New York University. After nearly 10 years of working as a Physicist and as a Professor of Physics, Dr. Chopp made a career change and turned his interest to translational research in neuroscience. Dr. Chopp's research has primarily focused on: 1) cellular and molecular biology of ischemic cell injury, 2) the pathophysiology of stroke, traumatic brain injury, peripheral neuropathy, multiple sclerosis, and glioma, 3) combination thrombolytic and neuro and vascular protective therapies for stroke, 4) mechanisms of neuroprotection, 5) cell-based and pharmacological neuro-restorative therapies for stroke, traumatic brain injury and neurodegenerative disease, 6) molecular and cellular mechanisms underlying neurogenesis and angiogenesis and the induction of brain plasticity leading to functional and behavioral recovery after neural injury, 7) treatment of glioma, 8) exosomes/ microRNA for treatment of neurological injury and disease, and 9) magnetic resonance imaging. Dr. Chopp has received multiple awards and recognitions for his research efforts, including the American Heart Association Thomas Willis Lecture Award, the Abraham White Distinguished Science Award, and the Lecture of Excellence and World Stroke Organization Award. Dr. Chopp has 623 peer reviewed publications and has given 414 plenary lectures and invited presentations. He has served on and chaired National Institutes of Health (NIH) study sections and has served as a consultant to government agencies, the U.S. National Institutes of Health, and the pharmaceutical industry.



ANTONIO FEDERICO

Prof. Antonio Federico, born in Polla (Sa) on the 25.08.48, from 1990 is full professor of Neurology at the University of Siena , Director of the Unit Clinical Neurology and Neurometabolic Disease.

He was Director of the Department of Neurological, Neurosurgical and Behavioural Sciences, University of Siena (2002-2008).

He received the degree in Medicine and specialization in Nervous and Mental Diseases, summa cum laude, at the University of Naples in 1972 and 1975 respectively. He received the Lepetit Award for the best degree dissertation in 1972.

His biological training was in the Institute of Biochemistry as student and after in Physiology of the University of Naples, and in the Centre de Neurochimie of CNRS, in Strasbourg, directed by prof. Mandel where he worked in the years 1973-75. He also collaborated with many international research groups, in different countries where he spent in the past years some times: in Montreal (Prof. Andermann, Karpati and Shoudgbridge), in London (dr A. Harding and prof. Morgan-Hughes), in Toronto (dr.Robinson), in Bonn (prof. von Bergmann) , in Paris (dr.Baumann), in Baltimore (proff. Moser and Naidu), in Oxford (prof. Matthews), etc. His clinical formation was made at the Medical School of the University of Naples, in the Dept, Neurology, and after in Siena, where he moved on 1980 with his mentor, prof. G.C. Guazzi. Associated professor in Neurology in 1982, since 1990 he is full professor of Neurology, Medical School, University of Siena. In 2013, he received honoris causa degree in Medicine at University Carol Davila, Bucharest, Rumania.

In the years 1990-96 he was Secretary of the Italian Society of Neurology. In the years 2006-08 was President of the Italian Society of Neurology. He coordinated the Study Group on Clinical Neurogenetics of the Italian Society of Neurology. He has been referee for projects evaluation in the area of Orphan drugs and Orphan diseases for Biomed Projects from EU, for MURST, CNR and Istituto Superiore di Sanita, and other national and international funding agencies, etc.

He is member of the Second Opinion Group of the American Leucodistrophy Association. Associated editor of Neurological Sciences , Springer-Verlag Editor from 2000. From 2012, he is Editor-in Chief.

He is author of more than 500 article quoted by Pubmed. He is author of a chapter on Cerebrotendinous Xanthomatosis, Vinken and Bruyn Edts, Handbook of Clincal Neurology, vol 49, Neurodystrophies and Neurolipidoses.

On the book McKusick's Mendelian Inheritance in Man,. Ed.1992, Catalog of Autosomal Dominant and Recessive Phenotypes he is cited for 3 different diseases. He was editor of the book Late Onset Neurometabolic diseases (A.Federico, K. Suzuki and N.Baumann Edts), Karger 1991, and many other books from Italian and international

Publishing Companies. Recently he published (2015) Manuale di Neurologia Pratica and Neurologia and Assistenza infermieristica, for students.

His main field of interest is related to neurometabolic, neurodegenerative and rare diseases, investigated from a genetic, metabolic, neuroimaging and clinical point of vue. Summary of the academic involvements: - Director of the Section Neurological Sciences, Dept Neurological , Neurosurgical and Behavioural Sciences (2000-2012) - Director of the Research Center for the Diagnosis, Therapy and Prevention of the Neurohandicap and Rare Neurological Diseases, until the 2010 - Vice-Dine of the Medical School, University of Siena (2003- 2006) - Director of the Postgraduate School of Neurology, University of Siena, from 2006 up to 2014. - Director of the PhD School in Cognitive and Neurological Sciences, University of Siena (from 2000 up to date) - Coordinator of the Section of the Univ. Siena of the PhD Program Neurosciences, Univ. Florence. - Research delegate for the Dept Medicine, Surgery and Neurosciences (2013-2018) - Vice-Rector of the University of Siena, from 1st april 2016 to november 2017.

Medical Involvements – Until November 2018 (date of retirement) Director of the OU Clinical Neurology and Neurometabolic Diseases, University Hospital of Siena Medical School. –He is still Director of the Regional Reference Center for Rare Diseases - Regional Coordinator of the Network for Rare Neurological Diseases, Tuscany Region. - Member of several Ministry of Health and Regional Committees National and International Commitments - President of the Italian Society of Neurology (2009-11) - Italian delegate to the World Federation of Neurology - Italian Delegate to the European Union of Medical Specialists (Section Neurology) - Italian Delegate and Chairman of the Neuromediterraneum Forum and President - Consultive Member of the European Brain Council - Editor – in – Chief of Neurological Sciences, Springer Verlag Editor. He is in the Editorial Board of many national and international journals. - Member of the American Panel United Leucodystrophies. – Member of the Scientific Committee of AISM (Associazione Italiana Sclerosi Multipla) - Chairman of Neurology. Member of the Scientific Societies: - Societa Italiana di Neurology (2014-2018) - Chairman of Neurology.

Past-President and Member of the Committee) - Society for the Inborn Errors of Metabolism - Italian Association of Neuropathology - SINDEM (Italian Association of Dementias) - Italian Association for Parkinson's disease - Italian Association of Neurogeriatrics (Member of the Scientific Committee) - Italian Stroke Forum - European Academy of Neurology (Member of the Board and Chairman of the Scientific Committee) - American Academy of Neurology - World Federation of Neurology (Co-Chair Section of Migration Neurology) - Neuromediterraneum Forum (President).



ALLA GUEKHT RUSSIA

Professor Guekht's research interests are in epilepsy, cognition, stroke and neuroepidemiology. She obtained the M.D. degree at the 2nd Moscow Medical Institute and completed residency in Neurology in the same Institute; she was then trained in neuropsychology and neurophysiology, participated in the training/fellow programs in the Munster University, University of Homburg/Saar (Germany), Thomas Jefferson Hospital and Philadelphia Comprehensive Epilepsy Center (USA). She received the PhD Diploma for the dissertation on EEG monitoring in carotid surgery and the Doctor of Medical Sciences Diploma for the dissertation on Brain plasticity and restoration after stroke. Currently she is the Professor of the Department of Neurology, Neurosurgery and Genetics, Russian National Research Medical University, Director of Moscow and Head of the Neurology Clinic of the Buyanov City Hospital in Moscow.

Prof. Guekht is the recipient of several prestigious international and national awards in medicine, including the Bruce S. Schoenberg International Award and lecture in Neuroepidemiology (American Academy of Neurology), European Educational Award on Epileptology and the Ambassador for Epilepsy Award from ILAE and the IBE, "Honored Physician of the Russian Federation" Award of the Government of Russia; "Priznanie" (Recognition) Award of the Russian Federation for multidisciplinary research in restoration after stroke and the award of the Major of Moscow.

She is the author of more than over 200 articles focusing on epilepsy, stroke (plasticity and restoration), dementia/cognitive decline after stroke, Parkinson's disease, including over 60 papers in peer-reviewed international journals and book chapters, 18 books (in Russian), including Manual in Neurology and National Guidelines in Neurology, 6 patents of the Russian Federation in the field of stroke, epilepsy, neurophysiology. She is the mentor to

many young neurologists with over 25 completed PhD and 4 doctoral dissertations.

She served in the Editorial Boards of Epilepsia, Epileptic Disorders; currently – in the Editorial Boards of the Journal of Neurological Sciences, Acta Neurologica Scandinavica, European Stroke Journal, Korsakov Journal of Neurology and Psychiatry. She acts as a regular reviewer for many international journals.

Alla Guekht served as the Member of the International Organizing/ Scientific Committee for many International /European Congresses, invited speaker at the Congresses of the WFN, EAN, EFNS, ESOC, European and International Epilepsy Congresses, CONy, Vascular Dementia Congress, World Congress on neurorehabilitation, other international and national conferences in neurology, epilepsy, stroke, rehabilitation.

She is currently the Vice-President-elect of the International League again epilepsy, member of the WFN Committee of Education, Steering Committee for the Action Plan for Stroke in Europe, Secretary of the Russian Society of Neurologists.

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MAX J. HILZ GERMANY

Studied medicine at the Universities of Cologne and Erlangen-Nuremberg in Germany. He first trained in Anesthesiology and Intensive Care Medicine and in Ear-Nose-and-Throat diseases, and then started his residency in Neurology and Psychiatry at the University of Erlangen-Nuremberg.

He specialized in Neurology, Clinical Neurophysiology, Neurological Intensive Care Medicine and Disorders of the Autonomic Nervous System (ANS). He holds German board certificates in Neurology and Psychiatry and in Psychotherapy. He also passed the board examination of the American Board of Electrodiagnostic Medicine.

He is licensed to practice medicine in Germany, the United Kingdom, and in the State of New York, USA.

From 1992 until 2013, he was Attending and Full Professor of Neurology, Medicine and Psychiatry at New York University, New York, NY. Until 2007, he also served as the Associate

Director of the Dysautonomia Evaluation and Treatment Center at New York University. In 2006, he was offered an Endowed Chair and tenured Professorship at New York University. From September 2016 to August 2017, he was the Chair in Autonomic Neurology, and Director of the Clinical Department of Autonomic Neurology at the University College London, Institute of Neurology, Queen Square, London, UK. Currently, Until April 2019, he was Professor of Neurology at the University of Erlangen-Nuremberg in Erlangen, Germany. Since June 2015, he is also Adjunct Professor of Neurology at Icahn School of Medicine at Mount Sinai, New York, NY, USA.

In December 2018, he received the academic degree of Doctor honoris causa (Dr. h.c.) from the "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Professor Hilz is the current Chair of the Autonomic Disorders Research Group in the World Federation of Neurology. He also co-chairs the Autonomic Nervous System Subspecialty Panel of the European Academy of Neurology, EAN. He was President of the German Autonomic Society, President of the European Federation of Autonomic Societies, and Chair of the Autonomic Section of the American Academy of Neurology. He is a member of the editorial board of Clinical Autonomic Research, and Associate Clinical Editor of Autonomic Neuroscience: Basic and Clinical. He also served as an advisor to the European Medicines Agency, EMA, on issues related to autonomic nervous system dysfunction.

He co-authored the guidelines of the German Neurological Society on syncope, the guidelines on erectile dysfunction and the guidelines of the German Diabetes Society on diabetic neuropathy. He has published more than 300 original and review articles in peer-reviewed journals and chapters in textbooks and presented his work at several hundred scientific conferences.

Prof. Hilz is experienced in the examination of small nerve fiber diseases and disorders of the peripheral and central autonomic nervous system, including hereditary sensory and autonomic neuropathies, diabetic neuropathies, and Fabry disease, and central autonomic disorders. He studied the pathophysiology of Familial Dysautonomia, also known as Hereditary Sensory and Autonomic Neuropathy Type III, of Fabry disease, and the effects of brain lesions of various etiologies on the central autonomic network and on autonomic function. He also described long-term changes in the central autonomic modulation of the cardiovascular system in patients with a history of traumatic brain injury, stroke, epilepsy, multiple sclerosis and other diseases.



VOLKER HÖMBERG GERMANY

Prof. Hömberg had his medical education at the Universities of Düsseldorf, Freiburg and Boston Massachusetts. After spending electives in Neurology at Boston City Hospital and the National Hospital for Nerv-ous Diseases Queens Square London he was a research fellow at the C. and O. Vogt Institute for Brain Research in Düsseldorf. In 1981 he started a residency in neurology with Prof. Hans Freund at Heinrich Heine University Düsseldorf. In 1987 he was appointed Director of the Neurological Therapy Centre (NTC) a newly founded Institute at Hein-rich Heine University in Düsseldorf. He was also founding Director of the NTC in Cologne . He was involved in the setup of many in-and outpa-tient rehabilitation hospitals in Germany. In 2001he started the St. Mauritius Therapy Clinic in Meerbusch near Düsseldorf and since 2011 he is Director of the Dept. of Neurology at the Gesundheitszentrum Bad Wimpfen and works as senior neurology group leader for the SRH-Group ,one of the biggest hospital groups in Germany.

He was founder, president and vice president of the German Society for Neurorehabilitation for many years. He serves as Secretary General for the World Federation of Neurorehabilitation (WFNR)for more than 12 years and is Vice President oft the European Federation of Neurorehabilitation Societies. (EFNR)

He is regular reviewer and co-editor for many international peer reviewing journals.

He is regular (co) -programme chairman for neurorehabilitation for major international meetings as the World- and European Neurorehabilitation Congresses (WCNR,ECNR), Controversies in Neurology (CONy) and the European Stroke Congress (ESC).

He has published more than 250 articles in international peer reviewed journals and many book chapters. His primary scientific interest are the fields of motor rehabilitation, cognition epistemiology, neurological music therapy and pharmacology in neurorehabilitation.



AMOS KORCZYN ISRAEL

Professor Korczyn graduated from the Hebrew University - Hadassah Medical School in Jerusalem in 1966 (MD), where he also received an MSc degree in pharmacology (cum laude) in 1966. He trained in neurology at Beilinson Hospital and at the National Hospital for Nervous Diseases, Queen Square, London. He was the Chairman of the Department of Neurology at the Tel-Aviv Medical Center since 1981 until 2002, and the incumbent of the Sieratzki Chair of Neurology at Tel-Aviv University, 1995-2010. Professor Korczyn has a particular interest in neurodegenerative diseases. He has authored or co-authored over 600 articles in peer-reviewed journals, as well as chapters in books, etc. He edited several books and Special Issues in Journals, and is co-Editor of the Journal of the Israeli Neurological Association (JINA) since 2009. He is or has been an Editorial Board member of 20 international journals, and organized several neurological conferences, mainly in the field of dementia. Parkinson's disease and other degenerative brain disorders, as well as CONy - the International Congress on Controversies in Neurology. Professor Korczyn also served on advisory boards in several drug discovery programs. Professor Korczyn is the Chairman of the Scientific Administrative Board of the Israeli Alzheimer's disease association (EMDA), and member of the SAB of Alzheimer Disease International, and has been the chairman of the WFN Research Committee for Neuropharmacology. Professor Korczyn is an honorary member of the neurological societies of Israel, Serbia, Poland and Russia. Professor Korczyn's H-index is 73.



PETER LACKNER AUSTRIA

Assoc.-Prof. PD Dr. Peter Lackner is head of the Department of Neurology at Otto-Wagner-Hospital, Vienna, Austria. The focus of the Department is post-acute long term care after critical neurological insults (stroke, traumatic brain injury) as well as long term neurocognitive rehabilitation in an outpatient setting. Prof. Lackner is a trained specialist in neurocritical care and has a long lasting publication record in clinical and experimental research done in the field.



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 and Co-Chair of the Neurotraumatology Scientific Panel 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: neuropiology 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 coorganizer 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 (209 papers indexed on Web of Science-ISI, H-index: 22) 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.



HARI SHANKER SHARMA SWEDEN

Hari Shanker Sharma, Director of Research (International Experimental Central Nervous System Injury & Repair, IECNSIR), University Hospital, Uppsala University is Professor of Neurobiology (MRC), Docent in Neuroanatomy (UU) and is currently affiliated with Department of Surgical Sciences, Division of Anesthesiology and Intensive Care Medicine, Uppsala University, Sweden. Hari Sharma was born on January 15, 1955 in an Industrialist town Dalmianagar (Bihar), India. He did his Bachelor of Science with Honors from the prestigious L. S. College Muzaffarpur in 1973 and secured 1st position in his batch. He obtained his Master Degree from Bihar University for securing 1st potion in the 1st Class. Hari Sharma joined the group of Professor Prasanta Kumar Dey, a neurophysiologist by training in the Department of Physiology, Institute of Medical; Sciences, Banaras Hindu University, Varanasi in 1977 to obtain Doctor of Philosophy Degree (D.Phil.) in Neurosciences

and was awarded Ph.D. in 1982 on "Blood-Brain Barrier in Stress." Hari Sharma after carrying out a series of Government of India funded Research Projects on the BBB and brain dysfunction (1982–1987), joined the lab of Neuropathology at Uppsala University with Professor Yngve Olsson in 1988 to investigate passage of tracer transport across the BBB caused by stress or traumatic insults to the Brain and Spinal cord at light and electron microscopy. Dr. Sharma awarded the prestigious Alexander von Humboldt Foundation Fellowship of German Government (1989–1991) to work on hyperthermia induced BBB dysfunction at the ultrastructural level in the laboratory of Professor Jorge Cervós-Navarro (a living "Legend in Neuropathology in Europe"). Dr. Sharma joined again Uppsala University and established a network of collaboration on "Experimental CNS Injury Research Group" as a lead investigator with eminent collaborators in various parts of Europe, USA, and Australia (1991–). On his work on hyperthermia Dr. Sharma received the prestigious Neuroanatomy award "Rönnows Research prize" of Uppsala University for "best neuroanatomical research of the year 1996" followed by the Award of the Degree of Doctor of Medical Sciences of Uppsala University in Neuroanatomy in 1999 and selected for the Best Thesis Award of the Medical faculty, "The Hwassers Prize" of 1999. On his meticulous works on the Blood Brain barrier and Brain edema (2000–2003) Dr. Sharma earned the prestigious title of "Docent in Neuroanatomy" of Medical Faculty, Uppsala University in April 2004. Currently his main research interest is Neuroprotection and Neuroregeneration, in relation to the Blood-brain barrier in stress, trauma, and drugs of abuse in health and disease.

Dr. Sharma on his research on brain pathology and neuroprotection in different models received the prestigious awards from The Laerdal Foundation of Acute Medicine, Stavanger, Norway, in 2005 followed by Distinguished International Scientists Collaboration Award by National Institute on Drug Abuse (NIDA), Baltimore, MD (2006-2008); NIH Grant on Alzheimer's Disease (2012-), Department of Defense Grant (2017-), NANO-Gov. Grant (2016-). His recent work on 5-HT3 receptor mediated neuroprotection in morphine withdrawal induced neurotoxicity won the coveted prize of Best Investigator Award 2008 and Best Scientific Presentation by European Federation of the International Association for Study of Pain (ISAP), and Awarded during their VI Annual Meeting in Lisbon, September 9–12, 2008. His recent research is aimed to find out the role of nanoparticles in Neurodegeneration and Neuroprotection using various treatment strategies that is supported by European Aerospace Research and Development (EOARD), London, UK and US Air Force Research Laboratory, Wright Patterson Air Force Base, Dayton, Oh, USA. On his works on Bloodbrain barrier in hypertension and diabetes together with Romanian colleagues, University of Medicine and Pharmacy "Iuliu Hatieganu," Cluj-Napoca, Romania awarded Dr. Sharma with Honorary Doctorate of Medical Sciences in 2009. Dr. Sharma's work over 30 years on the blood-brain barrier and brain edema won him the US Neurosurgeon Dr. Anthony Marmarou Award (2011) by the International Brain Edema Society at their 15th Congress in Tokyo, Japan, November 20–24, 2011. His works on Nanoneuroscience and development of nanomedicine to treat the CNS injuries has won accolades at various Government and International Scotties or Organization across the World. Accordingly Dr Sharma was decorated with the most prestigious "Hind Rattan Award 2012" (Jewel of India) on the eve of Republic Day of India 25th January 2012 and Mahatma Gandhi Pravasi Gold Medal on October 12, 2012 in House of Lords, London, UK. Based on his outstanding contribution in Nanoneuropharmacology and nanodrug delivery to treat central nervous system (CNS) diseases including Neurodegenerative diseases such as Alzheimer's and Parkinson's Hari Sharma bestowed with Prestigious Gujarat Govt. International Visionary Award 2012 in a glittering function in Ahmedabad, Gujarat on Nov 23, 2012. His further research on co-morbidity factors e.g., hypertension or diabetes may alter pathophysiology of brain injuries and require higher drug dose or nanodrug delivery of neuroprotective agents to minimize brain dysfunction is recognized by Govt. of India by presenting him one of the coveted "Bharat Jyoti Award 2013" (Glory of India) by His Excellency Governor Balmiki Prasad Singh in Hotel Le Meridien, New Delhi on Jan 12, 2013. Dr Sharma also received the highest Award of the Govt. of India "Navrattan Award 2013" (Nine Jewels of India) on the eve of 64th Republic Day of India (25th January 2013) by His Excellency Governor Bhishma Narain Singh, in Ashok Hotel, New Delhi. Hari Sharma is Founding President of the Global College of Neuroprotection & Neuroregeneration (2004-); Elected President of International Association of Neurorestoratology (IANR) (2014-); and selected Senior Expert of Asia-Pacific CEO Association, Worldwide (APCEO) (2012-) for his contribution to uplift scientific research in many countries Globally that may have better economic and social benefit for the mankind. Hari Sharma awarded coveted National Award "Sword of Honor" 2015 by Govt. of India on the eve of 66th Republic Day of India 25th January 2015 in New Delhi Eros Hotel International during the 34th Non-resident Indian (NRI) conclave by Speaker of Lok Sabha (Indian Parliament) the Hon'ble Mrs Meira Kumar of Indian national Congress (INC) Party for the continued extraordinary achievement in nanomedicine for public health awareness and possible therapeutic measures.

Based on his expertise in Nanoneuroscience, Hari Sharma was also invited to organize and chair Nanosymposium in Society for Neuroscience meetings in Chicago (2009), San Diego (2010), Washington DC (2011), New Orleans (2012), San Diego (2013) and Washington DC (2014, Nov 15-19, 2014), Washington DC Nov 11-15, 2017; San Diego October 3-7, 2018; Chair Neurobiology Symposium 14th Int. Amino Acid & Peptide, Vienna, Austria; Keynote speaker & Chair Nanotechnology-2015, Frankfurt, Germany. Hari Sharma is also the recipient of Prestigious US TechConnect Global Innovation Award 2013 at the National Innovation Summit & Innovation Showcase, Washington DC May 12-16, 2013 on his work on Nanowired cerebrolysin in Neuropathic Pain, followed by Nanodelivery of Cerebrolysin and Neprilysin for the treatment of Alzheimer's disease, Washington DC, May 14-17, 2017. This investigation is now selected for Defense Innovation in Miami Florida Oct 3-5, 2017 for further funding by Dept of Defense (DOD, US Govt). Hari Sharma Served as one of the Poster Judges in 2014 180th Annual Meeting of American Association of Advancement of Science (AAAS) Held in Chicago, IL, USA Feb 13-17, 2014 followed by 181st Annual Meeting of American Association of Advancement of Science (AAAS) held in San José, CA, USA Feb 12-16, 2015; 182nd AAAS Annual Meeting in Washington DC, USA Feb 11-15, 2016 & 183rd Annual Meeting of AAAS held in Boston, MA, USA Feb 16-20, 2017. Chair Nano World Boston, 2018; 2019, Hari Sharma has published over 350 research papers and 85 reviews, 14 monographs, and 80 international book chapters and edited 18 book volumes with Current H-index = 44 (ISI Database) as of today http://apps.webofknowledge.com/CitationReport. do?product=WOS&search mode=CitationReport&SID=F4HK58CYuRYrlSI6qbC&page=1&cr pgid=1&viewType=summary&colName=WOS.

He served as Guest Editor of Curr. Pharm. Desig. (2005, 2007, 2010–); J Neural. Transmiss. (2006, 2011–) and is the founding Editor-in-Chief of Int. J. Neuroprotec. Neuroregen. (2004–), UK and the European Editor of Central Nervous system-Neurological Disorders Drug Target (2013-). Dr. Sharma is on board of various International Journals including CNS and Neurological Disorders-Drug Targets, USA (2010), Journal of Neurodegeneration and Regeneration, USA (2009-); Austin Journal of Nanomedicine & Nanotechnology (2014-); and is associate editor of Journal of Nanoscience and Nanotechnology (Nanoneuroscience 2006-), USA, Review Editor—Frontiers in Neuroengineering (2007-), Frontiers in Neurorestoratology, and Associate Editor of Frontiers in Aging Neuroscience (2008-), Frontiers of Fractal Physiology (2010-), Switzerland, Journal of Neurorestoratology, Dove Medical press, London, UK (2012–), WebMD Central, Neurology Faculty, Advisory Board Member (2010–), World Journal of Pharmacology (2011–), Journal of Physical Medicine and Rehabilitation, USA (2012–). Dr. Sharma served as volume editor of several progress in Brain research series (Volumes 104, 115, 162 and 180, 245), International review of Neurobiology (Volume 82 and 102, 146) and other Springer Volumes on Spinal cord injury (1988) and Handbook of Neurochemistry (2009) apart from stand alone books (Elsevier, Springer and Academic Press since 1994). His latest edited and contributed Reference Book Drug and Gene Delivery to the Central Nervous System for Neuroprotection. Nanotechnological Advances from Springer Nature Publishing (June 2017; Sharma, Muresanu & Sharma Eds.) became a bestseller book on the subject. His new Volume of International review of Neurobiology (IRN) 137 "Nanomedicine in CNS Injury & Repair" Edited by Hari S Sharma & Aruna Sharma Academic Press, Elsevier, San Diego, CA, USA is just published on November 14, 2017. Dr. Hari Sharma is invited to join several National Academies of repute including New York Academy fo Science, USA (since 1994–); International Academy of Stress, New York (2003–), Swedish Academy of Pharmaceutical Sciences (2010–). Dr. Sharma has served as an expert evaluator and advisor to various Boards, Councils and Institutions for their Research Grants including Wellcome Trust, London, UK (2011–); Catalan Agency for Health Information and Quality, TV3 (2010-), European Commission Projects (2002-), European Nanomed Council (2009–), Ministry of Health Science Foundation; Medical research Council and University Commission of Grants in various countries in Europe, USA, UK, Canada, Hong Kong, Singapore and in Australia. Some of the notable organizations include: Australia and New Zealand Health Council (2000-); University Commission of Grants, Hong Kong (2002–), Singapore Medical Council, Singapore (2003–); UK Charity Organization "Research on Ageing: Help the Aged" (2003-); Euro Nanomed (2010-). Dr. Sharma is designated as ambassador of the City of Uppsala 2007, by Uppsala County administration and Uppsala Tourism for promoting Uppsala, Sweden as International Research Collaboration/Meetings and Conference Destination. Dr. Hari Sharma is married to Aruna Sharma (nee Bajpai) since 23rd April 1979 and has two sons. Dr Sharma is designated as Visiting Professor, University of Basque Country, Bilbao, Spain supported by Basque Govt. Foundation. His political affiliation belongs to Swedish Social Democrat Party (Socialdemokraterna, Sverige) where he is associated with the development of Education and Research matters in Sweden actively.



STEFAN STRILCIUC ROMANIA

Stefan Strilciuc is a public health specialist. His work is focused on management, data analysis, dissemination of interventional and observational clinical research studies, as well as economic evaluation in health. He serves on the Board of Governors of the European University of Brain and Technology (NeurotechEU) and the Health Technology Assessment Task Force of the Romanian Ministry of Health. He is a member of the Professional Society for Health Economics and Outcomes Research (ISPOR), currently working to reveal the economic burden of stroke in Romania within ongoing doctoral studies.

Strilciuc is also the Executive Director of the RoNeuro Institute for Neurological Research and Diagnostic, the Foundation of the Society for the Study of Neuroprotection and Neuroplasticity, and the Journal of Medicine and Life. In previous years, he has also worked with the Romanian Health Observatory on designing and disseminating original research reports and advocacy plans for patients in Eastern Europe.



JOHANNES VESTER GERMANY

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 completed the curriculum on biostatistics 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.

Since 1982 he holds > 100 advanced training courses on biometry for professionals in clinical research as well as teaching courses for universitary institutions and international societies.

From 1985 to 1995, he was member of the Ultrahigh Dexamethasone Head Injury Study Group and the leading biometrician of the German GUDHIS trial in Traumatic Brain Injury. Since 1995 he is Senior Consultant for Biometry & Clinical Research at the Institute for Data Analysis and Study Planning (IDV). He planned and evaluated about 150 randomized clinical studies worldwide and is member of various international Advisory Boards and Steering Committees including participation as biometric expert in regulatory authority panels, in FDA, EMA, and BfArM hearings, and in workshops of the International Biometric Society (IBS).

Statistical peer reviewer for leading medical journals such as Stroke (American Heart Association).

Since 2013 Statistical Expert and Elected Member of the International Scientific Committee of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN).

Since 2013 Statistical Expert and Elected Member of the World Academy for Multidisciplinary Neurotraumatology (AMN).

Since 2015 Member of the PhD Neuroscience International Faculty, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Since 2017 Invited Associate Professor, Department of Neuroscience, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Since 2018 Co-Chair EAN Guideline Task Force Neurorehabilitation.

Since 2018 Head Biometry & Clinical Research at the Institute for Data Analysis and Study Planning (IDV).

Since 2018 President of the Academy for Multidisciplinary Neurotraumatology (AMN).

GENERAL INFORMATION



GENERAL INFORMATION

LOGISTIC PARTNERS





Foundation for the Society for the Study of Neuroprotection and Neuroplasticity 37 Mircea Eliade Street, 400364, Cluj-Napoca, Romania Mr. Ovidiu Selejan: +40745255311 E-mail:office@ssnn.ro

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. Global Travel & More

21 Rapsodiei Street, Ap 15 Cluj Napoca, Romania tel.: +40364137103 office@global-t.ro

Synapse Travel

37 Calea Motilor, Ap 6 Cluj Napoca, Romania office@synapsetravel.ro synapsetravel.ro

Contact Details

Mrs. Doria Constantinescu, mobile: +40757096111 doria@synapsetravel.ro

FINAL PROGRAM & ABSTRACT BOOK

Available online <u>here</u>

TIME

The program hours are adjusted to Current Local Time in Bucharest, Romania, Eastern European Summer Time, UTC/GMT +3 hours

ORGANIZERS



Foundation of the Journal for Medicine and Life www.medandlife.org



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



"RoNeuro" Institute for Neurological Research and Diagnostic www.roneuro.ro



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"Danube" -University Krems www.donau-uni.ac.at



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