

15TH CONGRESS OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

IN CONJUNCTION WITH
THE 12TH ASIAN CONFERENCE ON
NEUROGENESIS AND NEUROPLASTICITY



8TH NOVEMBER 2019 | PULLMAN BAKU HOTEL | BAKU | AZERBAIDJAN

CONGRESS CHAIRMEN



DAFIN F. MUREȘANU

President of the European Federation of
NeuroRehabilitation Societies (EFNR)

Chairman of EAN Communication and Liaison Committee

Member of EAN Scientific Committee

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



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

FACULTY

IN ALPHABETICAL ORDER

Natan M. Bornstein / **Israel**
Michael Brainin / **Austria**
Michael Chopp / **USA**
Antonio Federico / **Italy**
Wolf Dieter Heiss / **Germany**
Max J. Hilz / **Germany**
Volker Hömberg / **Germany**
Axel Kohlmetz / **Austria**
Hyun Haeng Lee / **South Korea**
Dafin F. Mureşanu / **Romania**
Ignacio J. Previgliano / **Argentina**
Hari Shanker Sharma / **Sweden**
Ştefan Strilciuc / **Romania**
Nguyen Huy Thang / **Vietnam**
Johannes Vester / **Germany**

SCIENTIFIC PROGRAM



SCIENTIFIC PROGRAM

FRIDAY, NOVEMBER 8TH, 2019

08:45 – 09:00

WELCOME ADDRESS

PRESIDENTIAL SESSION

CHAIRPERSONS: Dafin F. Mureşanu (Romania), Natan M. Bornstein (Israel)

09:00 – 09:30

Dafin F. Mureşanu (Romania)

Stroke and microcirculation - is there a chance for an add-on therapy to improve post-stroke reperfusion and hemorrhagic transformation?

09:30 – 10:00

Natan M. Bornstein (Israel)

Predictors of post stroke cognitive impairment - The TABASCO study and beyond

10:00 – 10:30

Michael Brainin (Austria)

Cognitive disorders after stroke: classification and perspectives for therapy

10:30 – 11:00

Johannes Vester (Germany)

New vistas in TBI research – results from CAPTAIN studies and the multidimensional methodology

11:00 – 11:15

COFFEE BREAK

SESSION 2

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

- | | |
|---------------|--|
| 11:15 - 11:45 | Volker Hömberg (Germany)
How to deal with „proportional recovery“ in impairment - oriented neurorehab: role of pharmacological options in combination with training |
| 11:45 - 12:15 | Michael Chopp (USA)
Cerebrolysin - a potent microvascular therapy for stroke |
| 12:15 - 12:45 | Max Hiltz (Germany)
Altered autonomic responses to happy and fearful music in patients with a history of mild traumatic brain injury |
| 13:00 - 14:30 | LUNCH |

SESSION 3

CHAIRPERSONS: Max Hiltz (Germany), Michael Chopp (USA)

- | | |
|---------------|--|
| 14:30 - 15:00 | Axel Kohlmetz (Austria)
The relevance of case reports and case series |
| 15:00 - 15:30 | Nguyen Huy Thang (Vietnam)
Update of spontaneous intracerebral hemorrhage treatment |
| 15:30 - 16:00 | Ignacio Previgliano (Argentina)
Cognitive impairment in the post-ICU Syndrome: the potential of neurotrophic modulation for prevention and rehabilitation |
| 16:00 - 16:30 | Hyun-Haeng Lee (South Korea)
Synergistic effect of cerebrolysin and amantadine on disorders of consciousness secondary to acquired brain injury: a retrospective case control study |
| 16:30 - 16:45 | COFFEE BREAK |

SESSION 4

CHAIRPERSONS: Hari Shanker Sharma (Sweden), Antonio Federico (Italy)

- | | |
|---------------|--|
| 16:45 - 17:15 | Antonio Federico (Italy)
Genetic small vessel diseases: updates in CADASIL and related conditions |
| 17:15 - 17:45 | Hari Shanker Sharma (Sweden)
Methamphetamine exacerbates Alzheimer's disease pathology. Neuroprotective effects of nanowired neurotrophic factors with neprilysin |
| 17:45 - 18:15 | Wolf Dieter Heiss (Germany)
Non-invasive brain stimulation in rehabilitation after stroke |
| 18:15 - 18:45 | Ștefan Strilciuc (Romania)
Economic evaluation for stroke interventions in Romania: where do we start? |
| 18:45 - 19:00 | CLOSING REMARKS |

ABSTRACTS



PREDICTORS OF POST STROKE COGNITIVE IMPAIRMENT - THE TABASCO STUDY AND BEYOND

NATAN BORNSTEIN

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

After stroke patients frequently experience a spectrum of neuropsychological and motor deficits resulting in impaired activities; cognitive and functional. About 20%-25% of patients after stroke will develop cognitive impairment/dementia in the months following the event.

It is still not clear who are those patients that are prone to post-stroke cognitive decline. Who are the vulnerable patients?

The aim of the Tel-Aviv Brain Acute Stroke Cohort (TABASCO) is to characterize inflammatory, stress and neuroimaging biomarkers that may predict and detect the vulnerable subjects and might outline new concepts of early interventions and novel treatment strategies for those at higher risk. The TABASCO study and its findings will be discussed.

Currently the pharmacological treatment of Post-Stroke cognitive impairment includes AchE-Is with only modest benefit.

Another used treatment is CITICOLINE (cytidine 5 diphosphocholine - (CDP-Choline)). A meta-analysis of all the studies that was conducted in 2016 concluded that although citicoline appears to be safe and maybe beneficial, large clinical trials are needed to confirm its benefits.

Cerebrolysin, a multimodal drug, that mimics neurotrophic factors and maintains, protects and restores neuronal function. A COCHRANE review was conducted on the studies of cerebrolysin 10-30 ml/day in vascular dementia (2013) concluded it is beneficial and safe.

To conclude, the combination of behavioral and safe and effective pharmacological adjuvant therapies will significantly improve and promote brain recovery after stroke including cognitive impairment.

COGNITIVE DISORDERS AFTER STROKE: CLASSIFICATION AND PERSPECTIVES FOR THERAPY

MICHAEL BRAININ

President Elect, World Stroke Organisation

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

Disorders of cognition (neurocognitive disorders) following stroke occur between 7% in population-based studies of first-ever stroke patients and 41% in hospital-based studies which includes recurrent strokes. Milder forms of cognitive deterioration following stroke were found between 22% and 84% depending on definition, testing, and time of investigation. Incidence rates are 2-3% increasing annually at linear rates. Importantly, milder forms can also be quite disabling and hinder rehabilitation and reuptake of occupational and social roles. Probably all stroke patients are at risk of suffering from cognitive deterioration but some risk factors are more important than others such as location of stroke, initial stroke severity, previous strokes, level of pre-stroke cognition and presence of vascular risk factors. Genetic and inflammatory biomarkers are under investigation but observational data suggest that high levels of interleukins and C-reactive protein have predictive value. Cognitive and brain reserve can protect against cognitive deterioration and depends on education, leisure activities and social interactions. Moreover, diagnosis of post-stroke cognitive deterioration (mild neurocognitive disorder) varies according to test instruments used. Usually, a short bedside test is used and an extended neuropsychological test battery is applied later. Variations also result from speech disturbances, emotional disorders such as depression. CT and MRI confirm the diagnosis and provide additional information on location and size of infarct, previous infarcts, white matter lesions, microbleeds, and brain atrophy. Management focuses on prevention and includes cognitive training and modification of risk factors. Life-style modifications have been shown to be beneficial in preventing cognitive decline in persons at risk of dementia. To date, exploratory drug trials and case series have shown promising effects in stroke patients and are under further investigation.

For future clinical use, there are two options: one is to develop a highly selective drug which inhibits epigenetically triggered factors involved in harmful activation of immunomodulatory pathways and thus protects against decline in a yet to be specified, high-risk population. In these patients the high risk is defined by raised levels of circulatory markers or brain lesion analysis defined from neuroimaging. The other perhaps more promising option is based on a multiple factor causation of cognitive decline triggered by a cascade of events known to be triggered by ischemic lesions. For this approach, a less specific but multimodal approach

therapy can be applied to all post-stroke patients who are at risk for developing a post-stroke cognitive disorder. Currently efforts for both models are under way. Immune-modulatory substances known to foster remyelination in other neurological diseases are currently being tested (in a very narrow indication) and on the other hand the multimodal neuromodulator Cerebrolysin is being tested (in a very broad indication) for prevention of post-stroke cognitive disorders in a multicentre trial.

CEREBROLYSIN - A POTENT MICROVASCULAR THERAPY FOR STROKE

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 focus on Cerebrolysin as a vascular therapy which protects and restores the cerebral microvasculature to ensure the integrity of the blood brain barrier and to reduce any secondary post injury inflammatory effects. I will also propose the use of Cerebrolysin as an adjunctive therapy for mechanical thrombectomy (MT) and thrombolysis with tPA for the treatments of acute and subacute stroke.

The only approved treatments of acute ischemic stroke are: 1)mechanical thrombectomy (MT), performed within 24 hours of a large vessel arterial stroke, and 2) thrombolysis performed within 4.5 hours. These treatments although highly beneficial, are far from perfect. The majority of patients subjected to MT and thrombolysis do not have complete restoration of tissue perfusion and retain functional and neurological deficits post treatment. I will briefly review vascular changes that occur in the arterial and microvascular levels after MT and tPA thrombolysis. The clot itself while in the artery changes in time and becomes more platelet rich, making it more difficult to lyse with tPA. The arterial site of the clot also undergoes damage with the breakdown of vascular structure and upregulation of prothrombotic molecules. Even if the clot is removed within the appropriate time window, there is the well known no-reflow phenomenon. One can have a patent artery yet low tissue perfusion. Low tissue perfusion caused by secondary thrombosis and inflammatory changes within the microvasculature resulting in a prothrombotic, procoagulant and proinflammatory state of the microvasculature. This causes the growth of the penumbra and subsequent parenchymal cell

dysfunction. Importantly, a major contributor to the proinflammatory state within these vessels is the deposition of fibrin. Fibrin evokes potent proinflammatory conditions.

I will show that Cerebrolysin is fully capable of ameliorating the pro-coagulant-thrombotic and inflammatory state of the microvasculature post stroke. I provide data from an in vitro model of the human blood brain barrier and show that Cerebrolysin can obviate adverse vascular conditions caused by fibrin deposition and treatments with TPA.

I will then describe the underlying therapeutic mechanisms responsible for the beneficial effects of Cerebrolysin. I will demonstrate the Cerebrolysin stimulates vascular expression of the highly anti-inflammatory molecule Angiopoietin 1 (Ang1). Ang1 is a vascular protective and restorative molecule. In addition, I introduce microRNAs, non-coding RNAs which can concurrently regulate post-transcriptionally hundreds of genes. I note, based on our previous work that Cerebrolysin stimulates vascular and parenchymal upregulation of an important morphogen and transcription factor, Sonic Hedgehog (SHH). We have shown that SHH upregulates the expression of a very important family of microRNAs, miR-17-92. This miR -17-92 family promotes brain plasticity and neurovascular benefit post stroke and traumatic brain injury. Importantly, the miR-17-92 family has also been shown to ameliorate anxiety and depression. Thus, Cerebrolysin by stimulating tBACE generation and expression of important proteins and non-coding RNAs plays a vital role in neurovascular recovery. Particularly its impact on the microvasculature compels the investigation of Cerebrolysin in combination with presently approved MT and thrombolysis. We expect that the combination therapy of Cerebrolysin with MT/tPA would greatly augment their safety and therapeutic benefit leading to improved neurological outcomes post stroke. As a highly effective microvascular restorative treatment, Cerebrolysin has potent therapeutic potential for many cerebrovascular-based injuries and degenerative diseases.

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.

NON-INVASIVE BRAIN STIMULATION IN REHABILITATION AFTER STROKE

WOLF-DIETER HEISS

Emeritus Director of the Max Planck Institute for Neurological Research, Cologne, Germany

The functional deficit after a focal brain lesion is determined by the localization and the extent of the tissue damage. Since destroyed tissue usually cannot be replaced in the adult human brain, improvement or recovery of neurological deficits can be achieved only by reactivation of functionally disturbed but morphologically preserved areas or by recruitment of alternative pathways within the functional network. The visualization of disturbed interaction in functional networks and of their reorganization in the recovery after focal brain damage is the domain of functional imaging modalities such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI).

Longitudinal assessments at rest and during activation tasks during the early and later periods following a stroke can demonstrate recruitment and compensatory mechanisms in the functional network responsible for complete or partial recovery of disturbed functions. Imaging studies have shown that improvements after focal cortical injury are represented over larger cortical territories, an effect which appears to be dependent on the intensity of rehabilitative training. It has also been shown that the unaffected hemisphere in some instances actually inhibits the recovery of ipsilateral functional networks and this effect of transcallosal inhibition can be reduced by non-invasive brain stimulation.

Non-invasive brain stimulation (NIBS) can modulate the excitability and activity of targeted cortical regions and thereby alter the interaction within pathologically affected functional networks; this kind of intervention might promote the adaptive cortical reorganization of functional networks after stroke. Non-invasive brain stimulation (NIBS) uses direct current (DCS: excitation under the anode, inhibition under the cathode) or repetitive transcranial magnetic stimulation (rTMS: excitatory at high frequency, inhibitory at low frequency). Since recovery from poststroke deficits seems to be more effective in patients who recover function in the ipsilateral perilesional area, NIBS trials aimed to activate this region: this effect can be achieved by excitatory NIBS (high frequency repetitive transcranial magnetic stimulation, rTMS; intermittent theta burst stimulation, iTBS; anodal transcranial direct current stimulation, tDCS) to reactivate the

perilesional area or by inhibitory NIBS (low frequency rTMS or cathodal tDCS) to reduce increased activities in the contralesional homologous areas.

DCS as well as rTMS were applied in combination with rehabilitative measures in order to improve various symptoms after stroke, especially motor deficits and aphasia. In both applications recovery was improved with combined treatment in comparison to standard therapy without NIBS. All types of NIBS were used in rehabilitation of motor deficits after stroke and positive effects on recovery were observed. Among the different modalities low-frequency inhibitory stimulation of the motor cortex in the contralateral non-affected hemisphere seems to be the most prominent approach, but large controlled trials are still missing.

In poststroke aphasia several studies attempted to restore perilesional neuronal activity in the injured left inferior frontal gyrus by applying excitatory high frequency rTMS or iTBS or anodal tOCS to small series of patients in the chronic stage : They showed favorable effects in speech performance for several weeks to a few months. Only one study coupled ipsilesional anodal tOCS to language therapy in chronic nonfluent aphasia and observed improved speech / language performance for 1 week to 2 months. Most NIBS studies in poststroke aphasia employed inhibitory low frequency rTMS for stimulation of the contralesional pars triangularis of the right inferior frontal gyrus (BA 45) in order to reduce right hemisphere hyperactivity and transcallosal inhibition on the left Broca's area. Most studies reported single cases or small case series with chronic poststroke aphasia without any control condition and beneficial effects on speech performance lasting for several months. Only a few controlled studies including sham stimulation were performed in chronic stage after stroke. A controlled trial with inhibitory cathodal toes stimulation of the non-dominant right Wernicke area in patients with subacute global aphasia resulted in some improvement of comprehension in the treatment group. In one controlled randomized study changes in PET activation pattern in the subacute course were related to the clinical improvement. The shift of the activation pattern to the dominant hemisphere induced by inhibitory rTMS over the right inferior frontal gyrus could be demonstrated in the PET activation studies and correlated to improved performance in aphasia tests. NIBS might be a treatment strategy which could improve the effect of other rehabilitative efforts.

With NIBS positive effects were also obtained in hemineglect, memory dysfunction and cognitive decline after stroke. A combination of NIBS with multimodally acting drugs with neurotrophic efficacy might improve chances for recovery.

ALTERED AUTONOMIC RESPONSES TO HAPPY AND FEARFUL MUSIC IN PATIENTS WITH A HISTORY OF MILD TRAUMATIC BRAIN INJURY

MAX J. HILZ^{1,2}

RUIHAO WANG¹, KATHARINA M. HÖSL³, DAFIN FIOR MUREȘANU⁴, MAO LIU^{1,5}

1. Department of Neurology, University of Erlangen-Nuremberg, Erlangen, Germany
2. Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY, USA
3. Department of Psychiatry and Psychotherapy, Paracelsus Medical University, Nuremberg, Germany
4. Department of Neurosciences, Iuliu Hațieganu University of Medicine and Pharmacy and RONEURO INSTITUTE, Center for Research and Diagnosis of Neurological Diseases, Cluj-Napoca, Romania
5. Department of Neurology, Tongji Hospital and Medical College, Wuhan, Hubei Province, P.R. China

Background: Even after mild traumatic brain injury (mTBI) there may be long-lasting changes in autonomic responses to emotional stimuli. Happy or fearful music triggers emotional perception and autonomic responses. So far, these responses have not been evaluated in patients with a history of mTBI (post-mTBI-patients).

Objective: To assess cardiovascular autonomic responses to happy and fearful music in post-mTBI-patients.

Methods: In 24 post-mTBI-patients (35.3±2.7 years; 6 women, interval since mTBI 32.8±5.6 months) and in 26 healthy persons (30.4±2.3 years; 10 women), we monitored respiration, RR-intervals (RRIs), systolic and diastolic blood pressure (BPsys, BPdia) at rest and during presentation of 3-minute excerpts of “happy” music (Marriage of Figaro, Overture, K. 492) and “fearful” music (The miraculous Mandarin, Suite, Op. 19). Participants rated “happiness” and “fear” on Likert-scales from 1 to 5.

Results: Likert-scores assigned to happy and fearful music were similar in patients and controls. “Happy” music accelerated respiration only in controls (14.1±0.7 vs 16.0±0.7 bpm), increased BPsys in controls (134.0±3.5 vs 137.7±3.5 mmHg) and patients (129.6±3.0 vs 134.0±3.2 mmHg), but did not change BPdia and RRIs. “Fearful” music did not change respiration or RRIs, increased BPsys in controls (130.9±3.1 vs 135.1±3.3 mmHg) and patients (130.0±3.6 vs 134.3±3.7 mmHg), but increased BPdia only in controls (67.4±1.9 vs 68.8±2.1 mmHg).

Conclusion: The similar emotional ratings of the musical stimuli in patients and controls suggest that the patients’ emotional perception of “happy” and “fearful” music was not significantly compromised at the time of study, 32.8±5.6 months after the mTBI. In contrast, lack of respiration-acceleration with happy music and

BPdia-increase with fearful music in the patients indicates persistence of subtle changes in sympathetic processing of musical stimuli even months to years after mild TBI. The findings suggest that central autonomic regulation might be more vulnerable to mTBI than is the perception of emotional stimuli.

HOW TO DEAL WITH „PROPORTIONAL RECOVERY“ IN IMPAIRMENT - ORIENTED NEUROREHAB: ROLE OF PHARMACOLOGICAL OPTIONS IN COMBINATION WITH TRAINING

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. This is more than just a “philosophical” question because the necessary strategies may be different, following different neurobiological and behavioral rules. We have been very enthusiastic in successfully adopting elementary rules derived from basic work on motor learning into motor rehab by optimizing trajectories in patients who have maintained the ability to move at all (at least a little bit) , but we don’t really know if such “task-specific” motor learning is effective in people who cannot move at all.

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 demonstrated to apply for impairments in non-motor domains as neglect and language abilities (Lazar et al 2010, Marchi et al 2017). 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.

In animal experimentation so called „enriched environments“ have been proven to facilitate brain repair. There has however been no translation from this experimental animal world to the clinical bedside.

This enigma increases the need for better pharmacological options to improve impairment in 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 for the multimodal drug cerebrolysin, a mix of neurotrophic factors: The CARS trial (Muresanu et al 2016) documented for the first time after decades of frustrating attempts to achieve some sort of neuroprotective and/or neurorestorative effects that a multimodal drug can improve impairment after stroke. This was further corroborated in a consecutive trial (Guekht et al 2017) and further corroborated by a metaanalysis of stroke related trials with cerebrolysin (Bornstein et al 2018). The CAPTAIN trial looking at cerebrolysin effects in TBI in a multidimensional approach is on the way.

These trials 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.

Possible additional candidates for a true „impairment“ oriented treatment approach are neuromodulatory techniques such as peripheral neuromuscular and/ or sensory stimulation (eg. whole hand subliminal „mesh-glove“ stimulation) and more and more also noninvasive brain stimulation techniques such as repetitive transcranial magnetic stimulation and transcranial DC stimulation. Also the use of non-fatigable robotic devices to enable a high intensity massed movement treatment appear promising.

As treatment intensity is likely to be the key element for impairment reduction we certainly have to find clever and affordable ways: to increase the daily treatment time of our patients. Today even during inpatient rehabilitation treatment times hardly exceed three hours a day i.e. that we use only a small percentage of waking hours leaving long „idling“ time not filled by any treatment. In this sense we have

to “reinvent” neurorehabilitation within this sensitive post injury period to combat impairment with high frequency treatments combined with neuromodulatory techniques (robot use, peripheral and central stimulation, pharmaceuticals) .

Probably the most important impact in facilitating impairment reduction will however have clever, economically feasible, approaches to increase the net number of therapy or activity hours per day by creating true „ enriched environment“ for severely impaired patients. They should enable 6-8 hours of daytime treatment to avoid leaving our patients „inactive and alone“ in future.

References:

Wolf SL, Winstein CJ, Miller JP, Thompson PA, Taub E, Uswatte G, Morris D, Blanton S, Nichols-Larsen D, Clark PC

Retention of upper limb function in stroke survivors who have received constraint-induced movement therapy: the EXCITE randomised trial.
Lancet Neurol. 2008 Jan;7(1):33-4

Chollet F, Tardy J, Albucher JF, Thalamas C, Berard E, Lamy C, Bejot Y, Deltour S, Jaillard A, Niclot P, Guillon B, Moulin T, Marque P, Pariente J, Arnaud C, Loubinoux I.

Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial.

Lancet Neurol. 2011 Feb;10(2):123-30. doi: 10.1016/S1474-4422(10)70314-8. Epub 2011 Jan 7.

Muresanu DF, Heiss WD, Hoemberg V, Bajenaru O, Popescu CD, Vester JC, Rahlfs VW, Doppler E, Meier D, Moessler H, Guekht A

Cerebrolysin and Recovery After Stroke (CARS): A Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial

Stroke. 2016 Jan;47(1):151-9. doi: 10.1161/STROKEAHA.115.009416. Epub 2015 Nov 12

Alla Guekht, Johannes Vester, Wolf-Dieter Heiss, Eugene Gusev, Volker Hoemberg, Volker W. Rahlfs, Ovidiu Bajenaru, Bogdan O. Popescu, Edith Doppler, Stefan Winter, Herbert Moessler, Dafin Muresanu

Safety and efficacy of Cerebrolysin in motor function recovery after stroke: a meta-analysis of the CARS trials

Neurol Sci 2017 DOI 10.1007

Bernhardt J, Dewey H, Thrift A, Donnan G.

Inactive and alone: physical activity within the first 14 days of acute stroke unit care.

Stroke. 2004 Apr;35(4):1005-9.

Lazar RM, Minzer B, Antonietto D, et al.

Improvement in aphasia scores after stroke is well predicted by initial severity.

Stroke 2010;41:1485–1488.

Marchi NA1, Ptak R1, Di Pietro M1, Schnider A1, Guggisberg AG

Principles of proportional recovery after stroke generalize to neglect and aphasia.

Eur J Neurol. 2017 Aug;24(8):1084-1087. doi: 10.1111/ene.13296. Epub 2017 Jun 6.

Prabhakaran S, Zarahn E, Riley C, et al.
Inter-individual variability in the capacity for motor recovery after ischemic stroke.
Neurorehabil Neural Repair 2008;22:64–71.

Bornstein NM, Guekht A, Vester J, Heiss WD, Gusev E, Hömberg V, Rahlfs VW, Bajenaru O, Popescu BO, Muresanu D.
Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials.
Neurol Sci. 2018 Apr;39(4):629–640.

The FOCUS Trial Collaboration
Effects of fluoxetine on functional outcomes after acute stroke (FOCUS): a pragmatic, double-blind, randomised, controlled trial
Lancet 2019; 393: 265–74

THE RELEVANCE OF CASE REPORTS AND CASE SERIES

AXEL KOHLMETZ

Austria

Historically, case reports have been important for recognizing new or rare diseases, evaluating the therapeutic effects, adverse events, and costs of interventions; and improving problem-based medical education.

They provide evidence for effectiveness in a real-world setting, whereas clinical trials provide evidence for the efficacy of interventions in a controlled setting. Both are necessary. Case reports today make up an increasing percentage of the articles in peer reviewed medical journals and have provided key milestones in our understanding of specific diseases – examples will be part of the lecture.

Case reports have a high sensitivity for detecting novel treatment options and are a cornerstone of medical progress.

New guidelines and checklists, developed by an international group of experts were designed to increase the accuracy, transparency and usefulness of case reports. If strictly followed by authors, case reports:

- demonstrate early signals of benefits, harms, and value of a specific treatment
- provide information about resource utilization including cost
- support larger scale clinical research
- are a practice-base feedback for clinical practice guidelines (CPGs)
- are a valuable source for medical education

SYNERGISTIC EFFECT OF CEREBROLYSIN AND AMANTADINE ON DISORDERS OF CONSCIOUSNESS SECONDARY TO ACQUIRED BRAIN INJURY: A RETROSPECTIVE CASE CONTROL STUDY

HYUN HAENG LEE¹

SEUNGHWAN LEE¹, HYUN HAENG LEE¹, YEJIN LEE⁴, JONGMIN LEE^{1,2,3,*}

1. Department of Rehabilitation Medicine, Konkuk University School of Medicine and Konkuk University Medical Center, Seoul, Korea

2. Center for Neuroscience Research, Institute of Biomedical Science & Technology, Konkuk University, Seoul, Korea

3. Research Institute of Medical Science, Konkuk University School of Medicine, Seoul, Korea

4. Program in Occupational Therapy, Washington University School of Medicine, St. Louis, MO, USA

Background: Acquired brain injury (ABI) can cause disorders of consciousness (DOCs). A synergistic effect of cerebrolysin and amantadine has been postulated, but not systematically studied. The present study aimed to investigate the synergistic effect of them in patients with a DOC secondary to ABI.

Methods: We reviewed the patients diagnosed with a DOC after ABI. The patients were categorized into two groups: single regimen (amantadine only) and dual regimen (amantadine plus cerebrolysin). The patients' conscious state was assessed using the Coma Recovery Scale-Revised (CRS-R).

Results: We enrolled 89 patients. We found that the degree of CRS-R change and the ratio of patients with change of DOC category was higher in the dual regimen group than in the single regimen group. By analyzing the patients who had initially been in vegetative state before administration, we showed that the initial CRS was lower while the follow-up CRS was higher in the dual regimen group than in single regimen group, albeit without significance in either case.

Conclusions: We identified how amantadine plus cerebrolysin regimen and amantadine-alone regimen affected DOC patients. A future controlled trial is needed to investigate the efficacy of each regimen in patients with DOC secondary to ABI.

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

DAFIN F. MUREȘANU

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.

METHAMPHETAMINE EXACERBATES ALZHEIMER'S DISEASE PATHOLOGY. NEUROPROTECTIVE EFFECTS OF NANOWIRED NEUROTROPHIC FACTORS WITH NEPRILYSIN

HARI SHANKER SHARMA¹

***DAFIN F MURESANU^{2,3}, HERBERT MÖSSLER⁴, ALA NOZARI⁵, RUDY J CASTELLANI⁶, Z RYAN TIAN⁷,
SEAAH SAHIB⁷, ARUNA SHARMA¹***

1. International Experimental Central Nervous System Injury & Repair (IECNSIR), Dept. of Surgical Sciences, Anesthesiology & Intensive Care Medicine, Uppsala University Hospital, Uppsala University, SE-75185 Uppsala, Sweden;
2. Dept. Clinical Neurosciences, University of Medicine & Pharmacy, Cluj-Napoca, Romania;
3. "RoNeuro" Institute for Neurological Research and Diagnostic, 37 Mircea Eliade Street, 400364, Cluj-Napoca, Romania
4. Ever NeuroPharma, Oberburgau, Austria
5. Anesthesiology & Intensive Care, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, USA
6. Department of Pathology, University of Maryland, Baltimore, MD 21201, USA
7. Department of Chemistry and Biochemistry; University of Arkansas- Fayetteville; Fayetteville, AR 72701 USA

BACKGROUND

Alzheimer's disease (AD) is a devastating neurological ailment imposing lifetime disabilities causing heavy financial burden on the society. AD reflect lifetime behavior and stressors that affect the mental function culminating into the disease with advanced aging. Several risk factors of AD are well known such as traumatic brain injury, hypertension, diabetes and/or posttraumatic stress disorders (PTSD). These risk factors accelerate or exacerbate the pathogenesis of AD. However, apart from these well known risk factors of AD, studies on substance abuse

affecting AD pathology is still not well known. Use of methamphetamine (METH), cocaine, morphine, MDMA and other addictive substances are quite common in the society that affects mental and physical health. However their impact on AD pathophysiology are not known. In this study, we examined effects of METH on the pathogenesis of AD in an animal model.

METH when administered alone leads to hyperthermia and breakdown of the blood-brain barrier (BBB) permeability associated with edema formation and cell injuries. Thus, a possibility exists that METH users may have a high risk factor for developing AD.

Male Wistar rats (age 30-35 weeks) were administered METH (0.5 mg/kg, per day s.c.) for 1 week. This dose of METH causes slight hyperthermia on the first 3 days with abnormal behavior such as hyperlocomotion, mild jumping, grooming and restlessness. After that by 7th day these animals look quite normal and do not show abnormal behavior. These animals showed mild to moderate leaking of Evans blue in their brain on the 7th day showing BBB breakdown.

METHODS

AD like pathology was developed in naïve or chronic METH treated rats by administering A β P (1-40) intraventricularly (i.c.v.) in the left lateral ventricle (250 ng/10 μ l) once daily for 4 weeks. Control rats received saline instead of METH. In separate group of rats TiO₂ nanowired cerebrolysin (NWCBL 50 μ l) and or nanowired neprilysin (NWNPL, 100 ng/10 μ l) were administered (i.c.v.) once daily 3 weeks after the 1st A β P administration and continued for 1 week. After 30 days of the 1st A β P infusion, the rats were examined for BBB breakdown, edema, neuronal, glial injuries and A β P deposits in their brain.

RESULTS

Our observations showed that A β P infusion in METH intoxicated rats exacerbated 3- to 4-fold higher BBB breakdown to Evans blue albumin and radioiodine ([¹³¹I]-I) in several brain areas as compared to naïve rats after identical A β P treatment. The brain edema formation was also exacerbated by 1.5 to 2 fold in those brain areas showing BBB breakdown. Radioimmunoassay of A β P showed 60 to 120 % higher deposits in METH treated AD group whereas NPL measurement showed 40 to 68 % decrease in several brain regions in METH intoxicated AD group as compared to control AD rats. Cell injuries showed massive upregulation of neuronal injuries as seen by Nissl or H&E staining in AD group with METH intoxication as compared to normal AD rats.

Treatment with NWCBL and NWNPL together was significantly able to thwart BBB breakdown, edema formation and cell injuries in METH treated AD groups. In these

METH treated AD rats NWCBL and NWNPL therapy also restored NPL level and decreased A β P deposition in METH treated AD rats. However, in METH treated AD groups NWCBL alone or NWNPL alone showed only mild to beneficial effects.

CONCLUSIONS

These observations are the first to show that METH intoxication exacerbates AD pathology probably by higher accumulation of A β P deposits and greater reduction in NPL levels in the brain. Thus, METH users in the society are also highly vulnerable to AD pathology and for that awareness is needed to understand the dangers of METH abuse with regard to AD, not reported earlier.

*Acknowledgements. This investigation was supported by Grants from Swedish Medical Research Council Nr. 2710; Grants from the Alzheimer's Association (IIRG-09- 132087), the National Institutes of Health (R01 AG028679) and the Dr. Robert M. Kohrman Memorial Fund (MAS, RJC); Society for Neuroprotection and Neuroplasticity (SSNN), Romania; Astra Zeneca, Mölndal; Göran Gustafsson Foundation, Stockholm, Sweden; Alexander von Humboldt Foundation, Bonn, Germany; The University Grants Commission, New Delhi, India; Indian Council of Medical Research, New Delhi, India. The skillful technical assistance of Mr Om Prakash Gupta, Shiv Mandir Singh (Varanasi, India); Katja Deparade, Franzisca Drum, Elisabeth Scherer (Berlin, Germany); Secretarial assistance of Angela Ludwig (Berlin, Germany), Madeline Järild, Gunilla Åberg and Gunilla Tibling (Uppsala, Sweden) were highly appreciated.

COGNITIVE IMPAIRMENT IN THE POST-ICU SYNDROME: THE POTENTIAL OF NEUROTROPHIC MODULATION FOR PREVENTION AND REHABILITATION

IGNACIO J. PREVIGLIANO

Prof. of Neurology - Maimónides University, Buenos Aires, Argentina
Scientific Director - Federación Panamericana e Ibérica de Medicina Crítica
y Terapia Intensiva

Director Specialist Course on Critical Care Medicine - Maimónides University, Buenos Aires, Argentina

Director Hospital General de Agudos J. A. Fernández
Specialist in Neurology and Critical Care Medicine

In the last quarter-century, the description of the post-intensive care unit syndrome has led to a wider recognition of the prolonged disease burden affecting critical illness survivors. Prolonged physical disability, neuropsychiatric morbidity and cognitive impairment have been recognized as its hallmark features. Correlation between the degree of brain injury and prolonged cognitive impairment has been observed, and several secondary brain injury factors have been associated with the cognitive impairment that may follow critical illness. All of these factors are believed to overwhelm the natural defense mechanisms of the neurovascular unit

through various pathways, impairing the mechanisms that promote neuroplasticity, neuroprotection and neurogenesis in the central nervous system. Over the last years, research has established new muscle-brain interactions that may serve to potentiate these natural neuroprotective mechanisms through neurotrophic and anti-inflammatory signaling pathways, as well as the beneficial effects of synthetic neurotrophic factors such as Cerebrolysin in the context of primary brain injury in dementia, stroke, and traumatic brain injury. These appear as promising avenues of research to help prevent and reduce the burden of cognitive impairment following critical illness, as well as potentially beneficial agents for the cognitive rehabilitation of critical illness survivors.

ECONOMIC EVALUATION FOR STROKE INTERVENTIONS IN ROMANIA: WHERE DO WE START?

ȘTEFAN STRILCIUC^{1,2}

OVIDIU SELEJAN², DAFIN F. MURESANU^{1,2}

1. Department of Neurosciences, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

2. RoNeuro Institute for Neurological Research and Diagnostic, Cluj-Napoca, Romania

Stroke was the most important cause of death after heart disease in 2016. The economic burden for treatment and care is also continually increasing. In the EU, the estimated costs for treatment are 27 billion euros annually, out of which 18.5 billion for direct costs and 8.5 billion for indirect costs. Health systems face profound challenges in the management of involved contributors to morbidity and mortality of the disease. Economic evaluation in health is both necessary, given present health policy orientation toward value over quantity of services, and profitable for mature and widespread interventions, yielding guaranteed stable returns in a medium to long-term timeline. Understanding of the care processes that contribute to a better outcome has improved, and now enough proof exists to support interventions and care processes in both acute care and neurological rehabilitation after stroke.

In high-income countries, health systems have documented changes in secondary care provision over the last ten years, as stroke units have gained higher coverage globally, and patients have benefited from access to increased evidence-based care, and reductions in mortality and inpatient stay duration. Developing countries such as Romania face important hurdles with information and surveillance systems. A data crisis in this context profoundly inhibits informed policymaking for complex and burdensome diseases like stroke. The Romanian Ministry of Health has contracted technical assistance from an international consortium led by Oxford

Policy Management and Imperial College London for institution building of Health Technology Assessment (HTA) to replace Romania's existing underperforming framework. We suggest that mapping of available raw information is warranted before considering a novel HTA system proposal that is largely based on cost-effectiveness models from countries with significantly higher availability of data. While information sources for utility of interventions are available for Romania from international clinical trials, and may be used for economic evaluations for the proposed HTA methodology, data collection for the cost component that is required to calculate indicators such as incremental cost-effectiveness ratio or budget impact must be tailored to reflect healthcare expenditure, patient pathways, and overall efficiency of the Romanian Healthcare system. The Burden of Stroke in Europe report, drafted by King's College London for the Stroke Alliance for Europe is a limited attempt to capture the economic burden of stroke in Romania, due to its reliance on prevalence data with very wide confidence intervals from the Global Burden of Disease study, developed via extrapolation from other countries by the Institute for Health Metrics and Evaluation (IHME) at the University of Washington. We recommend that for economic evaluations for stroke that are relevant for policymaking in Romania, several information pre-requisites for economic evaluation that are related to the burden of disease and cost of care must be fulfilled as part of an integrated cost of illness study before any cost-effectiveness analysis is attempted. Collection of prevalence and direct and indirect costs must be performed from best available sources.

UPDATE OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE TREATMENT

NGUYEN HUY THANG

Chair, Department of Cerebrovascular Disease, 115 Hospital, Vietnam

Spontaneous intracerebral hemorrhage (ICH), defined as nontraumatic bleeding into the brain parenchyma, is the second most common subtype of stroke, with 5.3 million cases and over 3 million deaths reported worldwide in 2010. Case fatality is extremely high (reaching approximately 60 % at 1 year post event). Only 20 % of patients who survive are independent within 6 months. Factors such as chronic hypertension, cerebral amyloid angiopathy, and anticoagulation are commonly associated with ICH. Chronic arterial hypertension represents the major risk factor for bleeding. The incidence of hypertension-related ICH is decreasing in some regions due to improvements in the treatment of chronic hypertension. ICH is more common in Asians, advanced age, male sex, and low- and middle-income countries. The management of patients with hemorrhagic stroke is generally limited to

the supportive care or evacuation of the hematoma, although the efficacy of the surgical removal is variable and controversial. Medical management includes control blood pressure, venous thrombosis prophylaxis, gastric cytoprotection, and aggressive rehabilitation. Therefore, the need for a safe and effective treatment for patients with hemorrhagic stroke is urgently needed. There has been much interest in drugs that potentially protect neurons from the effects of ischemia, like NMDA receptor antagonists, antibodies to adhesion molecules, free radical scavengers, gangliosides, and apoptosis inhibitors. Encouraging results derive from studies in cell culture and in vivo stroke models after treatment with Cerebrolysin. It has been used in a number of European and Asian countries for various indications, for many years, having only rare and benign side effects reported. Recently, the treatment with Cerebrolysin is safe and well tolerated in ICH patients. Further studies with a higher number of patients need to prove positive results in the efficacy of Cerebrolysin in patients with hemorrhagic stroke.

NEW VISTAS IN TBI RESEARCH – RESULTS FROM CAPTAIN STUDIES AND THE MULTIDIMENSIONAL METHODOLOGY

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 clinically 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 methodological frameworks are available that are appropriate for this important new multidimensional approach.

Examples from the literature and current study designs in neurosciences are discussed and their implications related to future developments. 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.

Key Words: Clinical Research, TBI, Multidimensional, Methodology

CURRICULUM VITAE





NATAN M. BORNSTEIN
ISRAEL

Affiliation: Professor of Neurology at the Tel-Aviv University, Sackler Faculty of Medicine.

Director of the Brain Division at the Shaare-Zedek Medical Center

Head of Stroke Unit at the Tel-Aviv Medical Center (1989-2016)

Chairman of the ESNCH (2013)

Chairman of the Israeli Neurological Association (since 2009)

Vice President of the World Stroke Organization (WSO) (since 2008).

President of the European Neurosonology Society (2013).

Chairman of Neurology Department, Tel-Aviv Medical Center (2002-2007)

Consulting Editor of Stroke

Editorial Board of CVD, EJoN, Acta Neurologica Scandinavica, International Journal of Stroke, Neurosonology, Frontiers in Stroke, Journal of Annals of Medical Science.

Fellowship program in vascular neurology (stroke) in Toronto, Canada with Prof. John Norris (1984-87)

Main research interests are: Epidemiology of stroke, Stroke prevention, Vascular dementia, Inflammation and stroke, Neurosonology.



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

ITALY

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 Clinclal 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 view. 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 the Scientific Committee of the European Academy of Neurology (2014-2018) - Chairman of Neuromediterraneum Forum - Co-Chairman of Research group of WFN Migration Neurology. Member of the Scientific Societies: - Societa Italiana di Neurologia (Past Secretary, President, 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).



WOLF DIETER HEISS

GERMANY

Wolf-Dieter Heiss, born 31.12.1939 in Zell am See, Austria, graduated in medicine from the University of Vienna, Austria, in 1965. He achieved his training in neurology, neurophysiology, psychiatry and nuclear medicine at the University hospital in Vienna and spent research fellowships at the MIT, Cambridge, USA, the Physiological Institute in Stockholm, Sweden, the Department of Physiology of SUNY, Buffalo, NY and the Department of Neurology of the University of Minnesota, Minneapolis, USA. 1976 he was appointed associate professor at the Department of Neurology of the University of Vienna. In 1978 he became director of the Center for Cerebrovascular Research of the Max Planck Institute for Brain Research and of the Department of Neurology of the City Hospital Cologne-Merheim, Germany. 1981 he was appointed as director at the Max Planck Institute for Neurological Research. 1985 – 2005 he was professor of neurology and chairman of the Department of Neurology of the University of Cologne and director of the Department of General Neurology at the MPI in Cologne. He was president of the International Stroke Society 1992-96, was on the board of directors of the Society for Cerebral Blood Flow and Metabolism, deputy editor of the Journal of Cerebral Blood Flow and Metabolism and at present is associate editor of the Journal of Nuclear Medicine and section editor of Stroke. He was chairman of the program committee of the European Federation of Neurological Societies (EFNS) 1998 - 2001 and was president of the EFNS 2001 – 2005. Since 2005 he is Visiting Professor at the Danube University in Krems, Austria, and since 2009 Adjunct Professor at the McGill University in Montreal, Canada and since 2013 Associate Professor at the University of Cluj, Romania, where he received a Doctor Honoris Causa in December 2014.

Recent selected publications on the topic:

Contribution of Neuro-Imaging for Prediction of Functional Recovery after Ischemic Stroke.

Heiss WD. Cerebrovasc Dis. 2017 Sep 5;44(5-6):266-276.

Imaging effects related to language improvements by rTMS.

Heiss WD. Restor Neurol Neurosci. 2016 Apr 11;34(4):531-6.

Hybrid PET/MR Imaging in Neurology: Present Applications and Prospects for the Future.

Heiss WD. J Nucl Med. 2016 Jul;57(7):993-5.

Non-invasive repeated therapeutic stimulation for aphasia recovery: a multilingual, multicenter aphasia trial.

Thiel A, Black SE, Rochon EA, Lanthier S, Hartmann A, Chen JL, Mochizuki G, Zumbansen A, Heiss WD; NORTHSTAR study group. J Stroke Cerebrovasc Dis. 2015 Apr;24(4):751-8.

The ischemic penumbra: how does tissue injury evolve?

Heiss WD. Ann N Y Acad Sci. 2012 Sep;1268:26-34.

Relevance of experimental ischemia in cats for stroke management: a comparative reevaluation. Heiss WD, Graf R, Wienhard K. Cerebrovasc Dis. 2001;11(2):73-81



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 Nervous 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 Heinrich Heine University in Düsseldorf. He was also founding Director of the NTC in Cologne. He was involved in the setup of many in- and outpatient rehabilitation hospitals in Germany. In 2001 he 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 of 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.



HYUN HAENG LEE
SOUTH KOREA

Education

2018 Aug	M.S. College of Medicine, Seoul National University
2011 Feb	M.D. College of Medicine, Seoul National University
2007 Feb	B.S. Biological Sciences, College of Natural Sciences, Seoul National University

Training

2019 Mar – Current ,	a Clinical Assistant Professor, Department of Rehabilitation Medicine, Konkuk University Medical Center
2018 Mar – 2019 Feb,	a Clinical and Research Fellow, Department of Rehabilitation Medicine, Konkuk University Medical Center
2017 Mar – 2018 Feb,	a Clinical and Research Fellow, Department of Rehabilitation Medicine, Seoul National University Hospital
2013 Mar – 2017 Feb,	a Resident physician, Department of Rehabilitation Medicine, Seoul National University Hospital
2012 Mar – 2013 Feb,	an Intern, Seoul National University Hospital

Institutional appointment

2019 Mar – Current ,	a Clinical Assistant Professor, Department of Rehabilitation Medicine, Konkuk University Medical Center
----------------------	---

Licensure

2017 Feb Board Certificated Doctor of Physical Medicine and Rehabilitation,
South Korea (Number: 2091)

2011 Feb Medical Doctor, Ministry of Health, South Korea (Number: 106994)

Peer-reviewed publication (domestic)

Kim W-S, Bae H-J, Lee H-H, Shin H. Status of Rehabilitation After Ischemic Stroke: A Korean Nationwide Study. *Ann Rehabilitation Medicine*. 2018;42(4):528–535. doi:10.5535/arm.2018.42.4.528.

Lee H, Lee W, Seo H, Han D, Kim Y, Oh B-M. Current State and Prospects of Development of Blood-based Biomarkers for Mild Traumatic Brain Injury. *Brain Neurorehabilit*. 2017;10(1). doi:10.12786/bn.2017.10.e3.

Lee H, Shin E-K, Shin H-I, Yang E. Is WHODAS 2.0 Useful for Colorectal Cancer Survivors? *Ann Rehabilitation Medicine*. 2017;41(4):667. doi:10.5535/arm.2017.41.4.667.

Lee, Hyun Haeng, Se Hee Jung. Prediction of post-stroke falls by quantitative assessment of balance. *Annals of rehabilitation medicine*. 2017;41(3): 339–346. doi: 10.5535/arm.2017.41.3.339

Peer-reviewed publication (international)

Lee Y, Lee H-H, Uhm K, et al. Early Identification of Risk Factors for Mobility Decline among Hospitalized Older Patients. *Am J Phys Med Rehab*. 2019;1. doi:10.1097/phm.0000000000001180.

Do H, Seo H, Lee H, et al. Progression of Oropharyngeal Dysphagia in Patients with Multiple System Atrophy. *Dysphagia*. 2019;1–8. doi:10.1007/s00455-019-09990-z.

Seo HG, Lee HH, Oh B-MM. The Possible Effect of Oxytocin in Postpartum Recovery From a Stroke: A Case Report. *PM R*. 2018. doi:10.1016/j.pmrj.2018.04.005.

Lee H, Seo H, Kim K, et al. Characteristics of Early Oropharyngeal Dysphagia in Patients with Multiple System Atrophy. *Neurodegener Dis*. 2018;18(2–3):84–90. doi:10.1159/000487800.

Kang M-GG, Yun SJ, Shin HI, et al. Effects of robot-assisted gait training in patients with Parkinson's disease: study protocol for a randomized controlled trial. *Trials*. 2019;20(1):15. doi:10.1186/s13063-018-3123-4.

Park D, Lee H, Lee S, et al. Normal contractile algorithm of swallowing related muscles revealed by needle EMG and its comparison to videofluoroscopic swallowing study and high resolution manometry studies: A preliminary study. *J Electromyogr Kines*. 2017;36:81–89. doi:10.1016/j.jelekin.2017.07.007.



IGNACIO J. PREVIGLIANO
ARGENTINA

Prof. of Neurology - Maimónides University

Scientific Director - Federación Panamericana e Ibérica de Medicina Crítica y Terapia Intensiva

Director Specialist Course on Critical Care Medicine - Maimónides University

Director Hospital General de Agudos J. A. Fernández

Specialist in Neurology and Critical Care Medicine



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), Co-Chair EAN Scientific Panel Neurorehabilitation, Past President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), Member of the Romanian Academy, Member of the Academy of Medical Sciences, Romania, 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 Dăfin F. Muresanu is a specialist in Leadership and Management of Research and Health Care Systems (specialization in Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998 and several international courses and training stages in Neurology, research, management and leadership). Professor Dăfin 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 Neurotraumatology (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 400 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (193 papers indexed on Web of Science-ISI, H-index: 21) 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 with special expertise in Cell Biology in 1976 and awarded Gold Medal of Bihar University for securing 1st position 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 Blood–brain 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 Bishma 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=F4HK58CYuRYrISl6qbC&page=1&cr_pqid=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 of 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.



ȘTEFAN STRILCIUC
ROMANIA

Ștefan Strilciuc, a public health expert, is the Executive Director of the RoNeuro Institute for Neurological Research and the Society for the Study of Neuroprotection and Neuroplasticity. An active faculty member at Babeș-Bolyai University and Iuliu Hațieganu University of Medicine and Pharmacy in Cluj-Napoca, his research track is multidisciplinary, focused on clinical research, experimental medicine and public health.

As core member of the Romanian Health Observatory, Strilciuc has delivered valuable contributions for evidence-based policy-making through comprehensive analysis of the dynamics of Romania's healthcare system.



NGUYEN HUY THANG
VIETNAM

Board Certification

- Neurology, 1995
- Master of Neurology, 2002
- Stroke fellowship at The National University Hospital, Singapore 2005-2006
- Neurosonology (American Society of Neuroimaging), 2006
- Stroke fellowship at The University of Alabama at Birmingham, USA 2007-2008

National Committees:

Vice President of VietNam Stroke Association
President of HCM city Stroke Association
Member of the Asian Stroke Advisor Board Committee
Scientific Committee of the Asia-Pacific Stroke Congress

Journal Review:

Stroke Journal (The American Heart/Stroke Association), American Journal of Neuroimaging, Recent Patents on CNS Drug Discovery

Investigators:

- CLOTBUST-PRO
- DIAS 3, DIAS 4 : National leading Principle Investigator
- ENCHATED : National leading Principle Investigator and Steering committee member
- SOCRATES : National leading Principle Investigator
- AFFINITY : National leading Principle Investigator and Steering committee member
- TRIDENT : National leading Principle Investigator and Steering committee member

Publications

1. Thrombolysis in recurrent lacunar stroke. *European Journal of Neurology* 2008, 15: 1409–1411.
2. Prevalence and risk factors associated with reversed Robin Hood syndrome in acute ischemic stroke. *Stroke Journal* 2009. 40: 2738 – 2742.
3. Patients with Thrombolysed Stroke in Vietnam have an Excellent Outcome: Results from the Vietnam Thrombolysis Registry. *European Journal of Neurology* 2010, 17: 1188-1192
4. Preliminary experience with recombinant tissue plasminogen activator in Vietnam. *International Journal of Stroke* 2010, 5: 1-3
5. Real-Time Hemodynamic Assessment of Downstream Effects of Intracranial Stenose in Patients with Orthostatic Hypoperfusion Syndrome. *Cerebrovascular Diseases* 2010, 30: 335
6. Intravenous Thrombolysis. *International Journal of Stroke* 2010, 5: 516.
7. Whole body shaking due to intracranial blood flow steal. *Journal of Neurological Sciences*. 2011, 305;165
8. Current status of intravenous thrombolysis for acute ischemic stroke in Asia. *International Journal of Stroke*, 6: pp.523-530.
9. Case-fatality and functional status three months after first-ever stroke in Vietnam. *Journal of the Neurological Sciences* 365 (2016) 65–71
10. Health-related quality of life after stroke: reliability and validity of the Duke Health Profile for use in Vietnam. *Qual Life Res* (2015) 24:2807–2814
11. Low-Dose versus Standard-Dose Intravenous Alteplase in Acute Ischemic Stroke. *The New England Journal of Medicine* 2016; 374:2313-2323
12. The FOCUS, AFFINITY and EFFECTS trials studying the effect(s) of fluoxetine in patients with a recent stroke: statistical and health economic analysis plan for the trials and for the individual patient data meta-analysis. *Journal of Medical case reports* (2017) 1752-1947
13. The professional practice and training of neurology in the Asian and Oceanian Region: A cross-sectional survey by the Asian and Oceanian Association of Neurology (AOAN). *Journal of the Neurological Sciences* 2017
14. Low- Versus Standard-Dose Alteplase in Patients on Prior Antiplatelet Therapy: The ENCHANTED Trial (Enhanced Control of Hypertension and Thrombolysis Stroke Study). *Stroke Journal* 2017
15. Low-Dose vs Standard-Dose Alteplase for Patients With Acute Ischemic Stroke Secondary Analysis of the ENCHANTED Randomized Clinical Trial. *JAMA* 2017
16. XANAP: A real world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation in Asia. *Journal of Arrhythmia* 1 (2018) 883-2148
17. Intensive blood pressure reduction with intravenous thrombolysis therapy for acute ischaemic stroke (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial. *The Lancet* 2019
18. Applicability of ENCHANTED trial results to current acute ischemic stroke patients eligible for intravenous thrombolysis in England and Wales: Comparison with the Sentinel Stroke National Audit Programme registry. *International Journal of Stroke* 2019
19. Processes of stroke unit care and outcomes at discharge in Vietnam: findings from the REGistry of Stroke care Quality (RES-Q) in a major public hospital. *Journal of Stroke Medicine* 2019

Invited International Lecture

1. Thrombolysis in VietNam: Protocol and beyond. The Stroke Society of Australasia (SSA) 21st Annual Scientific Meeting of Stroke 2010.
 2. Intravenous thrombolysis in VietNam. The Asia Neuroscience Congress. Hong Kong, 2011.
 3. Acute stroke management in Viet Nam. The Asia Pacific Stroke Conference (APSC) Srilanka 2011.
 4. Solitaire Flow Restoration Device versus the Intra-Arterial tPA in Nonresponder Intravenous Thrombolysis Treated Patients: The Asia Pacific Stroke Conference (APSC) . Hong Kong 2013.
 5. Stroke in young adult in Vietnam. The Asia Pacific Stroke Conference (APSC) Taiwan 2014.
 6. Ischemic Penumbra. The Asia Neuroscience Congress. Taiwan 2014
 7. Provide stroke services in rural areas. The Asia Pacific Stroke Conference (APSC), Malaysia 2015.
 8. Endovascular in acute stroke management. The Asian Neuroscience Congress, Singapore 2015.
 9. Sleep apnea and stroke. Pacific Stroke Conference (APSC), Australia 2016.
 10. How hyperacute stroke units can be implemented in Australasia and Asia-Pacific. The Asia Pacific Stroke Conference (APSC) Australia 2016.
 11. Progress of Stroke Unit Care in Vietnam. The International Stroke Conference Houston, Texas 2-2017
 12. Stroke care in Vietnam. The World Stroke Congress, Canada 2018
-



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 studied biometric methods for pharmacology and clinical research at the Institute for Data Analysis and Study Planning in Munich.

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

From 1985 to 1995, he was member of the Ultrahigh Dexamethasone Head Injury Study Group and the leading biometrician of the German GUDHIS project in Traumatic Brain Injury, involving 10 Departments of Neurosurgery in Germany.

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

Since 1995 he is Senior Consultant for Biometry & Clinical Research. He planned and evaluated about 150 randomized clinical studies worldwide.

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

Since 2013 Elected Member of the World Academy for Multidisciplinary Neurotraumatology (AMN), since 2016 Elected Member of the Presidium of the 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

He is head of the Multidimensional Department at the Institute for Data Analysis and Study Planning, and statistical peer reviewer for leading medical journals such as Stroke (American Heart Association).

He 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)

GENERAL INFORMATION



GENERAL INFORMATION

CONGRESS VENUE:



PULLMAN BAKU

Mikayil Mushfig Street
1C, 1006, Baku, Azerbaijan
Tel: +994125389090
Fax: (+994)12/5389091
ha8j3@accor.com



GENERAL INFORMATION

REGISTRATION DESK

All materials and documentation will be available at the registration desk located at SSNN booth.

The staff will be pleased to help you with all enquiries regarding registration, materials and program. Please do not hesitate to contact the staff members if there is something they can do to make your stay more enjoyable.

LOGISTIC PARTNER:



Synapse Travel

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

Scientific Secretariat

Foundation of 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

Contact Details

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

GENERAL INFORMATION

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.

NAME BADGES

Participants are kindly requested to wear their name badge at all times. The badge enables admission to the scientific sessions and dinners.

FINAL PROGRAM & ABSTRACT BOOK

The participants documents include the program and abstract book which will be handed out at the registration counter.

COFFEE BREAKS

Coffee, tea and water are served during morning coffee breaks and are free of charge to all registered participants.

MOBILE PHONES

Participants are kindly requested to keep their mobile phones turned off while attending the scientific sessions in the meeting rooms.

CURRENCY

The official currency in Azerbaijan is Manat.

ELECTRICITY

Electrical power is 220 volts, 50 Hz. Two-prong plugs are standard.

TIME

The time in Azerbaijan is GMT +4.

ORGANIZERS



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



Journal for Medicine
and Life
www.medandlife.org



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



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



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



Romanian Society
of Neurology
www.neurology.ro



Romanian Academy of
Medical Sciences
www.adsm.ro

ACADEMIC PARTNERS



European Federation of
Neurological Societies
www.efnr.org
www.ecnr.org



World Federation for
NeuroRehabilitation
www.wfnr.co.uk



Uppsala University
www.uu.se



Tel Aviv University
www.tau.ac.il



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



Global College of
Neuroprotection and
Neuroregeneration



Banaras Hindu University
www.bhu.ac.in



“RoNeuro”

**Institute for Neurological Research and Diagnostic,
Cluj-Napoca, Romania**

Tel.: +40 374 46.22.22

str. Mircea Eliade nr. 37, 400364 Cluj-Napoca, România

Fax: +40 374.461.674; Email: receptie@roneuro.ro

www.roneuro.ro