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GENERAL INFORMATION

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Europa Hotel

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Republicii Street no 13, Eforie Nord, Constanta – Romania

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.

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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 Romania is RON.

ELECTRICITY

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

TIME

The time in Romania is Eastern European Time (GMT+2).



SCIENTIFIC PROGRAM



13TH INTERNATIONAL SUMMER SCHOOL OF NEUROLOGY

2-5 JULY, 2018 | EUROPA HOTEL | EFORIE NORD | ROMANIA

MONDAY, JULY 2ND, 2018

MODULE COORDINATORS: Volker Hömberg (Germany),
Hari Shanker Sharma (Sweden), Derek Mayer (USA)

08:45 – 09:00

WELCOME ADDRESS

Dafin F. Mureşanu (Romania), Natan Bornstein (Israel),
Valeria Caso (Italy), Ovidiu Băjenaru (Romania), Volker
Hömberg (Germany), Hari Shanker Sharma (Sweden),
Stanislav Groppa (Rep. Of Moldova)

09:00 – 10:30

Volker Hömberg (Germany)
The art of neurological examination

10:30 – 11:00

Dafin F. Mureşanu (Romania)
Anticorrelated processes in neurobiology - possible
consequences for neurorehabilitation strategies

11:00 – 11:30

David C. Good (USA)
Predicting clinical outcomes after stroke

11:30 – 12:00

COFFEE BREAK

12:00 – 12:30

Augustin Semenescu (Romania)
Inventions Presentation | Cranial implant with
osteointegrating structures and functional coatings and
Cranial endoprosthesis with a sliding system

| | |
|---------------|---|
| 12:30 – 13:00 | Hari Shanker Sharma (Sweden) Nanodelivery of Cerebrolsytin with 5-HT ₆ receptor antagonist induces superior neuroprotective effects following concussive head injury induced exacerbation of brain pathology in sleep deprivation |
| 13:00 – 13:30 | Stephen Skaper (Italy) Neuroinflammation: the risk of growing old |
| 13:30 | LUNCH |
| 18:00 – 18:30 | Johannes Vester (Germany) The concept of high quality, non-interventional comparative effectiveness in neurorehabilitation - new pathways within the framework of evidence-based medicine |
| 18:30 – 20:00 | Neurological case presentations Volker Hömberg (Germany), Dana Boering (Germany) |
| 20:00 | DINNER |

TUESDAY, JULY 3RD, 2018

MODULE COORDINATORS: Natan Bornstein (Israel),
Dafin F. Mureşanu (Romania)

| | |
|---------------|--|
| 09:00 – 09:45 | Natan Bornstein (Israel) Time is Brain, TIA as an Emergency |
| 09:45 – 10:30 | Natan Bornstein (Israel) Secondary stroke prevention |
| 10:30 – 11:15 | Natan Bornstein (Israel) Management of symptomatic carotid stenosis |

| | |
|---------------|---|
| 11:15 – 11:45 | COFFEE BREAK |
| 11:45 – 12:15 | Dafin F. Mureșanu (Romania) From neurobiology to evidence-based medicine concepts in neurorehabilitation after stroke |
| 12:15 – 12:45 | Dafin F. Mureșanu (Romania) Challenges and opportunities in stroke recovery |
| 13:00 | LUNCH |
| 18:00 – 20:00 | CASE PRESENTATIONS Natan Bornstein (Israel), Adina Stan (Romania) |
| 20:00 | DINNER |

WEDNESDAY, JULY 4TH, 2018

MODULE COORDINATORS: Bogdan Popescu (Romania),
Antonio Federico (Italy)

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|---------------|--|
| 09:00 – 09:30 | Antonio Federico (Italy) Genetic leucodystrophies as a model of oligodendrocyte dysfunction |
| 09:30 – 10:00 | Max Hilz (Germany) Transient loss of consciousness - a differential- diagnostic challenge |
| 10:00 – 10:30 | Ovidiu Băjenaru (Romania) Vascular cognitive impairment - pathophysiology and classification update |
| 10:30 – 11:00 | Ovidiu Băjenaru (Romania) Immunopathological considerations in relation to disease modifying therapies (DMT) in multiple sclerosis |

11:00 – 11:30

COFFEE BREAK

11:30 – 12:00

Angelo Antonini (Italy)
Updates on advanced Parkinson disease treatment

12:00 – 12:30

Peter Jenner (UK)
Multimodal drugs for a multimodal disease

12:30 – 13:00

Stanislav Groppa (Rep. Of Moldova)
Characteristics and predictive biomarkers of drug resistant epilepsy - a clinically oriented review

13:00 – 13:30

Tudor Lupescu (Romania)
Diabetic neuropathy diagnostics

13:30 – 14:00

Raluca Popescu (Romania)
The treatment of diabetic neuropathy and the prevention of diabetic foot

14:00

LUNCH

18:00 – 18:30

Amos Korczyn (Israel)
Mild cognitive impairment

18:30 – 19:00

Amos Korczyn (Israel)
Case presentations

19:00 – 19:30

Cristian Falup Pecurariu (Romania)
Dysautonomia in Parkinson's disease

19:30 – 20:00

Jozsef Szasz (Romania)
Management of advanced Parkinson's disease: DAT - limitations and unanswered questions (how early DAT should be initiated?)

20:00

DINNER

THURSDAY, JULY 5TH, 2018

MODULE COORDINATORS:

Michael Brainin (Austria),
Ovidiu Băjenaru (Romania)

| | |
|---------------|--|
| 09:00 – 09:30 | Josep Valls-Sole (Spain) Brain and non-brain stimulation therapy for neurological disorders |
| 09:30 – 10:00 | Bogdan Popescu (Romania) Microbiota, enteric nervous system and neurodegenerative diseases |
| 10:00 – 10:30 | Michael Brainin (Austria) The global stroke epidemic: Prevention is the Main Issue |
| 10:30 – 11:00 | Michael Brainin (Austria) Key elements of stroke care |
| 11:00 – 11:30 | COFFEE BREAK |
| 11:30 – 12:00 | Mihaela Simu (Romania) Focus on multidisciplinary approach in advanced Parkinson's disease |
| 12:00 – 12:30 | Cristina Tiu (Romania) ResQ registry of stroke care - filling the gaps between theory and practice |
| 12:30 – 13:00 | Rodica Bălașa (Romania) The use of serological biomarkers in multiple sclerosis treatment: a step toward personalized treatment |
| 13:00 – 14:30 | LUNCH |

| | |
|---------------|--|
| 14:30 – 15:00 | Anca Buzoianu (Romania) The neuropharmacology of N-PEP type peptides in neurocognitive impairment |
| 15:00 – 15:30 | Dafin F. Mureșanu (Romania) Combined neuropsychological, neurophysiological and psychophysiological assessment of the effects of N-Pep-12 on neurorecovery in patients after ischemic stroke – Case presentations |
| 15:30 – 16:00 | Mihaela Băciuț (Romania) The role of N-PEP peptide pharmacological support and peripheral magnetic stimulation in neurorehabilitation after surgery of developmental maxillofacial deformities |
| 16:00 – 16:30 | Ștefan Florian (Romania) The impact of N-PEP peptides on cognitive functions after traumatic brain injuries |
| 17:00 – 18:30 | <i>FINAL EXAMINATION</i> |
| 18:30 | <i>CONCLUDING REMARKS</i> |

ABSTRACTS



UPDATES ON ADVANCED PARKINSON DISEASE TREATMENT

ANGELO ANTONINI

Parkinson and Movement Disorders Unit, Department of Neurosciences (DNS)
University of Padua, Padua, Italy

Advanced stage of Parkinson's disease (PD) is now broader than in the past, encompassing various types and degrees of disability. It poses multiple management issues, because, despite levodopa still being unequaled in the symptomatic treatment of PD, its clinical effect tends to diminish with disease progression.

Advanced PD raises multiple management issues, as the patient carries the burden of the motor complications and non-motor symptoms making medication adjustments quite complex. Adequate control and optimal quality of life are often difficult to achieve and an integrate understanding of the pathophysiological mechanisms underlying the symptoms and of the multiple drug interactions is mandatory. While this fine balance can be generally achieved to various extents in experienced tertiary centers, mortality remains roughly unchanged, supporting thus the need for further research and therapeutic options that can truly modify PD progression and its milestones.

Motor complications tend to develop on average after four to six years of levodopa treatment. Motor fluctuations, though initially predictable, become more complex and unpredictable as the disease progresses. Dyskinesias are correlated with young age at PD onset, longer disease duration and higher LD doses. Symptoms with a poor response to LD include freezing of gait (FOG – affecting up to 80% of PD patients after 15 to 20 years of disease evolution), postural abnormalities, and dysarthria and dysphagia (present after 7 and 11 years after disease onset, respectively).

Potential risk factors for developing advanced PD have been outlined as clinical features and biomarkers. While age, sex and disease duration seem to be obvious determinants of development to advanced phase of PD, it is still debated whether the clinical phenotype at disease onset (tremor dominant, akinetic-rigid dominant, postural-instability dominant) is as predictor of PD evolution. However, other factors, among which presence of olfactory changes, rapid eye movement (REM) sleep disorders, cardiovascular autonomic dysfunction, as well as hallucinations and psychosis, may predict cognitive decline and dementia in PD, thus contributing to the overall clinical deterioration. Impulse control disorders have also been correlated with cognitive decline, particularly with executive dysfunction, as shown in one study.

Conventional therapies and routes of administration are making way for new, innovative approaches, either invasive, such as the duodenal administration of the levodopa/carbidopa intestinal gel, the apomorphine pump, or non-invasive, such as transdermal, nasal, sublingual or pulmonic routes, all intending to optimize delivery. Moreover, additional drugs like COMT and MAO-B inhibitors are required to adequately manage the full spectrum of emerging manifestations, characteristic of the advanced stage making an individualized integrated approach recommended.

VASCULAR COGNITIVE IMPAIRMENT – PATHOPHYSIOLOGY AND CLASSIFICATION UPDATE

OVIDIU BĂJENARU

University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania

About 25% of the survivors of a first stroke, develop a form of dementia during the first 5 years after a first stroke. While the neurodegenerative cognitive impairment still has no efficient disease-modifying treatment, the cerebrovascular disorders may be detectable and partly preventable. The different types of classification of vascular cognitive impairment (VCI) have variable degrees of sensibility and specificity, which make them – at least in some circumstances, difficult to use. These difficulties are even greater if we take into account that patients with cerebrovascular disorders, do not have only neurocognitive impairment due exclusively to vascular causes, but often they associate neurodegenerative disorders, in particular Alzheimer’s disease; so, most of these patients have VCI determined by mixed pathophysiologic mechanisms. The heterogeneity of VCI is even more complex, if we take into account the different types of vascular lesions and topographic locations, and the risk factors – including the genetic background of each patient. In the same time, nowadays there are important epidemiological, clinical and neuropathologic data demonstrating that at the level of the brain tissue and vascular walls, in particular in the brain microcirculation, there is a more severe evolution both of the neurodegenerative and neurovascular lesions, when both types coexist, generating a worse prognosis of these patients both of the vascular neurological deficits and of the neurocognitive impairment. Conceptually but also practically it is important to understand what “a brain at risk” means, to look for the modifiable risk factors of these patients and to treat them as early and efficient as possible, in order to prevent both stroke and dementia in later stages of evolution.



IMMUNOPATHOLOGICAL CONSIDERATIONS IN RELATION TO DISEASE MODIFYING THERAPIES (DMT) IN MULTIPLE SCLEROSIS

OVIDIU BĂJENARU

University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania

Multiple sclerosis is not only a chronic multifocal demyelinating disease of the CNS, as usually is still considered in clinical practice, but a chronic diffuse inflammatory immune-mediated disease of the CNS, with two essential types of consequent lesions: multifocal demyelination and axonal degeneration which is more extensive, much beyond the demyelination areas. The research in the biology and understanding the pathophysiology of this disease allowed a huge accumulation of data, demonstrating an interaction among genetic factors and the disturbances of the very complex immunopathologic mechanisms which are disturbed in this disease, at different molecular and cellular levels, implying both the systemic immunologic network but also the specific pathologic reactivity of the blood-brain barrier and CNS cellular components. The more and more profound understanding of these mechanisms allowed the development of many active immunomodulatory treatments, with pathologic and clinical disease modifying properties, some of which became available in the clinical practice and others being in different stages of clinical and preclinical research. These mechanisms and therapeutic molecules will be discussed.

THE USE OF SEROLOGICAL BIOMARKERS IN MULTIPLE SCLEROSIS TREATMENT: A STEP TOWARD PERSONALIZED TREATMENT

RODICA BĂLAȘA

University of Medicine and Pharmacy, Center of MS Treatment, Târgu Mureș, Romania

Multiple sclerosis (MS) is an immune-mediated inflammatory disease of the central nervous system (CNS) that affects young adults. MS is the first cause of neurological handicap in the 20–40 age group, more than 2.3 million people are affected by MS worldwide. There is no cure for MS, there are only disease modifying treatments (DMTs) that slow the MS progression and delay the accumulation of disability. MS is a heterogeneous disease from many points of view: pathogenic, immunological, clinical and treatment response to DMTs. EMEA has to date approved 12 DMTs for MS treatment, but today personalizing the treatment has become a health priority problem.

The immune system of the patient is dysregulated at multiple levels in MS. The DMTs approved have their mode of action at different levels of the immune system, either by reducing the proinflammatory players or increasing the regulatory networks. The peripheral immune dysregulation is mostly expressed in the relapsing remitting forms of MS (RRMS). There is an increased need to understand the immune pathogenic mechanisms so that the novel therapies might be optimally used.

For many years, MS was considered an inflammatory T cell-mediated disease. Among peripheral blood mononuclear cells, T lymphocytes play key roles in protective adaptive immune responses to a variety of pathogens. Regulation of T-cell responses is the key to maintaining immune balance. T helper 17 cells, through their interleukin-17, are considered the driving force of the immune cascade in MS

Lately, the understanding of the role of B cells in MS has progressed enormously. MS research targeting B cell is an example of translational medicine that resulted in a promising therapeutic approach. There is increasing evidence for peripheral B cell responses to be deeply involved in the immune pathology of MS: connection with pro- and anti-inflammatory capacities, stimulatory and regulatory functions and bystander activation. Initially, B cells were considered as antibody-producing cells with a secondary role in the MS pathogenesis, but now they are considered as main players together and in close interplay with T cells.

Personalized medicine in MS strategy requires further characterization of diverse T and B cell phenotypes and their different functions in the onset, propagation, and maintenance of inflammation/neurodegeneration. Our goal is to address in each patient a specific pathological mechanism. The use of specific biomarkers that could predict the patient's response to a certain DMT could contribute to decrease the loss of brain tissue and the accumulation of irreversible neurologic handicap .



MANAGEMENT OF SYMPTOMATIC CAROTID STENOSIS CEA VS. STENT

NATAN M. BORNSTEIN

Tel-Aviv University, Sackler Faculty of Medicine, Israel
Stroke Unit at Tel-Aviv Medical Center, Israel

Symptomatic severe carotid stenosis (>70%) carries a high risk of subsequent stroke of about ~ 30% over 2 years.

Carotid endarterectomy (CEA) was proved to reduce the risk of stroke significantly, with Relative Risk Reduction (RRR) = 65% and Number Needed to Treat (NNT) = 6 if performed safely (perioperative

S&D =5.8%) and should be executed within 2 weeks of TIA or minor stroke (NASCET & ECST).

For carotid stenting to replace CEA we need to know the comparative safety, durability and efficacy of the procedure. Only a few randomized, controlled studies comparing CEA and stenting were conducted (CAVATAS, SAPPHERE, EVA-3 and SPACE) with inconclusive results. There are still several ongoing studies (CREST in the USA and ICSS in Europe and Australia). Until more data will be available carotid stenting should be performed only in a selected group of patients with specific indications like: re-stenosis of the CEA, post neck radiation, inaccessible lesion for CEA and contra-indications for CEA.

SECONDARY STROKE PREVENTION

NATAN M. BORNSTEIN

Tel-Aviv University, Sackler Faculty of Medicine, Israel
Stroke Unit at Tel-Aviv Medical Center, Israel

Patients with TIA or ischemic stroke carry a risk of recurrent stroke between 5 and 20% per year. In patients with TIA or ischemic stroke of noncardiac origin antiplatelet drugs are able to decrease the risk of stroke by 11-15% and the risk of stroke, MI and vascular death by 15-22%. Aspirin is the most widely used drug. It is affordable and effective. Low doses of 50-325 mg aspirin are as effective as high doses and cause less gastrointestinal side effects. Severe bleeding complications are dose-dependent. The combination of aspirin with slow release dipyridamole is superior to aspirin alone for stroke prevention (ESPS-2 and ESPRIT1). Both studies have shown approximately 20%-24% relative risk reduction (RRR) of stroke and death. Clopidogrel is superior to aspirin in patients at high risk of recurrence by

about 8.7% RRR (CAPRIE2). The combination of aspirin plus clopidogrel is not more effective than clopidogrel alone but carries a higher bleeding risk (MATCH3 and CHARISMA4). None of the antiplatelet agents is able to significantly reduce mortality. The recent results of the PROFESS trial 5,6 showed no difference between clopidogrel and aspirin with slow release dipyridamole in secondary stroke prevention.

References

1. Lancet 2006;367:1665-73
2. Lancet 1996;348:1392-1339
3. Lancet 2004;364:331-337
4. N Eng J Med 2006;354(16):1744-6
5. Cerebrovasc Dis 2007;23:368-380
6. N Engl J Med 2008;359:1238-51

TIME IS BRAIN, TIA AS AN EMERGENCY

NATAN M. BORNSTEIN

Tel-Aviv University, Sackler Faculty of Medicine, Israel
Stroke Unit at Tel-Aviv Medical Center, Israel

Transient Ischemic Attack (TIA) should be considered as an emergency and work-up has to be done within 24 hours like acute unstable angina pectoris. It is known that about 23% of stroke are preceded by TIA. Several studies have shown that the risk of subsequent stroke in the first 2 weeks after a TIA is about 1% per day. In 2 published well conducted studies, EXPRESS (P. Rothwell) and SOS_TIA (P. Amarenco) it was shown that very early management in a TIA clinic will reduce the risk of subsequent stroke by 80% at 3 months. Therefore, work-up evaluation has to be performed within 24 hours in a dedicated organized structure.

Several stroke registries reported that carotid stenosis is the cause of embolic stroke in about 25%-30% of all ischemic strokes. Current guidelines recommend immediate intervention either by carotid endarterectomy (CEA) or stenting (CAS) in patients with symptomatic carotid stenosis greater than 50%.

Carotid duplex is a reliable, non-invasive, accessible tool for evaluation of carotid stenosis with very high level of accuracy. Therefore, carotid duplex should be the first line tool for rapid evaluation of every patient with TIA in order to detect a potential treatable carotid stenosis for stroke prevention. It is recommended to establish an "Acute TIA clinic" equipped with immediate accessible Duplex device to enable rapid evaluation of the carotid system in order to detect potential treatable carotid stenosis.

THE GLOBAL STROKE EPIDEMIC: PREVENTION IS THE MAIN ISSUE

MICHAEL BRAININ

Danube University Krems, Austria

Today, there is an increase in stroke mortality which is most dramatic in low and middle income countries. If we include prevalence rates and the overall burden of the disease, dementia and stroke combined are by far the most burdening diseases globally. Moreover, in countries with aging populations the increase is also seen due to demographic changes.

More recently, several studies have shown that a decrease of incidence rates is possible by improving modifiable risk factors, mostly of life style. For example, The Global Burden of Disease Study and the Interstroke Study both report that the burden of stroke is strongly influenced by modifiable risk factors and up to 90% of stroke occurrence can be explained by these risk factors. Conversely, a major reduction of incidence might be expected if behavioral and metabolic risk factors are managed appropriately. Recently, environmental factors (indoor and outdoor air pollution and lead exposure) have been recognized as major risks. Air pollution alone explains 30% of the stroke risk burden globally.

Prevention on a population scale can only be effective if large programs are established that target not only high-risk persons but aim also at medium risk and low risk persons. The WHO led initiative of reducing the NCDs (non-communicating diseases such as heart disease, cancer, diabetes, stroke and cardiopulmonary disease) can only become effective if the prevention issues are carried across diseases and are not only focused on one specific illness. This NCD Alliance has published a WHO Global Action Plan 2013-2020 which aims at reducing the NCD burden by 30% in 2030 (30 by 30). Regional assessments of the effectiveness of such initiatives show that in some world regions this may be reached but in others the targets will be missed if additional efforts are not made.

KEY ELEMENTS OF STROKE CARE

MICHAEL BRAININ

Danube University Krems, Austria

Organised stroke care is a form of care provided in hospital by nurses, doctors and therapists who specialise in stroke patients and work as a co-ordinated team. An updated systematic review has confirmed significant reductions in death (3% absolute reduction), dependency (5% increase in independent survivors) and the

need for institutional care (2% reduction) for patients treated in a stroke unit, compared with those treated in general wards. All types of patients, irrespective of gender, age, stroke subtype and stroke severity, appear to benefit from treatment in stroke units. These results have been confirmed in large observational studies of routine practice. Stroke units may also improve patients' quality of life, and improvements in outcome may persist for several years. Of available therapies in the acute phase of stroke (antiplatelet therapy, intravenous thrombolysis, stroke unit care), stroke unit care has the overall largest benefit because this principle of care may potentially be applied to all patients with acute stroke.

The core components of stroke unit care include

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

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

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

Thrombolytic therapy should be used by personnel trained in its use in a centre equipped to investigate and monitor patients appropriately. Currently thrombolysis is only approved for treatment within 4.5 hours of symptom onset. Thrombolysis requires admission of stroke to hospital and it cannot easily be given in small local hospitals. More recently, endovascular thrombectomy has become standard treatment for large thrombuses in the M1 or 2 segment of the ACM which usually causes severe strokes with NIHSS values of 15 or more. This therapy can only be applied within 6 hours of onset, in selected cases even up to 24 hours, and must be performed in specialized comprehensive stroke centers.

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

Strategies to prevent further strokes should be initiated already when the patient is under early treatment for a first stroke. All patients with stroke (ischemic, hemorrhagic, and stroke of unknown cause) will benefit from systematic swallowing assessment for determination of dysphagia risk, and early detection and management of temperature elevation, very high blood pressure, and cardiac arrhythmia or decompensation. Later on, modification of life style changes, in particular cessation of smoking, and blood pressure reduction with a diuretic and an ACE-inhibitor should be considered. Blood pressure reduction should not be started until after the acute phase.

Patients with ischemic stroke benefit from long-term use of antiplatelet therapy as well as from a statin.

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

DYSAUTONOMIA IN PARKINSON'S DISEASE

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Among the non-motor symptoms found in Parkinson's disease (PD), the dysfunctions concerning the autonomic nervous system are prevalent and constitute an important cause of disability for the patients. Even if some of these dysautonomic manifestations might predate the development of the motor symptoms, and thus, the diagnosis of PD, the most of them are more severe and prominent as the disease advances and were found to adversely affect the activities of daily living and the quality of life.

Nearly all patients with PD have at least one sign of abnormal function of the autonomic nervous system. The spectrum of autonomic dysfunction is broad and includes olfactory abnormalities, gastrointestinal symptoms (salivary excess, dysphagia, gastroparesis, constipation), cardiovascular dysautonomia (syncope, orthostatic hypotension), bladder dysfunctions (urgency, frequency), etc. The neurodegeneration of the central autonomic networks and of the peripheral pre-ganglionic and post-ganglionic projections neurons is the main proposed neuropathological mechanism. There are several assessment methods of dysautonomia, including scales or specific tests. This review will focus on characterizing the principal symptoms of autonomic dysfunction encountered in PD, their interconnections, and will provide up-to-date insights regarding the assessment and management of dysautonomia.

GENETIC LEUCODYSTROPHIES AS A MODEL OF OLIGODENDROCYTE DYSFUNCTION

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Leukodystrophies are a group of orphan genetic diseases that primarily affect the white matter (WM) of the brain. Glial cells play a major role in the structural, metabolic and trophic support of axons.

Diversity of the genetically determined defects that interfere with glial cell functions explain the large heterogeneity of leukodystrophies that may be classified:

- According to neuropathology (staining: orthochromatic, metachromatic, sudanophilic; site of demyelination: sparing U fibres, etc; associated findings)
- According with clinical aspects (peripheral nerve, muscle, eye involvement, macrocephaly, tendinous xanthomas, premature aging, skin and bone changes, endocrine involvement: adrenocortical or ovarian insufficiency, diabetes, etc)
- According to biochemical abnormalities
- According to molecular genetic abnormalities.

We will report the main well known forms (Adrenoleucodystrophy, Metachromatic Leucodystrophy, Krabbe Disease) and some rarer conditions as Vanishing White Matter disease, Vacuolating Leucodystrophy, Alexander disease, Spheroid leukoencephalopathy, etc, and also some recently identified forms, describing the clinical findings for clinical suspicion and the pathogenetic mechanisms.

PREDICTING CLINICAL OUTCOMES AFTER STROKE

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Worldwide, stroke is the second most common cause of death and the third leading cause of disability. Low and middle income countries account for two thirds of all stroke cases. The burden of disability is high among stroke victims who survive. It is estimated that approximately 50% of all stroke victims survive beyond five years and 50% sustain significant disabilities. Recent estimates indicate that stroke-related disability adjusted life years (DALY's) will increase from 38 million DALY's in 1990 to 61 million DALY's in 2020. It is estimated that 33% to 42% of patients require assistance for activities of daily living 3-6 years after stroke, and 36% of patients are institutionalized after 5 years.

Predicting who will have disability following stroke is an important goal. There is no general agreement about what constitutes "recovery" after stroke. Much functional improvement after a cerebral injury is really compensation. The term "brain plasticity" is widely used, but not easily defined. It may refer to changes at many levels ranging from molecular events to behavior.

In acute stroke, neuroimaging is helpful in predicting long-range outcome. In most ischemic stroke patients there is a core of infarction surrounded by tissue at risk of further damage, the penumbra. CT and MR perfusion images can help identify tissue at risk. CT angiograms and MR angiograms may demonstrate an occluded

artery due to a clot which can be removed using endovascular approaches. Once MR diffusion weighted images are positive, tissue is generally not salvageable and not amenable to endovascular approaches. Once a stroke is stable, the outcome depends mostly on the severity of the initial neurologic deficit. The type of neurologic deficits (motor, sensory, visual, etc.) also are important in determining outcome, which also varies by the pathophysiology of the stroke (ischemic versus hemorrhagic). Recovery of function generally follows a predictable pattern in most subjects with improvement “plateauing” by 3 to 6 months following the stroke. Disability status at one month is generally a reliable proxy for final outcome. Stroke severity is clearly a crucial predictor of clinical outcome. In a recent multinational study of acute ischemic stroke, the baseline NIHSS was the most important predictor for outcome in a multivariate analysis, followed by age.

Simple clinical measures can be useful in predicting motor function following stroke. If there is no voluntary movement in the upper extremity by 15 days, or no measurable grip at one month, prognosis for useful arm function is poor. If there is voluntary hip movement by one week, ambulation is possible, but often with the use of an assistive device or orthosis. Arm weakness is less likely to recover than leg weakness and recovery almost always occurs initially in the proximal muscles of both the upper and lower extremity. Between 35% and 40% of patients experience aphasia immediately after stroke. Considerable recovery occurs in most patients during the first 6 months. Recovery from speech disorders often takes longer than motor recovery. Recent studies have shown that the location of the stroke is highly predictable for aphasia improvement after stroke. Lesion load in the left posterior superior temporal gyrus and superior longitudinal fasciculus/arcuate fasciculus is most important.

Depression is another negative predictor for stroke outcome. It is often underdiagnosed and undertreated. 30% to 50% of patients with stroke have at least minor depression. This clearly affects the ultimate degree of recovery and can be successfully treated with antidepressants. Post-stroke depression is associated with dependence in ADL's, and increases the time to recovery. Depression can be a major barrier in engaging patients in exercise and recovery programs. In addition to association with poor functional outcome, depression is also associated with poor cognition. Depression before or at the time of stroke also results in a greater than threefold risk of subsequent mortality in subsequent years. Fortunately, there are many pharmacologic treatments for depression including the SSRI's, and serotonin-norepinephrine re-uptake inhibitors such as venlafaxine.

Evaluating the ability of biomarkers to predict stroke prognosis is an active area of research. These include biochemical markers as well as neuroimaging and neurophysiological markers. Subjects with the Met/Met or VAL/MET alleles at

codon 66 in the BDNF gene have a statistical association with poorer outcome. COMT is an enzyme that influences availability of dopamine in the synaptic cleft and patients who are Met158 allele carriers perform better than Val158 allele carriers. Copeptin and NT-proBNP are also independent variables predicting all-cause mortality in patients with ischemic stroke. Obviously, much more work needs to be done on the value of genomic and biochemical markers to improve recovery.

An important question raised within the past five years concerns the question as to whether there are biological limits to recovery. Could recovery be hard wired? The “70% rule” suggests that upper and lower limb motor impairment resolves by a fixed proportion, which is 70% of the maximum possible improvement. This seems to be true for patients of all ages, both genders, and in countries with different rehabilitation services. Although the majority of patients fit the prediction models of motor recovery, a smaller percentage do not achieve predicted recovery at six months. Further investigation suggests that these “non-fitters” have certain characteristics including no finger extension at 72 hours, severe facial palsy, severe impairment of lower extremity motor function at 72 hours, and a large infarction in the middle cerebral artery distribution. It has been suggested that patients with low potential to recover should be taught compensation strategies early, instead of therapy focused on improving impairment. A number of studies have shown that proportional recovery of motor function depends on the integrity of the corticospinal tract. CST integrity can be determined neurophysiologically by measuring the motor response to transcranial magnetic stimulation (TMS). Patients with no response to cortical stimulation usually have a poor outcome. CST can also be evaluated by measuring fractional anisotropy using diffusion tensor imaging (DTI). In at least one study, resolution of motor impairment depended completely on the presence CST and was independent of physical therapy doses. Cortical network connectivity may also be important in re-establishing a motor output via the CST. Is it possible therapy could assist in improving cortical network connectivity? In the end, however, the integrity of the CST appears to be the ultimate determinant of motor recovery.

The proportional recovery principle may also explain recovery from non-motor impairments, including aphasia and visual-spatial deficits. However, not as much work has been done in these areas. Recent studies in rats have demonstrated proportional recovery of motor function following experimental stroke, suggesting this may be a cross-species phenomenon.

In summary, predicting recovery from stroke may be determined at different time points. Neuroimaging may be important in acute stroke, the clinical examination in acute and subacute stroke, and neurophysiological testing and DTI imaging in later phases of stroke. Genomics and biochemical markers may also play a role in

predicting recovery in the future. The ability to predict recovery following stroke is extremely important not only to patients and their families, but also to clinicians. In the future, perhaps an individual rehabilitation plan can be based on predictive markers.

CHARACTERISTICS AND PREDICTIVE BIOMARKERS OF DRUG RESISTANT EPILEPSY - A CLINICALLY ORIENTED REVIEW

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Patients who have drug resistant epilepsy (DRE) have increased risk for premature death, injuries, psychosocial problems, (e.g. under-education, unemployment, and impaired socialization), psychiatric disturbances, and death. They usually require treatment with higher doses of antiepileptic drugs and/or polytherapy, often resulting in adverse effects and leading to poorer quality of life (QOL).

In spite of the drastic increase in cost, medical and surgical treatment of epilepsy has not changed significantly, and epilepsy remains a disease with high morbidity. The up-to-date management strategies of refractory epilepsy fall into three main categories: pharmacotherapy, epilepsy surgery, and alternative treatment strategies including neurostimulation, ketogenic diet, and lifestyle changes.

The identification of valid biomarkers for outcome prediction of diseases and improvement of drug response, as well as avoidance of side effects is an emerging field of interest in medicine. The concept of individualized therapy is becoming increasingly important in the treatment of patients with epilepsy, as predictive markers for disease prognosis and treatment outcome are still limited. Therefore, there is an urgent need for valid predictive biomarkers to guide patient-tailored individualized treatment strategies in epilepsy, a research area that is still in its infancy.

The mechanisms of drug resistance are not completely understood and are likely to be multifactorial.



Negative predictors for seizure remission include history of status epilepticus, number of failed drug therapies, total number of tonic-clonic seizures, neurologic insult, duration of epilepsy, and developmental disability. Other factors associated with increased risk for intractability include early onset of epilepsy, symptomatic etiology, and large number of seizures prior to treatment.

The likelihood of seizure freedom does not differ substantially whether an established or a new-generation anticonvulsant is used. Focal epilepsy and frequent seizures before antiepileptic drug treatment initiation are also more often associated with drug resistant epilepsy.

Studies have shown higher occurrence of DRE with cortical dysplasia, mesial temporal sclerosis, and dual pathology. Besides that, remote head trauma or brain infection, perinatal pathology, febrile seizures, family history of epilepsy, abnormal neurological status and mental retardation lead to elevated risk for development of drug resistance in individuals with drug resistant epilepsy.

Multivariate analysis showed that frequent seizures during the first two years of disease manifestation, polytherapy, seizure polymorphism and epileptiform discharges on EEG are four independent factors associated with drug resistant epilepsy, and in combination, there is up to 98% certainty that case will be in the drug resistant epilepsy group. Various combinations of these four variables also increase probability of developing drug resistant epilepsy.

Complete seizure freedom and prevention of drug toxicity are stronger and more consistently established drivers of a better QOL in patients with epilepsy than a simple reduction in seizure frequency. Nevertheless, improvement in genomic technologies and research methodology is expected to increase the chances of uncovering truly predictive genetic markers for DRE and further the advancement of epilepsy pharmacogenomics.

TRANSIENT LOSS OF CONSCIOUSNESS – A DIFFERENTIAL-DIAGNOSTIC CHALLENGE

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Transient loss of consciousness (TLOC) defines the various, rather frequent conditions with an abrupt onset of apparent loss of consciousness. Within a short

time (i.e. within minutes), patients have a spontaneous and complete recovery. During TLOCs there is: 1) loss of normal motor control either with flaccid muscle tone or with stiffness that may be accompanied by jerking movements, 2) loss of postural control associated with falls, and 3) unresponsiveness and amnesia for the time period of the event. TLOC can be caused by a trauma such as a concussion, or by non-traumatic pathomechanisms. One of the most essential diagnostic steps is the solid assessment of the patient's history.

The most common cause of non-traumatic TLOC is syncope. Syncope may be neurally mediated (for example reflex syncope or vasovagal syncope). Syncope may also be caused by orthostatic hypotension with blood pressure decreasing upon orthostasis below the lower blood pressure limits of stable cerebral autoregulation. Syncope may also be triggered by cardiac arrhythmias or by structural heart diseases such as aortic valve stenosis. The most relevant differential diagnosis of syncope - and second most common cause of non-traumatic TLOC - are primary or secondary generalized epileptic seizures. The differentiation between syncope and seizure has significant therapeutic consequences but is often difficult, particularly if patients have a convulsive syncope. Rapid recovery with full orientation, very shortly after TLOC, supports the diagnosis of syncope.

Other causes of (non-traumatic) TLOC are 'pseudoseizures' and 'pseudosyncope', conditions during which patients seem to be unconscious although they have not lost consciousness. Misdiagnoses may be frequent and require careful history taking, monitoring of blood pressure, heart rate, respiration and preferably also electroencephalography during the functional 'pseudoseizures' or 'pseudosyncope'. Finally, there are miscellaneous disorders such as vertebrobasilar transient ischemic attacks which are rarely associated with a complete loss of consciousness, the subclavian steal syndrome, cataplexy which is not associated with a loss of consciousness, and excessive daytime sleepiness, metabolic disorders (e.g. hypoglycemia) or 'drop attacks' which are also not associated with loss of consciousness.

Together with the key clinical aspects, the history often supports the differential diagnosis and helps to determine whether the patient experienced an epileptic loss of consciousness, syncope or functional ("psychogenic") loss of consciousness, conditions that are not uncommon in clinical routine.



THE ART OF NEUROLOGICAL EXAMINATION

VOLKER HÖMBERG

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In this course the art of a rational neurological examination will be taught:

More than in any other clinical discipline the history and examination in neurology are the most informative source of information for the clinician. This is of course due to the fact that structure and function of central and peripheral nervous system are clear and informative.

Clinical skills for optimal examination of cranial nerves, motor and sensory functions and screening approaches for cognitive and linguistic analysis will be presented. So the students will soon learn that neurologic examination is much more than just looking at "reflexes".

Also fields notoriously estimated as being difficult (such as eye movements, nystagmus, diplopia etc.) will not be spared but elucidated in an "easy to understand and remember" mode.

MULTIMODAL DRUGS FOR A MULTIMODAL DISEASE

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Parkinson's disease (PD) is now considered to be a multisystem disorder involving pathology and biochemical change in both the central and peripheral nervous system and characterised by both motor and non-motor symptomatology. The complexity of PD offers an opportunity for the development of non-dopaminergic drugs acting on those pathways responsible for the expression of both motor and non-motor components. However, attempts to manipulate non-dopaminergic systems using targeted novel drug molecules has met with only limited success and very few novel dopaminergic approaches have been introduced. The approach used has been that commonly employed in the pharmaceutical industry to develop single action, highly targeted molecules with the objective of avoiding 'off target' actions leading to unwanted adverse events.

However, the complex nature of PD would then require a polypharmacy approach to individualise treatment for each symptom so increasing the risk of drug

interactions. In contrast, understanding why some complex drugs are more effective than others in treating PD has been ignored until recently.

L-dopa is considered to be the gold standard treatment for PD and it is generally considered to reflect a dopamine replacement therapy approach. The dopaminergic actions of L-dopa affect all dopamine receptor subtypes in brain, in contrast to most synthetic dopamine agonists and some dopamine is also converted to noradrenaline. L-dopa is decarboxylated to dopamine in 5-HT neurones and alters serotonergic transmission and it may also act as an aminoacid neuromodulator itself. In addition, L-dopa exerts not only a short duration effect but also produces a long duration response that is poorly characterised but contributes to the overall action of the drug in PD. All of this leads to the conclusion that L-dopa is a complex multimodal drug and this may explain its superior effectiveness in PD. Applying the same analysis to apomorphine which is considered to be the only dopamine agonist with efficacy equivalent to that of L-dopa reveals a similar picture. Apomorphine has broad spectrum effects at dopamine receptors in brain but also possesses significant activity at a range of serotonergic and noradrenergic receptors. It too appears to be multimodal in nature.

Recently, safinamide has been introduced in to the treatment of PD as a reversible selective MAO-B inhibitor. However, safinamide possesses a range of pharmacological actions and it these that separate it from other agents. In particular, safinamide has sodium channel blocking properties and these can lead to a decrease in glutamate release thought to underlie dyskinesia in PD. Indeed, safinamide both increases motor function and decreases the intensity of dyskinesia when tested in MPTP treated primates and to some degree in man. Safinamide also has effects on non-motor symptoms of PD with activity on pain, cognition and mood. So, safinamide is a recent example of how multimodal drugs are relevant to the treatment of PD. In a similar vein, zonisamide is now being used to treat motor symptoms of PD based on its multiple pharmacological effects that include MAO-B inhibition and sodium channel blocking activity.

The general view is that drugs with multiple targeted actions are a useful but underused approach to treating the symptoms of PD and that a multimodal approach will be useful for the future therapy of PD.



MILD COGNITIVE IMPAIRMENT (MCI)

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Mild cognitive impairment (MCI) is considered an intermediate state between normal aging and dementia. However, MCI is a heterogeneous entity, it has multiple etiologies, different clinical presentations [e.g. amnestic, executive, behavioral], vague diagnostic criteria and variability in clinical outcomes over time and in rates of progression (and not infrequently regression!). Delivery of MCI diagnosis means no more than saying that the person, while not demented, has some recently acquired cognitive deficits that may be predictive of further cognitive and functional decline and dementia. Giving a person this diagnosis may have a detrimental effect as the subject may interpret this as meaning that (s)he is on an accelerated downhill slope while in fact, a significant number of people who are diagnosed as having MCI may maintain stability or revert to normality. On the other hand, patient's awareness of the diagnosis may be advantageous as these subjects and their caregivers do need diagnostic workup, ongoing monitoring, support and treatment, if available, and may choose to be knowledgeable about their prognosis in order to reach significant decisions as long as they are cognitively capable to manage their affairs.

DIABETIC NEUROPATHY – DIAGNOSIS

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Diabetes mellitus has a very high prevalence in the general population all over the world. Statistics show that neuropathy can be observed in almost half of the diabetic patients. Thus, diabetic neuropathy due to its frequency, medical complications and healthcare costs can be considered a social problem. The most frequent form of neuropathy is the distal symmetric sensory polyneuropathy, but other forms can also be encountered (mononeuropathies, entrapment neuropathies, autonomic neuropathy, treatment induced neuropathy). Among the mononeuropathies, carpal tunnel syndrome is by far the most frequent, but also ulnar neuropathies at the elbow, fibular neuropathies and meralgia paresthetica can be encountered. Cranial nerve involvement can be seen in neuropathies of the oculomotor nerves and facial

nerve. The radiculoplexus neuropathies are characterized by regional involvement (cervical, thoracoabdominal or lumbal), a typical temporal profile, intense pain and lasting weakness. A specific syndrom results from an aggressive treatment of hyperglycaemia – the treatment induced neuropathy is characterized by pain and long evolution. The diagnosis involves a correct clinical evaluation and the use of different paraclinic methods. Electroneuromyography is a good tool, but provides information regarding only the large fibers. Small fiber involvement requires other methods: skin biopsy, with determination of the intraepidermal nerve fiber density, is very specific. The corneal confocal microscopy evaluates “in vivo” the density and length of corneal small nerve fibers. QSART, QST, laser evoked potentials belong more to research areas and are not common in clinical settings. Small nerve fibers have sensory and autonomic functions; both are involved in neuropathies. Evaluation of the electrochemical skin conductance with Sudoscan evaluates autonomic nerve fibers changes, that are correlated with the sensory nerve fibers disorders.

FROM NEUROBIOLOGY TO EVIDENCE-BASED MEDICINE CONCEPTS IN NEUROREHABILITATION AFTER STROKE

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Brain damage affects all three levels of structural and functional organization: cellular and molecular level, circuitries level and dynamic network level and launches an endogenous continuous brain defense response which consists in neuroprotection (the immediate response) and neurorecovery (a later response).

Endogenous neuromodulation represents at the cellular and molecular level the optimization of common biological processes that could potentially generate cell death or promote neurodegeneration. At the circuitries and dynamic network levels, it represents the tendency in reinbalancing of functional connectivity in resting-state networks.

In the last years, there has been a substantial effort in understanding the brain functioning and how to enhance endogenous neuromodulation and neurorehabilitation in general, by using a large spectrum of neurotechnologies such as imaging techniques (functional magnetic resonance imaging, ligant-based positron emission tomography, diffusion-tensor imaging), quantitative electroencephalogram, magnetoencephalography, eye tracking, optogenetics,

transcranial magnetic stimulation, transcranial direct current simulation, deep brain stimulation, computational neuroscience and brain-computer interfaces. The combination between these technologies provide valuable information about the structure-function relationship underlying resting-state networks, about the dynamic cross-talk between networks and about the abnormalities in the functional connectivity in different pathologies.

Neurorecovery can be enhanced by pharmacological intervention, physical activity, electromagnetic stimulation, psychological support, environmental stimulation or any demonstrated combinations of these factors capable of improving the patient's condition after brain and spinal cord injuries. From the pharmacological perspective, it is clear that the focusing on molecules that are capable of mimic the function of endogenous molecules with multimodal and pleiotropic neuroprotective effects is the best approach in neurorecovery, especially when they are associated with intensive physical training.

Biological agents (e.g., neurotrophic factors and related molecules) with modulating and multimodal effects are better pharmacological agents for brain and spinal cord protection and recovery, because they usually have also pleiotropic neuroprotective effect. That is why they are capable of pharmacologically bridging acute neuroprotective processes with the long-term recovery processes.

There are many animal and human studies trying to elucidate the cellular and molecular mechanisms of plasticity of the nervous system. A better understanding of the mechanisms underlying the neuroplasticity will reflect in a more efficient and comprehensive treatment.

Over the last decades, therapeutic approaches for stroke have significantly evolved and improved as a consequence of the implementation of modern stroke units, improvement of general medical care and more structured and early administered rehabilitation schemes.

Thrombolytic therapy with rt-PA (recombinant tissue plasminogen activator) has been developed and a number of clinical trials have recently confirmed the effectiveness of thrombectomy to be better than rtPA alone.

Except thrombolytic therapy and thrombectomy there is still no widely accepted therapy for acute ischemic stroke. Current data shows that even if advanced procedures can be used, 60% of stroke patients die or remain with a certain level of deficit. As it is widely accepted that immobilization-related complications cause over 50% of stroke patients' deaths, rehabilitation plays an important role in stroke care.

CHALLENGES AND OPPORTUNITIES IN STROKE RECOVERY

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It is getting clearer that multimodal drugs may play an important role in pharmacological support of neurorehabilitation after stroke.

The results of recently published large and well-controlled clinical studies show a positive effect of Cerebrolysin on neurological recovery after acute ischemic stroke. The newly published CARS study assessed the efficacy and safety of Cerebrolysin in combination with a standardized rehabilitation program. The primary study endpoint was the Action Research Arm Test (ARAT) at day 90, assessing upper-limb motor functions. Cerebrolysin was administered for 21 days, starting within 48-72 hours after ischemic stroke.

The study showed a statistically significant group difference in the upper-limb motor function (ARAT) at day 90 – primary end point. Cerebrolysin was also superior over placebo in most of the secondary endpoints like the NIHSS, Barthel Index and mRS. Also, at day 90, patients treated with Cerebrolysin showed less depressive symptoms and better quality of life. In addition, the most important measure for early benefit, the NIHSS at day 21, showed statistically significant superiority of Cerebrolysin. Analysis of the safety parameters did not show any clinically statistical significant differences between the treatment groups. The trial indicates that early combination of rehabilitation with a multimodal medication of neuroprotective and recovery properties is a valid therapeutic approach.

Furthermore, CARS 1 and CARS 2 meta-analysis provides evidence that Cerebrolysin has a beneficial effect on motor function recovery in early rehabilitation patients after stroke. All pre-planned primary meta-analytic results were statistically significant.

ANTICORRELATED PROCESSES IN NEUROBIOLOGY - POSSIBLE CONSEQUENCES FOR NEUROREHABILITATION STRATEGIES

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1. INTRODUCTION

Clinical studies in neurorehabilitation face several problems such as high heterogeneity regarding their methodology, the lack of efficacy that usually characterizes single-intervention rehabilitation, the difficulty of conducting a clinical trial that follows a holistic approach, the difficulty of creating protocols with personalized interventions, and the difficulty of shifting recently developed neurophysiological concepts from imagistic studies into clinical practice. One of the principles heavily promoted by Corbetta et al. is the need to combine specific interventions for motor function with a cognitive-behavioral intervention. The rationale behind this approach is based on the dynamic interconnectivity among the brain circuits involved in motor execution, executive function, attention and memory (Corbetta M, 2011).

2. LEVELS OF CNS ENDOGENOUS MODULATION AND NEURORESTORATION

The concept of endogenous neuromodulation (Muresanu DF, 2012) refers to the brain's capacity to balance anti-correlated processes, such as pro-survival signaling mechanisms versus pro-death signaling mechanisms at the cellular and molecular level, long-term potentiation versus long-term depression at the local circuit level, synchronization versus desynchronization at the dynamic network level. Every level in turn comprises several sublevels, each of which is characterized by a multitude of anti-correlated processes.

Synergism is an essential propriety of complex biological systems such as the nervous system, through which multiple mechanisms at different levels converge to the same result, such as rebalancing neurobiological processes after an insult. Failure of endogenous defense activity triggers a pathological "synergism" that leads to a stable, robust state that characterizes the chronic status after stroke when rehabilitation procedures are less efficient.

The relationships among the brain's levels of organization

Regarding brain function, three levels of organization have been described: the cellular and molecular level, the circuitry level, and the dynamic network level, all of which have been implicated both in maintaining endogenous homeostasis and in pathophysiological processes. These levels are inter-correlated; alterations that directly affect the cellular and molecular level also affect the circuitry and dynamic network levels.

The neurovascular unit (NVU) has an essential role in modulating brain homeostasis and is characterized by dynamic communication among neurons, astrocytes, smooth muscle cells, endothelial cells, pericytes, basement membranes, and extracellular matrix. Beyond the damage to the NVU caused by the primary lesion, secondary mechanisms also have a negative impact upon neurovascular coupling. Spreading depression, which represents the propagation of a depolarization wave associated with transmembrane ionic and water shifts, represents an important mechanism in the propagation of tissue damage during stroke and leads to the alteration of neurovascular coupling beyond the ischemic/hemorrhagic lesion (Hinzman JM, 2014).

In a recent study that combined fMRI, pulsed arterial spin labeling (PASL) and carotid Doppler, hemodynamic lag was observed in stroke patients (stroke onset less than 2 weeks before); this lag was considered to be related to impaired neurovascular coupling due to microvascular damage at the cellular level, especially impaired astrocyte and pericyte reactivity. Interestingly, there was a higher rate of lag in patients who received tPA, probably because of the microvascular damage that followed reperfusion. Hemodynamic lag contributes to neural communication impairment and network structure alteration and is thus associated with a higher risk of developing executive dysfunction and neglect (Siegel JS, 2015).

Inter-hemispheric functional connectivity

Inter-hemispheric connectivity is considered to modulate the informational flow in the brain; increased synchronization of the two hemispheres in the gamma frequency is considered to be essential for cognitive processes (Helfrich RF, 2014). Additionally, reduced/imbalanced connectivity is associated with cognitive-behavioral disturbances (Ben-Shimon E, 2015; Luo C, 2015; Qiu YW, 2016). Numerous studies have focused on the imbalance of interhemispheric functional connectivity after stroke by using either imaging or neurophysiological techniques. This imbalance consists of reduced activity on the lesioned side and increased excitability on the contra-lesioned side. The hyper-excitability has been explained by axonal sprouting and dendritic branching on the cellular/molecular level and by the recruitment of circuits normally involved in other functions and the loss of inhibitory influence from the lesioned hemisphere at the circuitry level. The imbalance starts as a compensatory mechanism, providing support for the affected side, but it can also be detrimental by exercising an inhibitory effect on

the lesioned side. This inter-hemispheric conflict has been found to have an impact on the recovery of motor deficits, aphasia or attention deficits after stroke (Teki S, 2013; Blesneag AV, 2015; Lim JS, 2015; Petitet P, 2015).

Interconnectivity of behavioral processes

Multiple behavioral processes have been described in accordance with each functional domain (motor, language, attention, memory, etc.); these processes were assigned to lesions in specific areas. However, these behavioral processes are highly correlated, such that stroke can trigger a variety of deficits even if it directly affects only a few structural connections. (Corbetta M, 2015). For example, neglect patients have concomitant multiple deficits due to altered fronto-parietal cortical networks – the dorsal attention network (DAN) and the ventral attention network (VAN). The DAN is responsible for both top-down and bottom-up types of attention, while the VAN is predominately responsible for bottom-up attention; these two networks function through a dynamic interaction. Although stroke usually determines structural alteration of the VAN only, it triggers a functional imbalance between these two anti-correlated circuits that also affects the DAN. This connectivity imbalance explains why patients with neglect can also develop low arousal, impaired working memory and lower attentional capacity deficits, including motor attention deficits (He BJ, 2007). Additionally, language networks such as the fronto-temporo-parietal network (FTPN) comprise both brain regions specialized in this function as well as regions with role in cognitive control (Fedorenko, 2014). This explains why aphasia is usually also associated also with executive dysfunction and attention deficits that can have a negative impact upon rehabilitation (Murray LL, 2012; Brownsett SL, 2014; Geranmayer F, 2014).

Integration and segregation of functional networks

Currently, functional connectomics, especially regarding cognitive function, is viewed as a dynamic balance between anti-correlated networks that function by activation (synchronization) and deactivation (desynchronization) in response to different tasks (Fox MD, 2005). Synchronization is responsible for the integration of information, while desynchronization is responsible for segregation of information. This balance between integration/segregation provides both stability and flexibility within brain circuits (Tognoli E and Kelso J, 2014). The extent of the damage or the need to rebalance these networks has important consequences upon cognitive rehabilitation. For example, a successful speech therapy is accompanied by higher activity in the left FTPN and lower activity in the default mode network (DMN) during speech, and a failure of rehabilitation is associated with high activity in both the right FTP and the DMN. Another example of reduced segregation is neglect patients who present a reduced anti-correlation between dorsal attention/sensory-motor networks and default/fronto-parietal networks (Baldassarre A, 2014). However, components of resting state networks are also activated during tasks and have

a facilitating action upon task-positive networks such as the posterior cingulate cortex (PCC), which is part of the DMN, but is activated along with the FTPN during speech tasks (Geranmayer F, 2016). Such common regions (hubs) are usually characterized by “rich club organization”, meaning that they have a high degree of connectivity with other brain regions and are responsible for the integration of internal cognitive processes with sensory and motor information (de Pasquale F, 2015). Altered integration of information affects communication between separate cognitive networks and is observed in patients with small vessel disease, who have reduced cognitive flexibility and altered executive function.

Network efficiency

Stroke, including small vessel disease (SVD), results in decreased structural connectivity, as measured by fractional anisotropy (FA) (Van Meer MP, 2012; Reijmer YD, 2016). Structural reorganization results in changes regarding functional efficiency. Small-worldness, which has been described based on graph analyses as being the best combination possible of short path length between regions of interest and an increased clustering coefficient, is considered the optimal organization for a functional cognitive status, being a balanced compromise between minimizing the energetic costs of wiring and maximizing information processing (Douw L, 2011; Bullmore E and Sporns O, 2012). After a medium/large stroke, the initial loss of structural connections triggers, as a compensatory mechanism, hyper-excitability in surrounding regions and on the non-lesioned side, which is characterized by synchronization loss and increased random integration, leading to increased small-worldness (Van Meer MP, 2012). During the rehabilitation process, small-worldness can either decrease or normalize, depending on the recovery of function: it decreases in patients who develop mainly compensatory mechanisms and normalizes in patients in whom physiological connections are successfully restored (Cheng L, 2012; Caleo, 2015; Lee J, 2015).

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MICROBIOTA, ENTERIC NERVOUS SYSTEM AND NEURODEGENERATIVE DISEASES

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Human beings are populated by trillions of bacteria, used to live in a mutually advantageous symbiosis with our bodies. However, studies from recent years suggest that this microbiota could influence triggers for different human pathologies, including neurodegeneration. Neurodegenerative diseases have still no elucidated etiology and no disease-modifying treatment. Brain and gut are connected through a massive enteric nervous system, which might accumulate unfolded proteins and transport them to the brain. In the present work I will try to evaluate the most recent data regarding neurodegenerative disorders and microbiota.

THE TREATMENT OF DIABETIC NEUROPATHY AND THE PREVENTION OF DIABETIC FOOT

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Peripheral diabetic neuropathy (PDN) is worldwide the most common chronic complication of diabetes. Approximately one of three diabetic patients is affected by distal symmetric polyneuropathy representing a major problem of health due to clinical manifestations which are associated with high morbidity, reduced quality of life and increased mortality. The early recognition and an appropriate management of diabetic neuropathy is mandatory in order to make an efficient secondary prevention.

Screening for symptoms and signs of diabetic neuropathy at every visit of the patient in diabetes clinic may detect the neuropathy even in earliest stage of it. Thus, recognition and a proper treatment for diabetic neuropathy may improve symptoms, outcome and quality of life.

Treatment of diabetic neuropathy is based on three principles: 1. maintaining a good metabolic control and reduction of cardiovascular risk factors; 2. pathogenic treatment of neuropathy; 3. symptomatic treatment .

Nowadays, antioxidant alpha lipoic acid used in order to reduce oxidative stress and benfotiamine are available as pathogenic treatment for diabetic polyneuropathy in several countries only. Several meta-analyses suggest that alpha lipoic acid is an effective drug even for symptomatic diabetic polyneuropathy. The symptomatic treatment remains a challenge for the physician. Centrally acting analgesic drugs are frequently used to treat neuropathic pain, but these agents may have side effects, especially in the central nervous system, which may limit their use and in the same time, they not slow the progression of the neuropathy.

Diabetic foot syndrome is one of the most frequent cause of admission among diabetic patients, one of its main causes being the presence of sensory-motor diabetic neuropathy. Up to 50% of PDN may be asymptomatic; if it is not recognized and if preventive foot care is not implemented, patients are at risk for injuries to their insensate feet. Furthermore this pathway lead to acute or chronic ulcer. For this reason, the correct diagnostic of foot lesions, rapid and appropriate treatment of them (by a combined approach gathering podiatrist, diabetologist, neurologist, surgeon, etc) and education in foot care are the cornerstones of the diabetic foot treatment.

CRANIAL ENDOPROTHESIS WITH A SLIDING SYSTEM

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The invention relates to a cranial endoprosthesis with a sliding system, used to repair the traumatic defects of the skull, by the surgical procedure of cranioplasty. The cranial endoprosthesis consists of a superior sliding layer, a lower sliding layer and a fastening system, and the sliding layers are made up of mobile cells with sliding system. For assembling, the lower sliding layer is positioned in a non-sliding state, tangent to the lower surface of the skull, and for actuating and sliding the movable cells of the lower layer, an actuator key is required.

CRANIAL IMPLANT WITH OSTEOINTEGRATING STRUCTURES AND FUNCTIONAL COATINGS

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The invention relates to the structure and fastening method of a mesh implant with functional coatings having the role of osteointegration, used for cranioplasties and reconfigurations of major cranial defects. The implant made of pure Ti or a biocompatible Ti alloy with osteointegration structures, consists of two layers, one fixed and the other movable, interconverted so that translations in two perpendicular directions can be made while maintaining the fixed layer. The cells of the two layers are arranged in two directions whose intersection at any point forms a specific angle α .

NANODELIVERY OF CEREBROLSYIN WITH 5-HT₆ RECEPTOR ANTAGONIST INDUCES SUPERIOR NEUROPROTECTIVE EFFECTS FOLLOWING CONCUSSIVE HEAD INJURY INDUCED EXACERBATION OF BRAIN PATHOLOGY IN SLEEP DEPRIVATION^s

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Sleep deprivation (SD) in military leads to often decline in cognitive and higher mental functions. Since a close link between SD and onset of Alzheimer's Disease (AD) is established, it appears that SD may worsen brain pathology in AD. Previously, we showed that 48 or 72 h SD alters serotonin (5-hydroxytryptamine, 5-HT) metabolism and induces brain pathology that is significantly reduced by 5-HT₃ receptor antagonist ondansetron. Recent reports suggest that treatment with

5-HT₆ receptor antagonists has also beneficial effects in attenuating behavioral and cognitive functions in AD.

We found that Cerebrolsyin, a balanced composition of several neurotrophic factors and active peptide fragments when delivered through TiO₂-nanowired-technology results in superior neuroprotective effects on brain pathology in AD. Thus, we examined whether AD brain pathology is aggravated in SD and nanodelivery of 5-HT₆ receptor antagonist SB-399885 together with Cerebrolsyin may have synergistic enhanced therapeutic effects in AD in combination with SD.

Male Wistar rats (age 20 to 25 weeks) were subjected to 72 h SD using an inverted flowerpot model placed in a pool of water maintained at 1 cm below the surface so that animals are deprived of restful sleep. After 72 h of SD these animals were administered amyloid-beta peptide (A β P, 250 ng/10 μ l, i.c.v.) in the left lateral ventricle once daily for 4 weeks to develop AD like symptoms and brain pathology. Control group received 0.9 % saline instead of A β P.

Our observation shows that A β P infusion in SD rats resulted in marked exacerbation of brain pathology (2 to 3 fold higher) after 4 weeks in terms of A β P deposition in the brain, neuronal damages in cortex, hippocampus and cerebellum, blood-brain barrier (BBB) breakdown and edema formation as compared to identical A β P infusion in control rats. These SD rats also showed much worse behavioral performances on Rota-Rod treadmill, inclined plane angle test, and water maze apparatus.

TiO₂-nanowired delivery of 5-HT₆ receptor antagonist SB-399885 (3 mg/kg) together with Cerebrolsyin (2.5 ml/kg) intravenously once daily for 2 weeks starting from 1 week after the onset of A β P infusion resulted in marked neuroprotection in AD brain in SD group as compared to these drugs either given alone or without nanotechnology under identical conditions. Interestingly, nanowired delivery of drugs in combination also improved behavioral function remarkably in SD rats after A β P infusion. These observations are the first to show that a combination of 5-HT₆ receptor antagonist with Cerebrolsyin using nanodelivery has superior neuroprotective effects in AD induced brain pathology in SD, not reported earlier.

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Aruna Sharma, MD is Secretary of Research International Experimental Central Nervous System (CNS) injury & Repair (IECNSIR) currently working at Uppsala University Hospital, Uppsala University, Sweden. She is a qualified experimental Neuropathologist and received her training at Karl Marx University Leipzig, Institute of Neurobiology (1987-1988); Semmelweis University Medical School, Department of Human Morphology and Developmental Biology, Budapest, Hungary (1988-1989), Free University Berlin, Germany (1989-1991) and Neuropathology Institute Uppsala (1992-1995). Her main interest is now focused on Indian Medicinal drugs and their effects on the Central Nervous System Function, toxicology, neurorepair and neuroprotection. She is also investigating neurotoxicological profiles of many Ayurvedic traditional drugs with special reference to those containing metal oxide or metal ashes. Dr Sharma is member of various Distinguished American Organizations and elected to receive the prestigious award "Women of the Years Representing Sweden Award 2009". She earned Top 15 % technology Award of 2016 at Global Innovation Summit & Showcase on her recent Innovation on "Neuroprotective effects of Nanowired delivery of Cerebrolysin together with alpha melanocyte Stimulating hormone (-MSH) in concussive head injury in sleep deprivation, US Govt. Washington DC, May 22-25, 2016". She is also "Visiting Professor" of University of Basque Country, Bilbao, Spain supported by Basque Govt. Foundation (2015-2018) where she is engaged in nanodelivery of drugs affecting CNS Injury in neurodegenerative diseases e.g., Alzheimer's and Parkinson's Diseases. Aruna is selected as one of the Poster Judges in Brain & Behaviour-Neuroscience by the American Association for advancement of Science in their 184th Annual Conference, Austin TX, Feb 15-19, 2018. She has published over 140 original research papers in Reputed Neuroscience Journals with an H-index = 19 (ISI database, 143 citations) as of today.

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FOCUS ON MULTIDISCIPLINARY APPROACH IN ADVANCED PARKINSON'S DISEASE

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Parkinson's disease (PD) is a complex progressive neurodegenerative disorder characterized mainly but not exclusively by loss of dopaminergic neurons in the basal ganglia. Motor problems such as bradykinesia, tremor and rigidity tend to predominate early in the disease. Later in the course of the illness, patients present motor complications and a plethora of non-motor symptoms, with diverse functional and psychosocial consequences. And all these symptoms disease related are frequently "wrapped" in various comorbidities.

The advanced therapies for PD - subcutaneous apomorphine pump, levodopa-carbidopa intestinal gel (LCIG) and deep brain stimulation (DBS), – require specialized multidisciplinary teams (MDT) to ensure successful implementation. Moreover, most non-motor features do not respond satisfactorily to dopaminergic drugs and some might get even worse. Therefore, a MDT, combining pharmacological treatment with non-pharmacological interventions is needed in order to manage such a complex disorder.

Clinical experience suggests that optimal management requires a multidisciplinary approach, with multifactorial health plans tailored to the needs of each individual patient and up to 20 different health care professionals may provide beneficial interventions.

It has been proven that a MDT approach improves the motor function and the quality of life (QoL) in patients with PD and QoL for their caregivers; therefore, it is increasingly recommended in PD treatment guidelines.

NEUROINFLAMMATION: THE RISK OF GROWING OLD

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Frailty is a common geriatric syndrome characterized by age-associated declines in physiologic and cognitive reserves across multi-organ systems, resulting in an increased vulnerability for adverse health outcomes. Chronic (non-resolving) inflammation is likely a key pathophysiologic process that contributes to the frailty syndrome directly and indirectly through other intermediate physiologic systems, and complex multi-factorial etiologies such as obesity and diabetes. Aging is associated with elevated levels of circulating cytokines and pro-inflammatory markers, and age-related changes in the immune system (often referred to as 'immunosenescence' or 'inflammaging'). Hippocampal processing is more easily disrupted in old animals than in younger ones when the peripheral innate immune system is stimulated, suggesting that aging can facilitate neurobehavioral complications associated with peripheral infections. Innate immune cell types, especially mast cells and microglia, are likely to contribute importantly to non-resolving inflammation in the context of aging. Although we think of aging as a general slowing down of the body's cellular activities, the latter cell populations actually appear to become more reactive. As an animal ages, mast cells express alterations in degranulation behavior. Microglial cell reactivity/sensitivity persist throughout the entire lifespan, and may explain how stimulation of microglia early in life can induce long-term changes in brain function. Senescence of resident microglia (and astrocytes) might contribute to the age-related increase in risk for neurodegenerative diseases. Dystrophic (senescent) rather than activated microglia are found in mouse brain with aging. Experimental models of aging show aberrant microglial cell behaviors, e.g. in terms of an increased inflammatory state, in which microglia are 'primed' to be activated and resistant to regulation. Primed microglia are more sensitive to a secondary inflammatory stimulus, thus leading to an exaggerated inflammatory response. Microglial priming might be explained also by mechanisms that underlie trained immunity (enhancement of inflammatory responses by epigenetic mechanisms mobilized after first exposure to an inflammatory stimulus). Primed microglia may over-react to a second challenge, resulting in an enhanced pain intensity and duration. Challenge to the aged brain's immune system leads to amplification /prolongation of microglia activation that may, over a long period of time, manifest itself in deleterious behavioral and cognitive consequences. A mast cell - microglia dialogue may likely contribute to exacerbate the effects of aging on pro-inflammatory behaviors. Obesity and diabetes are both states of chronic low-grade inflammation. A general rise in occurrence of the latter conditions with age may, in effect, place the elderly

in 'harms way' for exposure to low-grade, non-resolving inflammation. Indeed, an endotoxin-induced, persistent state of low-grade inflammation is associated with innate immune 'programming' or 'memory'. Given the close link between blood-brain barrier integrity and cognitive dysfunction in aging, acute and chronic inflammatory pain states, including neuropathic pain (which is associated with low-grade chronic inflammation), may well alter barrier permeability. Identifying safe and efficacious treatments for chronic pain remains a prime public health concern, especially considering the progressive increase in the world's elderly population, and the challenge of age-related pharmacokinetic/pharmacodynamic issues and polypharmacy.

BRAIN AND NON-BRAIN STIMULATION THERAPY FOR NEUROLOGICAL DISORDERS

JOSEP VALLS-SOLE

Senior Consultant in the Neurology Department of the Hospital Clinic of Barcelona, Spain

Brain-stimulation-based treatments (BSBT) have shown a short-lived effect on a variety of neurological and psychiatric disorders. However, non-brain-stimulation-based treatments (nBSBT) have also shown benefits that, similarly, last for a short time. I intend to present a review of many forms of therapeutic stimulation, which reported some benefit. Some benefit, measured with various outcome scores, may not be higher than placebo but this may still be acceptable if there are no side effects. Effectiveness are often measured using behavioral or performance tasks and subjective-rating scores, which stresses the importance of the patient feelings. Most novel forms of treatment are based on electrical stimulation and not necessarily direct to the brain but implying peripheral nerves (nBSBT), which effect can combine input to the brain and feedback from target organs. There is a tendency to use simplified methods. While repetitive transcranial magnetic stimulation or transcranial direct current stimulation require relatively complex machines, a clinical setting and physician supervision, new proposals are limited to set portable stimulation devices and there is a tendency for home-based therapeutic applications that can be remotely supervised. New treatments are applied while subjects perform motor tasks or are immersed in sensory experiences. BSBT may set the right level of excitability in brain circuits to enhance sensory experiences or improve performance. While BSBT may have its place in a hospital setting and research, some nBSBT treatments are well suited to take home and be self-administered by the patient at the desired time and frequency as an add-on therapy. The combination of both, BSBT and nBSBT, as it may be the case with illusions derived from visual, auditory, haptic and olfactory inputs in a virtual reality environment, may be the next step.

MANAGEMENT OF ADVANCED PARKINSON'S DISEASE: DAT - LIMITATIONS AND UNANSWERED QUESTIONS (HOW EARLY DAT SHOULD BE INITIATED?)

JÓZSEF SZÁSZ

University of Medicine and Pharmacy Targu-Mures, Romania

Parkinson's disease (PD) is one of the most important, increasingly prevalent and progressively disabling neurodegenerative disorder of later life. None of the available treatments influence the progression of the disease. Since the discovery of levodopa as the mainstay of pharmacotherapy in the early 1960s, the pharmacological treatment of PD has been continuously debated and adapted, mainly as a result of the pharmacokinetic properties and changing pharmacodynamics of this drug during the disease progression, as this changes inevitably lead to predictable and unpredictable response fluctuations, both motor and non-motor. Motor fluctuations and dyskinesias affect almost all patients with PD at some point during the disease course, with major implications in global health status. There are now several treatment options for switching from intermittent, non-invasive therapy (oral, transdermal patch) to device-aided treatment (DAT). The continuous intra-jejunal infusion of levodopa (Levodopa-Carbidopa Intestinal Gel, LCIG) or apomorphine infusions offer significant benefits for selected patients and can be considered an option prior to surgery (Deep Brain Stimulation, DBS). The indications for using one of the available DAT are similar and include: pronounced motor and/or non-motor fluctuations, with or without dyskinesias, severe conventional oral dopaminergic therapy-related complications. In spite of undisputable improvements during the last years, many patients remain significantly disabled, and a fully satisfying management of motor complications is still an important unmet need of PD therapy.

CAN WE APPLY PERSONALIZED MEDICINE TO MS PATIENTS?

CRISTINA TIU

Department of Neurology, University Hospital Bucharest, Romania
"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

As we are getting closer to the first quarter of the 21st century, 150 years after Charcot has described MS, we still do not have a cure for this terrible disease, affecting thousands and thousands of young adults. This sounds awfully disappointing at a first glance, but if you are a MS neurologist you are pleased to work in an era where you already need some guidance to choose between the multitude of immunomodulatory drugs coming on stage year after year. Do we

have criteria to choose one drug or another for a certain patient? Is the drug we have chosen the best for our patient? Do we play the card of safety or of efficacy? Can we have both? Is it possible to reach the NEDA 4 status? How do we know a drug works? These are just a part of the multitude of questions that MS patients ask their doctor. The unmet needs of MS neurologists and MS patients, beside the Holy Grail of curing the disease, are better diagnostic tools and a method to select the most appropriate treatment for each patient. As we still do not have such tools we rely on monitoring the disease, on selection of treatments based on the activity and aggressivity of the disease, and the medical history of the patient in order to avoid serious adverse reactions to a certain drug. We look forward to get some results from the current research activity around the world, and as a neurologist who started the professional activity when prolonged corticotherapy was the treatment of choice in MS, I keep hope that before ending my career, I will have the opportunity to apply personalized medicine to my patients.

***THE CONCEPT OF HIGH QUALITY, NON-INTERVENTIONAL
COMPARATIVE EFFECTIVENESS IN NEUROREHABILITATION - NEW
PATHWAYS WITHIN THE FRAMEWORK OF EVIDENCE-BASED MEDICINE***

JOHANNES VESTER

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

Evidence-based practice knocks on the door of clinical research in neurorehabilitation. The clinical trial is the mechanism for comparing and testing therapeutic interventions to determine their effect in human subjects and thus their value in rehabilitation practice (Terrin, 2003, Behrman 2013). But how are the chances to improve therapeutic concepts within the demanding framework of evidenced-based medicine?

While there is growing demand for information about comparative effectiveness (CE), there is substantial debate about whether and when observational studies have sufficient quality to support decision making.

Methodological challenges for analysis and the interpretation of results, as well as the lack of accepted principles to assess quality have limited the practical use of observational research.

Non-randomized studies have been relegated to lower tiers in commonly used hierarchies of evidence, largely because of their heterogeneity, the potential for bias in the results, and the challenges involved in their conduct and interpretation. Within the GRADE system (guidance for use of the Grading of Recommendations Assessment, Development, and Evaluation), observational studies start as low quality evidence and even can be rated further down if relevant evidence comes from studies that suffer from a high risk of bias.

Recent calls for using the full range of high-quality comparative effectiveness (CE) research to inform decisions about medical diagnostics and interventions have brought forth a spate of consensus offerings about recognizing quality in observational CE studies and meta-analysis.

An important milestone has been achieved by implementing the GRACE Principles for High-Quality Observational Studies of Comparative Effectiveness. This important guidance provides a hierarchy of evidence for observational research on comparative effectiveness that can be used by decision-makers, as well as key elements of good practice including defining research questions and methods a priori; collecting valid, clinically relevant data; analyzing, interpreting and reporting data, including sensitivity analyses and alternative explanations for findings; and conducting these studies in accordance with accepted good practices.

In this lecture, current perspectives of evidence-based medicine, classic and modern approaches to comparative effectiveness research, future pathways to improve the quality of CE trials, are discussed with examples from different fields of neurorehabilitation.

CURRICULUM VITAE





ANGELO ANTONINI

ITALY

Angelo Antonini graduated in Medicine in 1986 and completed Neurology training in 1990 at the University of Rome "La Sapienza" in Rome where he developed skills in neuropharmacology and movement disorders. After obtaining a scholarship in 1990, in 1991 he started a PhD in Neuroradiology with PET and MRI at the University of Zurich and the Institute of Physics Paul Scherrer in Villigen, Switzerland, which he completed in 1994. PET studies focused on the dopaminergic system, metabolic disorders and cerebral blood flow in healthy subjects, in Parkinson patients and with other movement disorders as well as psychiatric disorders. MRI studies focused on the study of signal T2 and its relationship with free iron as degeneration biomarkers. After one year as Post- Doc in Zurich, in October 1995 he continued his research at the Neuroimaging Laboratory of NY Shore University Hospital and was promoted to Assistant Professor at New University York. During this period, the research focused on the study of brain networks and their modulation with pharmacological and surgical interventions. In November 1997, he returned to Italy in Milan at the Parkinson Institute where he contributed to the development of a research centre for Parkinson's disease and implemented clinical trials and functional surgery at the Department of Neuroscience in collaboration with the University of Milan -Bicocca. In 2010 he moved to Venice in the National Research Institute San Camillo where he is responsible of the Unit for Parkinson and Movement Disorders and became Professor of Neurology at the University of Padua.

During his career, he received several academic awards and funding (including an ongoing Horizon2020 project), published over 340 peer reviewed manuscripts, has a H-Index (Scopus) of 64 and over 13500 citations. He has been an invited speaker at national and international neurology congresses in over 40 countries around the world. He has organized international courses and conferences. He is an honorary member of the Society of Neurology of France and of Romania. It serves as a reviewer for the main neurological journals. He is a Fellow of the European Academy of Neurology, President Elect of the European Section of the Movement Disorders Society and Auditor of the Italian Parkinson's and Movement Disorders Academy.



MIHAELA BĂCIUȚ

ROMANIA

Professor, Department of Maxillofacial Surgery and Implantology,
Faculty of Dental Medicine, „Iuliu Hatieganu” University of Medicine and Pharmacy Cluj-
Napoca, Romania

UNIVERSITY STUDIES

Faculty of Dental Medicine and Faculty of Medicine, „Iuliu Hatieganu” University of Medicine
and Pharmacy Cluj-Napoca

POSTGRADUATE SPECIALIZATION

Oral and maxillofacial surgery

POSTGRADUATE TRAINING

Oral Implantology, 1994, Microsurgery, 1994, International Cancer Management Course,
1998, Competence course in maxillo-dental radiodiagnostic, Ultrasonography, Orthognathic
surgery, Lasertherapy, Cleft surgery and management

SCIENTIFIC AND PROFESSIONAL SOCIETIES

Founding member of the Romanian Society of Reconstructive Microsurgery

Vicepresident of the Romanian Society of Oral and Maxillofacial Surgery
(SRCOMF)

- Member: Romanian Society of Angiology and Vascular Surgery 1991, International Association of Oral and Maxillofacial Surgeons (IAOMS) 1994, European Association of Cranio-Maxillofacial Surgery (EACMFS) 1994, Association of Transylvanian Dermatologists 1996, Romanian Society of Plastic and Esthetic Surgery 2001, Romanian Society of Ultrasonography in Medicine and Biology 1998, Romanian Society of Oral Implantology and Biomaterials 2000, Romanian Society of Lasers in Dentistry 2003

SCIENTIFIC ACTIVITY

- Scientific articles and studies - 190 papers
- Books and textbooks - 10 books authored and coauthored
- Papers communicated in conferences – 71 papers

OTHER PROFESSIONAL ACTIVITIES

Member of the Editorial Board Journal of Cranio-Maxillofacial Surgery – the



official journal of the
European Association of Cranio-Maxillofacial Surgery

Member of the editorial boards:

- Dento-Medica (Sibiu, Romanian – French Dental Association, “Victor Papilian” Faculty of Medicine 1996)
- Quo Vadis (Cluj-Napoca, Humanitarian Foundation “Hipocrate” 1997)
- Romanian Journal of Ultrasonography 1999
- Transilvania Stomatologică 2001

DOMAINS OF RESEARCH AND INTEREST

- Neuroregeneration and neuroplasticity of cranial nerves
- Stem cell based regeneration
- Craniofacial surgery of complex congenital malformations
- Orthognathic surgery of facial deformities and asymmetry
- Oral implantology
- Biomaterials
- Medical rapid prototyping and medical imaging to optimize healthcare

systems

- Craniofacial bone reconstruction and regeneration
- Osteogenesis using callus distraction
- Lasertherapy
- Craniofacial ultrasonography

Research projects – national and international - 22





OVIDIU BĂJENARU

ROMANIA

Corresponding Member of the Romanian Academy

Member of the Romanian Academy of Medical Sciences of Romania

Professor of Neurology and Director of the Clinical Neuroscience Department at the University of Medicine and Pharmacy "Carol Davila" Bucharest, Chairman of the Department of Neurology – University Emergency Hospital Bucharest

- Graduate of the Faculty of Medicine – University of Medicine and Pharmacy (UMF) „Carol Davila” Bucharest (1983)
- Specialist in Neurology (1989), Senior Neurologist (1994); competence in MRI diagnostic in neurologic disorders (1991)
- PhD (1993) - UMF „Carol Davila” Bucharest
- 2006: Doctor Honoris Causa –University „Ovidius” – Constanta
- Postdoctoral specialization at the University „René Descartes” (Paris) during 1993-1994, in clinical Neurology (CHU „Saint-Anne” and „Kremlin-Bicetre”) and research grants in Clinical and Experimental Neurophysiology (CHU „Cochin-Port Royale” and Faculté de Medecine Paris V)
- 2001-2013: President of the Romanian Society of Neurology
- Since 2013: Honorary President ad vitam of the Romanian Society of Neurology
- Since 2001: Coordinator and Chairman of all annual National Congresses of the Romanian Society of Neurology and many other scientific events and teaching courses organized for neurologists in Romania
- Visiting Professor in Vietnam (2013) and Kazakhstan (2015), on behalf of WFN
- Member of the Executive Committee of ENS (European Society of Neurology) between 2005-2009, of the Scientific Committee of ECTRIMS (2004-2009)
- Member of European Academy of Neurology (since 2014), American Academy of Neurology, International Parkinson's Disease and Movement Disorders Society, European Stroke Organisation, Danube Neurological Association (member of the Scientific Board and Deputy Secretary General), and others
- Since 2008: official representative of Romania for UEMS - European Board of Neurology (secretary of the Executive Committee between 2010-2015) and member of the examination board for the title of European Neurologist
- Author of more than 1000 scientific papers reported and published in scientific journals, among 147 cited in ISI Web of Science (Hirsch index 16) and Pubmed. Author of chapters in 2 international books of neurology and author and co-author in more than 15 medical books published in Romania.

- Coordinator of the National Diagnostic and Treatment Guidelines in Neurological Disorders
- National Principal Investigator and Investigator in more than 50 international, multicentric, controlled clinical trials in: stroke, Parkinson's disease and movement disorders, multiple sclerosis, dementia, epilepsy, and others.
- Director of more national research grants
- 9 awards of excellency in medicine from different socio-professional national and international organizations, the Romanian Ministry of Health and the Romanian Orthodox Patriarchate
- Initiator and coordinator of the National Medical Programs of the Ministry of Health and National Health Insurance System for the treatment of: acute stroke, multiple sclerosis, rare neurological diseases, advanced Parkinson's disease (1999 – 2015)
- President of Consultative Commission of Neurology of the Ministry of Health and National Health Insurance System (2008 – 2015)



RODICA BĂLAȘA
ROMANIA

Prof. Rodica Balasa is the head of the 1st Neurology Clinic of Tirgu Mures Emergency County Clinical Hospital and of Regional MS center with more than 800 MS patients being diagnosed, followed and treated ever since 2003.

Prof. Balasa's scientific activity is seen in more than 150 publications with a Total Impact Factor over 50.

The main fields of her research are: multiple sclerosis, especially the neuro-immunology aspects, other primary or secondary demyelinating diseases of the central nervous system, cerebrovascular diseases and interdisciplinary research in neurological pathology associated with other diseases such as diabetes mellitus, endocrine disease, hematological diseases and neoplasm.

Since 2017, prof. Balasa is vice-rector and director of the Doctoral School of the University of Medicine and Pharmacy from Tirgu Mures. She is also a member of AAN, EAN and SNR.



DANA BOERING
GERMANY

EDUCATION:

1. Secondary School I. Slavici Arad, Romania
2. Medical School: Facultatea de medicina si Farmacie I.M.F. Cluj-Napoca, Romania

ACADEMICAL QUALIFICATIONS:

1. Dr. medic: I.M.F. Cluj Napoca 1981
2. German acknowledgement as Dr. med. 1987
3. Specialty qualification: Neurologist 1994
4. Further specialty qualification: Neurorehabilitationist 2001, Neurophysiologist 2002

EMPLOYMENT:

St. Mauritius Therapieklinik Meerbusch 2002-2016
SRH Gesundheitszentrum Bad Wimpfen since 2016

PROFESSIONAL APPOINTMENTS, SCIENTIFIC ACTIVITIES:

1994-2002 Collaboration with the University of Essen in the field of plasticity after stroke, with an emphasis on the role of the cerebellum in motoric learning tasks

Since 2002 Collaboration with the University of Düsseldorf in the field of plasticity after stroke

Since 2009 Collaboration with the Coma Science Group Liege Belgium
Member of the DOC special interest group of the IBIA





NATAN BORNSTEIN

ISRAEL

EDUCATION

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

FURTHER EDUCATION

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

ACADEMIC AND PROFESSIONAL EXPERIENCE

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

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

PROFESSIONAL ACHIEVEMENTS- EDITORIAL BOARD

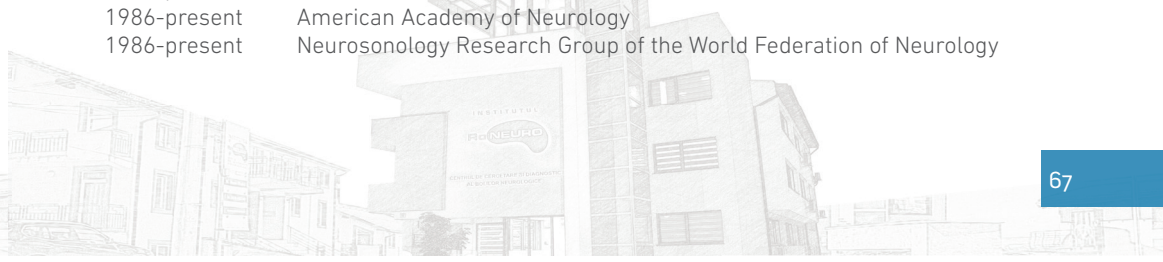
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| 1991-present | Neurological Research Journal, Guest Editor |
| 1991-present | STROKE, Member of the editorial board |
| 1998-present | European Journal of Neurology, Member of the editorial board |
| 1999-present | Journal of Cerebrovascular disease, Member of the editorial board |
| 2000-present | Journal of Annals of Medical Science, Consulting Editor |
| 2001-present | Journal of Neurological Science (Turkish), Member of the editorial board |
| 2001-present | Acta Clinica Croatica, Member of the editorial Council |
| 2003-present | Italian Heart Journal, International Scientific Board |
| 2003-present | Journal of Neurological Sciences, Guest Editor |
| 2004-present | Turkish Journal of Neurology, International Advisory Board |
| 2005-present | Archives of Medical Sciences (AMS) , Member of the Editorial Board |
| 2006-present | Journal of Cardiovascular Medicine, International Scientific Board |
| 2006-present | International Journal of Stroke, Editorial Board |
| 2006-present | Acta Neurologica Scandinavica, Editorial Board |
| 2009-present | American Journal of Neuroprotection& Neurogeneration (AJNN) Member of the Editorial Board |
| 2010 | Neurosonology, International Editorial Board |
| 2010 | Frontiers in Stroke, Review Editor |

PROFESSIONAL ACHIEVEMENTS- REVIEWER

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

MEMBERSHIP IN PROFESSIONAL SOCIETIES

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



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



MICHAEL BRAININ
AUSTRIA

Michael Brainin, MD PhD Dr(hons) FESO FAHA FEAN;
Professor of Neurology at the Danube University Krems, Austria and Chair of the Department of Clinical Neurosciences and Preventive Medicine since 2000. From 1994-2016 he was head of the Department of Neurology at the University Clinic Tulln, Austria. He was co-founder of the national stroke unit network and national stroke registry in 2003. He has been conducting international courses and Master's programs in Stroke Medicine and was Chairman of the WSO Education Committee 2008-2017. He currently chairs the World Stroke Academy. He was President of the European Stroke Organisation (2012-2014) and is President elect of the World Stroke Organisation and will take office in 2018. His scientific interest is in stroke treatment, recovery, and cognition. He received numerous awards, honorary doctorates and honorary memberships from scientific societies around the world. He has published more than 200 peer-reviewed papers and has given more than 1.000 invited lectures. He is associate editor of the European Journal of Neurology and senior consulting editor of Stroke.



ANCA BUZOIANU

ROMANIA

Anca Dana Buzoianu, MD, PhD, is Professor of Clinical Pharmacology, Senior Clinical Pharmacologist, Senior Pediatrician, Dean of the Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, President of the Romanian Association of the Medical School's Deans, General Executive Secretary of the Romanian Society for Pharmacology, Therapeutics and Clinical Toxicology. She is also member of 8 scientific international Societies, and 4 national one.

Postgraduate specialization. Professor Anca Buzoianu is senior clinical pharmacologist and also senior pediatrician. She is the Head of the Department of Pharmacology at Medical Faculty of Cluj, and the leader of a dynamic research team of the department, and member of the Neuroscience Research Center of the Iuliu Hatieganu University of Cluj-Napoca. Professor Anca Buzoianu and her colleagues are actually involved in Pharmacogenetics studies regarding the metabolizing status of some drugs such the oral anticoagulants, antiepileptic drugs, biologic products etc. Other research themes are the therapeutic approach of multiple sclerosis and stroke, pharmacogenetics of the drugs used in dermatological diseases, the effects of some new compounds in pain and inflammation etc. Professor Buzoianu has conducted 8 national grants, 1 international educational project and participated in the research team in another 16 research projects.

Professor Buzoianu has a valuable expertise in Academic Leadership and Management, also in the Management of the Health Care System (Master in the Health Care Management 2009), and in the Quality Assurance evaluation process, being evaluator for the Higher Education for several years. She is President of the Clinical Pharmacology and Toxicology Committee of the Romanian Health Ministry, President of the Pharmacology Committee of the Romanian Physician College, member of the Institutional Evaluation Committee of the Romanian Agency for Quality Assurance in Higher Education.

Scientific and professional societies

- CIDMEF – Conference Internationale de Doyens et de Facultes de Medicine d'Expresion Francaise - member de Bureau Permanent,
- European Association of Clinical Pharmacology and Therapeutics,
- International Association for Medical Education,
- International Association of Medical School,
- The Society for the Study of Neuroprotection and Neuroplasticity



- European College of Neuropsychopharmacology
- International Advisory Board - European Society of Clinical Neuropharmacology
- Balkan Medical Union.
- Romanian Association of the Medical Faculties Deans - president
- General Executive Secretary of the Romanian Society for Pharmacology, Therapeutics and Clinical Toxicology
- Romanian Association for the Study of Pain
- Romanian Society of Addiction and Pharmacovigilance,

Scientific activity

- Articles and studies - 80 papers indexed ISI and in other international data bases
- Books and chapter in books - 12

Prizes

Professor Anca Dana Buzoianu has been honored with the "Victor Papilian" prize of the Cluj Medical Faculty in 2006 for her first volume of "Pharmacology" textbook. In 2007 she received the great "Iuliu Hatieganu" Award for her contribution to the development of a novel domain of academic learning in the frame of the Doctoral School.

In 2011 Professor Anca Dana Buzoianu has received the honorary medal of the National Council of the Physicians of the National Order of Doctors de France

In 2012 Professor Buzoianu Anca has been honored with the Excellence Award for Academic Management - "Dean of the year" with the occasion of the "Health Gala" - offered by the Romanian Ministry of Education and Health Ministry

In 2013 she won again the great Prize "Iuliu Hatieganu" of the University of Medicine and Pharmacy for her contribution for the obtaining of the quality certificate "Label CIDMEF" by the Medical Faculty of Cluj-Napoca.





CRISTIAN FALUP-PECURARIU

ROMANIA

Cristian Falup-Pecurariu is Head of the Department of Neurology, County Emergency Clinic Hospital from Brasov, and is Lecturer of Neurology at the Transilvania University from Braşov, Romania. He received his medical degree from the University of Medicine and Pharmacy "Iuliu Haţieganu" from Cluj-Napoca.

He hold a 1 year fellowship of the European Neurological Society in movement disorders and sleep medicine at Hospital Clinic, University of Barcelona, Spain.

During his career Cristian Falup-Pecurariu was President of the European Association of Young Neurologists and Trainees (EAYNT), EAYNT Liason Officer with World Federation of Neurological Society, co-representative of Europe on the International Working Group for Young Neurologists and Trainees (World Federation of Neurology). He was also Secretary of the EFNS/MDS-ES Panel on Movement Disorders, member of the Educational Committee of MDS-ES and currently is member of the MDS Leadership Task Force, European Academy of Neurology Scientific Panel Movement Disorders, MDS-ES Executive Committee, MDS Rating Scales Translation Committee. He is member of EUROPAR (European Parkinson's Group) and International Parkinson and Movement Disorders Society Non motor study group.

He is the initiator and Course Director of the Movement Disorders Teaching Course held in Brasov.

His research focuses on non-motor aspects of Parkinson's diseases and restless legs syndrome.





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 Sanità, and other national and international funding agencies, etc.

He is member of the Second Opinion Group of the American Leucodystrophy Association.

Associated editor of Neurological Sciences in the past 3 years. 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 Clinical 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-)
- Vice-Rector of the University of Siena, from 1st april 2016.

Medical Involvements

- Director of the OU Clinical Neurology and Neurometabolic Diseases, University Hospital of Siena Medical School.
- 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
- Chairman of Neuromediterraneum Forum
- Co-Chairman of Research group of WFN Migration Neurology

Member of the Scientific Societies:

- Società 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)

His present positions are:

full professor of Neurology, University of Siena, Medical School

- Director of Unit Clinical Neurology and Neurometabolic Diseases, Siena Hospital.
- Past-Director of the Section Neurological Diseases of the Department of Neurological and Behavioural Sciences of the University of Siena since the 2012, at the fusion of this Department in the Dept Medicine, Surgery and Neurosciences.
- Italian Delegate to the World Federation of Neurology and to European Academy of Neurology Council.
- Past- President of the Italian Society of Neurology (President years 2009-2011)
- From 1995 he is Director of a PhD Programme on Applied Neurological Sciences at University of Siena, from 2004 of the European PhD Programme and European School of Doctorate of Applied Neurological Sciences. Since 2011 he is director of the PhD Programme on Cognitive and Neurological Sciences at University of Siena.
- He is Italian member of the Committee of European Union of Medical Specialists, in the section Neurology.
- Delegate for Research in the Dept. Medicine, Surgery and Neurosciences.
- Coordinator for the Tuscany Region of the Network on Rare Neurological Diseases.
- On 2013, he received Honoris Causa degree from the University Carol Davila, Bucharest
- Chairman of the Neuromediterraneum Forum



- Editor in Chief of Neurological Sciences, Springer-Verlag Editor.
- Co-Editor of many international journals.
- On the 2014 was nominate WHO consultant for Rare Neurological Diseases.
- From june 2014, he is Chairman of the Scientific Committee and Member of the Board of the European Academy of Neurology
- From February 2015 Co-Chairman of the Research Group Migration Neurology of the World Federation of Neurology.
- From the 1st april 2016, vice-Rector of the University of Siena.



ȘTEFAN FLORIAN
ROMANIA

- Senior Neurosurgeon, Head of Department of Neurosurgery, Cluj County Emergency Hospital, Cluj-Napoca
- President of the Senate of the University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, President of the Romanian Society of Neurosurgery, Corresponding Member of the Romanian Academy of Medical Sciences
- As a senior neurosurgeon, up to now, he performed over 15000 surgeries, with no less than 750 surgeries per year in the last decade.
- His main areas of interest are aimed at the cerebrovascular pathology, neurooncology and paediatric neurosurgery
- As a university professor, the educational, scientific (7 books, 24 chapters, 48 indexed ISI publications) and research activities (16 research grants) are highly important to him. One of his major educational objectives is to offer continuous medical education to all young neurosurgeons (during the last 10 years he organised 2 international congresses and 7 national congresses with international participation, 5 neurosurgery masterclasses and 10 Romanian-German courses and also delivered over 230 lectures at various national and international meetings and congresses).
- Member of various international professional societies (WANS, EANS, EANO, WFNS, AANS, CNS, AMN, SSNN, SeENS, EASA), President of EMN (Euroacademia Multidisciplinaria Neurotraumatologica), Second Vice President at large of WFNS





DAVID C. GOOD

USA

Dr. David Charles Good is Professor and Founding Chair of Neurology at the Milton S. Hershey Medical Center of the Penn State College of Medicine. Dr. Good received a Bachelor of Science degree in biochemistry and a Doctor of Medicine degree from the University of Wisconsin at Madison. Dr. Good performed an internship in Internal Medicine at the Hennepin County Medical Center and University of Minnesota Hospital and a completed residency in Neurology and a stroke fellowship at the University of Minnesota Hospital, Minneapolis. Dr. Good has been the director of rehabilitation at Southern Illinois University School of Medicine in Springfield, Illinois and Wake Forest University Baptist Medical Center in Winston-Salem, North Carolina. He accepted a position at Penn State in 2005 as the first chair of Neurology. He has held leadership positions at his institution, nationally, and internationally. He is a fellow of the American Academy of Neurology and the American Neurological Association. He is a charter member of the American Society of Neurorehabilitation, and has served in a number of capacities in the ASNR including President of the organization. He is past chairman of the Neurorehabilitation and Neuro Repair section of the American Academy of Neurology. He previously chaired the Accreditation Council of the United Council for Neurological Subspecialties. He served on the National Advisory Board for Medical Rehabilitation Research at the NIH. He has served on a number of study sections and has been an ad-hoc reviewer for a number of journals. He is the president-elect of the World Federation for Neurological Rehabilitation, serves on the Presidium, and is the regional vice president for North America. His research interests in recent years have focused on motor recovery in stroke, especially the role of the unaffected hemisphere in stroke recovery.

In addition to many presentations nationally and internationally, Dr. Good is widely published, with three books, multiple book chapters, peer-reviewed papers, and abstracts to his credit.



STANISLAV GROPPA

REPUBLIC OF MOLDOVA

Stanislav Groppa, MD, PhD, University Professor, Academician of Moldavian Academy of Science, Neurologist, Head of Neurology Chair of "N. Testemitanu" State Medicine and Pharmacy University, Director of the Neurology Neurosurgery Department (Institute of Emergency Medicine), Head of the Neurobiology and Medical Genetics Laboratory

He has graduated of the "N. Testemitanu" State Medicine and Pharmacy University in 1979. At age of 29 he got his doctor of medical science degree, and at 35 - doctor habilitat and at 39 years is conferred the title of university professor.

In 2007, he became a member of the Moldavian Academy of Sciences, and shortly after he was elected academician-coordinator of the Medical Department of the Moldavian Academy of Science. In 2012 Prof Groppa is elected as member of the Moldavian Academy of Science. Between 2015 -2016 hee is vice-president of the Moldavian Academy of Science. He is a Honorary Member of the of Medical Sciences Academy from Romania.

He has been trained in Medical centers from Russia, USA, Germany, China, Australia, Italy, and many others. Established a strong collaboration connections with researches and scientific institutions from all around the world.

Under the leadership, 18 doctoral theses were performed, including doctor habilitat thesis. His scientific interests are in the field of stroke prevention and early management, epilepsy, and pain relief.

Also, he is a member of international organizations, American Neurology and Stroke Association, European Academy of Epileptology; Member of the European Academy of Neurology, Member of Romania Academy of medical Schience, Member of Romania Stroke Association.

Professor S. Groppa is President of the Moldavian League against Epilepsy, President Moldavian Stroke Association, Vice-President of the Moldavian Neurology Society. He is a member of the editorial staff of Moldavian and not only Medical Journals.





MAX HILZ
GERMANY

He studied medicine at the Universities of Cologne and Erlangen-Nuremberg in Germany. After he had defended his doctoral thesis, he first trained in Anesthesiology and Intensive Care Medicine and in Ear-Nose-and-Throat diseases. Then, he 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), and 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 held appointments at New York University, New York, NY, as Professor of Neurology, Medicine and Psychiatry. Until 2007, he also served as the Associate Director of the NYU Dysautonomia Evaluation and Treatment Center. He was deeply involved in clinical research regarding the pathophysiology of Familial Dysautonomia, also known as Riley-Day syndrome or Hereditary Sensory and Autonomic Neuropathy Type III, and in studies of Fabry disease that led to the approval of enzyme replacement therapy in the USA. He is 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. From September 2016 to August 2017, he served as 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.

Professor Hilz is a member of 16 national and international scientific societies and is on the board of several autonomic nervous system societies. He currently co-chairs the Autonomic Nervous System Subspecialty Panel of the European Academy of Neurology, EAN. He also is Past-President of the German Autonomic Society, Past-President of the European Federation of Autonomic Societies, and Past-Chair of the Autonomic Section of the American Academy of Neurology. He is ad hoc reviewer for more than 25 international scientific journals, a member of the editorial board of Clinical Autonomic Research, and Associate Clinical Editor of Autonomic Neuroscience: Basic and Clinical. 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 autonomic nervous system, including hereditary sensory and autonomic neuropathies, diabetic neuropathies, and Fabry disease, and central autonomic disorders. He also served as an advisor to the European Medicines Agency, EMA, on issues related to autonomic

nervous system dysfunction.

Prof. Hilz conducted various studies showing improvement of neuropathic pain, small fiber neuropathy, and autonomic cardiovascular control in Fabry patients receiving biweekly 1.0 mg/kg enzyme replacement therapy.



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 out-patient 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-reviewed 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 interests are the fields of motor rehabilitation, cognition, epistemology, neurological music therapy, and pharmacology in neurorehabilitation.





AMOS KORCZYN

ISRAEL

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

Professor Korczyn is the Chairman of the Scientific Administrative Board of the Israeli Alzheimer's disease association (EMDA), and member of the SAB of Alzheimer Disease International, and has been the chairman of the WFN Research Committee for Neuroparmacology.

Professor Korczyn is an honorary member of the neurological societies of Israel, Serbia, Poland and Russia.

Professor Korczyn's H-index is 39.



PETER JENNER
UK

Prof Peter Jenner is a world-renowned specialist in preclinical aspects of Parkinson's and other neurodegenerative diseases. He has expertise in drug metabolism and pharmacokinetics but neuropharmacology based on functional models of neurodegenerative diseases has formed the major focus of his work. Following 14 years as Head of Pharmacology, Peter is now Emeritus Professor of Pharmacology at King's College London, and a Fellow of the Royal Pharmaceutical Society, the British Pharmacological Society, the Royal Society of Medicine and of King's College London. He has published more than 700 peer reviewed papers along with many chapters and monographs. Aside from his illustrious academic achievements, Professor Jenner also has considerable industrial experience, being a Founder, Director and CSO of Proximagen, is currently CSO of Chronos Therapeutics and consults for a number of pharmaceutical companies, including USB, Teva and Lundbeck. Professor Peter Jenner Currently Emeritus Professor of Pharmacology at King's College London, Peter is a world-renowned specialist in preclinical aspects of Parkinson's and other neurodegenerative diseases. He was previously a founder and CSO of the biotech Proximagen and is also currently CSO of Chronos.



TUDOR LUPESCU
ROMANIA

Tudor Lupescu obtained his medical degree from "Carol Davila" University of Medicine in Bucharest, in 1989. After 3 years of training at Colentina Clinical Hospital he became Specialist in Neurology in 1994. Since 2006 he is running the Neurology Department at Agrippa Ionescu Hospital in Bucharest. 1998, he qualified as Consultant Neurologist. Since his early years of training in Neurology, Tudor Lupescu has shown a special interest in Clinical Neurophysiology. In 2000 he earned a Competence in Clinical Neurophysiology (EEG, EMG, and Evoked Potentials). 1997 he was the first to use Transcranial Magnetic



Stimulation in Romania. This was also the subject of his PhD thesis presented in 2005. Since 2008, Tudor Lupescu is President of ASNER – Romanian Society of Electrodiagnostic Neurophysiology. He is also founding member and vicepresident of the Romanian Society of Diabetic Neuropathy.

Dr Tudor Lupescu is Fellow of the American Academy of Neurology, and associate member of the American Association of Neuromuscular and Electrodiagnostic Medicine. Between 2008 and 2014 he was also member of the Neurophysiology Subcommittee of ENS, and since 2015, he is member of the Neurophysiology Subcommittee of the European Academy of Neurology.



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 (EFNRS), Past President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), 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 Dafin 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 Dafin F. Muresanu is coordinator in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of many educational projects: European and international schools and courses (International School of Neurology, European Stroke Organisation summer School, Danubian Neurological Society Teaching Courses, Seminars - Department of Neurosciences, European Teaching Courses on Neurorehabilitation) and scientific events: congresses, conferences, symposia (International Congresses of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), International Association of Neurorestoratology (IANR) & Global College for Neuroprotection and Neuroregeneration (GCNN) Conferences, Vascular Dementia Congresses (VaD), World Congresses on Controversies in Neurology (CONy), Danube Society Neurology Congresses, World Academy for Multidisciplinary 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 (176 papers indexed on Web of Science-ISI, H-index: 18) 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.



BOGDAN O. POPESCU
ROMANIA

Born March 8th, 1971 in Bucharest, Romania.

Address: Department of Neurology, School of Medicine, 'Carol Davila' University of Medicine and Pharmacy, Colentina Clinical Hospital, 19-21 Sos. Stefan cel Mare, sector 2, 020125, Bucharest, Romania.

Scientometrics: 50 ISI full text articles, Over 1000 ISI citations, Hirsch index 18.

ACADEMIC EDUCATION AND APPOINTMENTS

| | |
|-------------|--|
| 1996 | MD, 'Carol Davila' University School of Medicine, Bucharest, Romania |
| 2000 - 2009 | Assistant Professor, 'Carol Davila' University School of Medicine |
| 2001 | PhD, 'Carol Davila' University School of Medicine - suma cum laudae |
| 2002 - 2008 | Neurologist, University Hospital Bucharest |
| 2004 | PhD, Karolinska Institute, Stockholm, Sweden |

- 2005 - Head of Laboratory of Molecular Medicine, 'Victor Babeş' National Institute of Pathology, Bucharest, Romania
- 2008 - Senior Neurologist
- 2009 - 2012 Lecturer, 'Carol Davila' University School of Medicine
- 2009 - Senior Researcher, 'Victor Babeş' National Institute of Pathology, Bucharest, Romania
- 2012 - 2015 Associate Professor, 'Carol Davila' University School of Medicine and Head of Neurology Unit II, Colentina Clinical Hospital
- 2015 Professor of Neurology, 'Carol Davila' University School of Medicine, Colentina Clinical Hospital

AWARDS

- 1999 Beaufour-Ipsen prize for the best research study in neurology
- 2000 Young histochemist award - International Society of Histochemistry and Cytochemistry
- 2004 Diploma of scientific merit - 'Victor Babeş' National Institute of Pathology
- 2007 'Victor Babeş' Award of Romanian Academy for medical research
- 2010 Science and Art National Foundation Award of Excellence for research in the field of Neuroscience and Neuropathology
- 2014 'Brain Networking' Foundation Award of Romanian Academy of Medical Sciences, for developing Neurology nationally and internationally.

OTHER CURRENT ACTIVITIES

- Editor in Chief of Romanian Journal of Neurology (2016 -) and former Executive Editor (2001-2016)
- President of the Romanian Society of Neurology (2017 -) and former Secretary General (2001-2013)
- Research director of the Society for the Study of Neuroprotection and Neuroplasticity (2005 -)
- Vicepresident of 'Carol Davila' University of Medicine and Pharmacy Bucharest (2016 -)
- Vicepresident of Bucharest College of Physicians (2015 -)

SELECTED PUBLICATIONS

1. Wallin A, Kapaki E, Boban M, Engelborghs S, Hermann DM, Huisa B, Jonsson M, Kramberger MG, Lossi L, Malojcic B, Mehrabian S, Merighi A, Mukaetova-Ladinska EB, Paraskevas GP, Popescu BO, Ravid R, Traykov L, Tsvigoulis G, Weinstein G, Korczyn A, Bjerke M, Rosenberg G. Biochemical markers in vascular cognitive impairment associated with subcortical small vessel disease - A consensus report. BMC Neurol. 2017; 17:102.
2. Ceafalan LC, Popescu BO. Juxtacerebral Tissue Regeneration Potential: Telocytes Contribution. Adv Exp Med Biol. 2016;913:397-402.
3. Gheorghiu M, David S, Polonschii C, Olaru A, Gaspar S, Bajenaru O, Popescu BO, Gheorghiu E. Label free sensing platform for amyloid fibrils effect on living cells. Biosens Bioelectron. 2014, 52:89-97.
4. Enciu AM, Gherghiceanu M, Popescu BO. Triggers and effectors of oxidative stress at blood-brain barrier level: relevance for brain ageing and neurodegeneration. Oxid Med Cell

Longev. 2013;2013:297512.

5. Popescu BO, Gherghiceanu M, Kostin S, Ceafalan L, Popescu LM. Telocytes in meninges and choroid plexus. *Neurosci Lett*. 2012, 516:265-9.

6. Hort J, O'Brien JT, Gainotti G, Pirttila T, Popescu BO, Rektorova I, Sorbi S, Scheltens P; EFNS Scientist Panel on Dementia. EFNS guidelines for the diagnosis and management of Alzheimer's disease. *Eur J Neurol*. 2010, 17:1236-48.

7. Popescu BO, Toescu EC, Popescu LM, Bajenaru O, Muresanu DF, Schultzberg M, Bogdanovic N. Blood-brain barrier alterations in ageing and dementia. *J Neurol Sci*, 283:99-106, 2009.

8. Cowburn RF, Popescu BO, Ankarcrona M, Dehvari N, Cedazo-Minguez A. Presenilin-mediated signal transduction. *Physiol Behav*. 2007;92:93-7.

9. Popescu BO, Cedazo-Minguez A, Benedikz E, Nishimura T, Winblad B, Ankarcrona M, Cowburn RF. Gamma-secretase activity of presenilin 1 regulates acetylcholine muscarinic receptor-mediated signal transduction. *J Biol Chem*. 2004;279:6455-64.

10. Cedazo-Minguez A, Popescu BO, Blanco-Millán JM, Akterin S, Pei JJ, Winblad B, Cowburn RF. Apolipoprotein E and beta-amyloid (1-42) regulation of glycogen synthase kinase-3 β . *J Neurochem*. 2003;87:1152-64.



RALUCA POPESCU
ROMANIA

Dr. med., senior specialist in Diabetes, Nutrition and Metabolic Diseases

Lecturer in Diabetes, Nutrition and Metabolic Diseases Department, University of Medicine and Pharmacy, Iasi, Romania

Treasurer of Society for Diabetic Neuropathy





AUGUSTIN SEMENCESCU

ROMANIA

WORKPLACE

University Politehnica of Bucharest, Faculty of Materials Science and Engineering and Faculty of Engineering in Foreign Languages, Romania - 313 Splaiul Independentei, District 6, 060042 - Bucharest – Romania

OCCUPATION OR POSITION HELD

- Professor Eng., Mat., Ec., M., PhD., Habil.
- Professor Eng., Mat., Ec., M., PhD
- National Expert for the European Commission-Research Directorate-General -Research Fund for Coal and Steel
- Associate professor PhD. Eng. M.Ec.
- Assistant Professor PhD. Eng.
- University Assistant Eng.
- Designer Engineer III
- Deputy Director «International Cooperation»
- National Contact Point for SMEs-FP6-European Commission

MAIN ACTIVITIES AND RESPONSIBILITIES

- Education activities for higher education (Bachelor and Master). Design and scientific research and development activity, innovation in the fields of metallurgical engineering, modeling-mathematical simulation, statistics for engineers and economists, organization of production systems, marketing and forecasting research, science policy. Technical expertise in the field of metallurgical equipment and installations. Doctorate coordination in the field of ENGINEERING and MANAGEMENT.
- Education activities for higher education (Bachelor and Master). Design and scientific research and development activity, innovation in the fields of metallurgical engineering, modeling-mathematical simulation, statistics for engineers and economists, organization of production systems, marketing and forecasting research, science policy. Technical expertise in the field of metallurgical equipment and installations.
- Management of Coal and Steel Scientific Projects- European Commission-Research Directorate-General -Research Fund for Coal and Steel
- Education activities for higher education (Bachelor and Master). Design and scientific research and development, innovation in metallurgical processes engineering, mathematical simulation modeling, optimization of industrial processes, statistics for engineers and economists, applied informatics (Mathcad, MatLab), TP / C ++

programming, organization of production systems, science policy, marketing research and forecasting.

- Education activities for higher education (Bachelor and Master). Design and scientific research and development, innovation in metallurgical processes engineering, mathematical simulation modeling, optimization of industrial processes, statistics for engineers and economists, applied informatics (Mathcad, MatLab), TP / C ++ programming, organization of production systems, science policy
- Coordination of research, development and innovation projects. Design and scientific research, in metallurgical processes engineering, mathematical simulation modeling, optimization of industrial processes, statistics for engineers and economists, organization of production systems, science policy
- Design, research, development, innovation
- Management and marketing of innovation and technology transfer activities
- Developing partnerships between national and transnational universities

NAME AND ADDRESS OF EMPLOYER

- University Politehnica of Bucharest, Faculty of Materials Science and Engineering and Faculty of Engineering in Foreign Languages, Romania - 313 Splaiul Independentei, District 6, 060042 - Bucharest- Romania
- University Politehnica of Bucharest, Faculty of Materials Science and Engineering and Faculty of Engineering in Foreign Languages, Romania - 313 Splaiul Independentei, District 6, 060042 - Bucharest – Romania
- European Commission-Research Directorate-General -Research Fund for Coal and Steel, Bruxelles, Belgium
- University Politehnica of Bucharest, Faculty of Materials Science and Engineering, Faculty of Transports Technical College No.2 and Faculty of Engineering in Foreign Languages, Romania - 313 Splaiul Independentei, District 6, 060042 - Bucharest – Romania
- University Politehnica of Bucharest, Faculty of Materials Science and Engineering, Faculty of Transports Technical College No.2 and Faculty of Engineering in Foreign Languages, Romania - 313 Splaiul Independentei, District 6, 060042 - Bucharest – Romania
- University Politehnica of Bucharest, Faculty of Materials Science and Engineering and Faculty of Engineering in Foreign Languages, Romania - 313 Splaiul Independentei, District 6, 060042 - Bucharest – Romania
- National Institute for the Design of Metallurgical Sections and Plants IPROMET SA –20 Constructorilor Av., District 6, Bucharest, Romania -
- Managerial Agency for Scientific Research, Innovation and Technological Transfer of Politehnica -MASRITT/AMCSIT Politehnica (Government Agency) - 313 Splaiul Independentei, Rectorate Building, R 102, R 103, AN 033, District 6, 060042 - Bucharest - Romania
- National Contact Point for SMEs-FP6-European Commission

MAIN SUBJECTS STUDIED / PROFESSIONAL SKILLS ACQUIRED

- Habilitation Thesis: "CONTRIBUTION TO INCREASING INSTITUTIONAL PERFORMANCE

BY IMPLEMENTING ACADEMIC ENTREPRENEURSHIP" Domain of university doctoral studies: ENGINEERING AND MANAGEMENT (when the title of doctorate coordinator was awarded, Minister Order no.5121 from 28.092017), HABILITATION COMMITTEE -Prof. Ion ABRUDAN, Eng., PhD-President, Prof. Constantin BUNGĂU Eng., PhD, Habil. - Member, Prof. Constantin OPREAN Eng., PhD, - Member

- Bachelor of Science Paper: NUMBER SEQUENCES -APPLICATIONS OF FIBBONNACI NUMBER SEQUENCES.COMPUTING PROGRAMS FOR NUMBER SEQUENCES LIMITS (C/ C++, TP)
- Bachelor of Science Paper: ROMANIAN STOCK MARKET; INDICATORS, FINANCIAL INSTRUMENTS AND CLIENT APPLICATIONS (Java, .Net Framework si PHP)
- PhD Thesis:" COMPLEX CONTROL AND MATHEMATICAL MODELING OF RING-TYPE BAKING FURNACES"
- Automations and Computers
- Technical skills of metallurgical engineering and design of Aggregates and Technological Installations
- Technical skills for impact studies and environmental balances
- Technical skills for FP 6 projects

SCIENTIFIC ACTIVITY

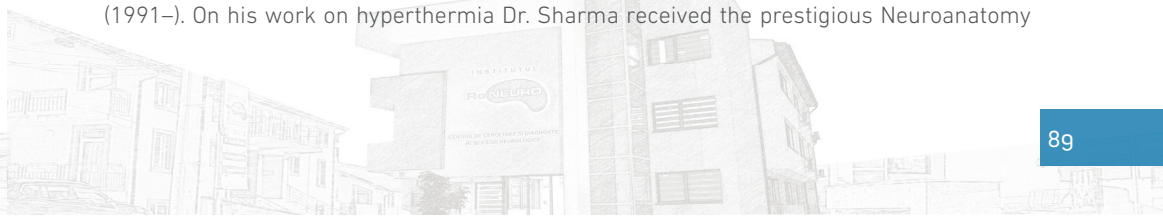
- Ci - BOOKS PUBLISHED AT INTERNATIONAL PUBLISHING HOUSES: 2
- Ca - BOOKS COURSES (MANUALS) PUBLISHED AT RECOGNIZED PUBLISHING HOUSES:31
- Cb - SPECIALTY BOOKS PUBLISHED AT RECOGNIZED PUBLISHING HOUSES:11
- Cc- BOOKS PUBLISHED AT OTHER ISBN PUBLISHING HOUSES,:9
- I- PUBLISHED COLLECTIONS AND GUIDANCE BOOKS:19
- D- WRITING OF THEORETICAL CHAPTERS: 6
- RIS- ISI, RECOGNIZED INTERNATIONAL SPECIALIST JOURNALS OR INDEXED IN FIELD SPECIFIC INTERNATIONAL DATA BASES, WHICH SELECT THE JOURNALS BASED ON PERFORMANCE CRITERIA: 59
- RIO- OTHER INTERNATIONAL SPECIALIST JOURNALS:27
- RNS- INTERNATIONAL SPECIALIST JOURNALS RECOGNIZED BY CNCIS:76
- VI- VOLUMES OF RECOGNIZED INTERNATIONAL ISSN OR ISBN SCIENTIFIC MANIFESTATIONS NATIONAL OR FROM ABROAD, ISI RATED OR INDEXED IN INTERNATIONAL DATA BASES: 89
- VN- VOLUMES OF NATIONAL SCIENTIFIC MANIFESTATIONS: 26
- PATENTS OF INVENTION IN INTERNATIONAL DATA BASES - Derwent Innovations Index and Espacenet : 54
- PI- INTERNATIONAL COMPETITION RESEARCH PROJECTS BASED ON CONTRACT / GRANT : 19
- PARTICIPANT IN BILATERAL PROJECTS: 11
- PN- NATIONAL COMPETITION RESEARCH PROJECTS BASED ON CONTRACT / GRANT - AS PROJECT MANAGER: 27
- PROJECTS AS RESEARCH COLABORATOR: 65
- International Grants Coordinator - European Commission -RESEARCH AND INNOVATION - Research Fund for Coal and Steel (RFCS) as Scientific Officer TG8 (20017-2008) : 38
- INTERNATIONAL SCIENTIFIC PRIZES: 122, of which

- Medals of GOLD:73
- Medals of Silver:10
- Medals of Bronze:2
- Diplomas, Trophies and Special Prizes:122
- INTERNATIONAL SCIENTIFIC PRIZES: 13
- INNOVATION PATENTS (applied in practice): 23
- INTERNATIONAL ORDERS AND MEDALS: 3



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). 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 Bhishma Narain Singh, in Ashok Hotel, New Delhi. Hari Sharma is Founding President of the Global College of Neuroprotection & Neuroregeneration (2004-); Elected President of International Association of Neurorestoratology (IANR) (2014-); and selected Senior Expert of Asia-Pacific CEO Association, Worldwide (APCEO) (2012-) for his contribution to uplift scientific research in many countries Globally that may have better economic and social benefit for

the mankind. Hari Sharma awarded coveted National Award “Sword of Honor” 2015 by Govt. of India on the eve of 66th Republic Day of India 25th January 2015 in New Delhi Eros Hotel International during the 34th Non-resident Indian (NRI) conclave by Speaker of Lok Sabha (Indian Parliament) the Hon’ble Mrs Meira Kumar of Indian national Congress (INC) Party for the continued extraordinary achievement in nanomedicine for public health awareness and possible therapeutic measures.

Based on his expertise in Nanoneuroscience, Hari Sharma was also invited to organize and chair Nanosymposium in Society for Neuroscience meetings in Chicago (2009), San Diego (2010), Washington DC (2011), New Orleans (2012), San Diego (2013) and Washington DC (2014, Nov 15-19, 2014); 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. 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. 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 = 38 (ISI Database) as of today. 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), International review of Neurobiology (Volume 82 and 102) 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). 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.



MIHAELA SIMU
ROMANIA

Mihaela Simu is presently working as Professor and Chairman of the Neurology Department II of University of Medicine and Pharmacy “Victor Babes” - Timisoara.

Professor Simu is currently Vicepresident of the Romanian Society of Neurology, one of the coordinators of the National Programme for the treatment of Multiple Sclerosis in Romania, active member of ENS, EFNS, American Academy of Neurology, and MDS.

Professor Simu has been and is involved as principal investigator in more than 20 international and national multicentric trials and 4 national research grants, and is presently the Romanian project leader in the BIOMARK HURO project (cooperation between Szeged and Timisoara medical Universities). Her interests are directed mainly in clinical neurology, in particular in multiple sclerosis, Parkinson disease, dementia, cerebrovascular and focal dystonias.

As author or co-author, has published and reported more than 100 national and international scientific papers, 3 medical books and 2 neurology courses in a bilingual (Romanian / English) version.





STEPHEN SKAPER

ITALY

STUDIES: B.S. (chemistry) Illinois Institute of Technology (1969); Ph.D. (biochemistry) University of South Dakota (1973); Laurea in chemistry, University of Padua (1990)

CAREER: NIH Postdoctoral Fellow, Department of Medicine, University of California, San Diego (1973-1976); Fellow in Human Genetics, Department of Pediatrics, Case Western Reserve University, Cleveland, Ohio (1977); Postgraduate Research Biologist, Department of Biology, University of California, San Diego (1978); Assistant Research Biologist, Department of Biology, University of California, San Diego (1979-1982); Associate Research Biologist, Department of Biology, University of California, San Diego (1983-1987); Head, Laboratory of Neuropharmacology, Neuroscience Research Laboratories, Fidia S.p.A. - Abano Terme, Italy (1987-1993); Principal Scientist and Head, Laboratory of Cell Biology, Researchlife S.c.p.A. (a Lifegroup Company), Biomedical Research Center, St. Thomas Hospital, Castelfranco Veneto (TV), Italy (1993-1996); Visiting Professor, Department of Pharmacology, University of Padua, Padua, Italy (1997); Assistant Director, Molecular Neurobiology Research, SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Harlow, United Kingdom (1998-2001); Senior Group Leader, Migraine and Stroke Research, Neurology & GI Centre of Excellence for Drug Discovery, GlaxoSmithKline R & D Limited, Harlow, United Kingdom (2002-2003); Senior Group Leader, Neurodegeneration Research, Neurology & GI Centre of Excellence for Drug Discovery, GlaxoSmithKline R & D Limited, Harlow, United Kingdom (2004-2007); Senior Group Leader, Target Validation (Cognition and Pain), Centre of Excellence for Drug Discovery, GlaxoSmithKline R&D Limited, Harlow, United Kingdom (2008); Adjunct Professor, Department of Pharmacology and Anesthesiology, University of Padua, Faculty of Medicine, Padua, Italy (2009-present).

PROFESSIONAL MEMBERSHIPS: Sigma CI (The Scientific Research Society); Phi Lambda Upsilon (honorary chemistry society); Alpha Chi Sigma (professional society in chemistry/chemical engineering); Society for Neuroscience; International Society for Cerebral Blood Flow and Metabolism

JOURNALS EDITED: Editor-in-Chief, CNS & Neurological Disorders – Drug Targets; Associate Editor, American Journal of Neuroprotection and Neuroregeneration; Editorial Board Member, Scientific Reports (Neuroscience); Councilor, International Association of Neurorestoratology
REVIEW PANELS: The Wellcome Trust (UK), Biotechnology and Biological Sciences Research Council (BBSRC) (UK), Austrian Science Fund (ad hoc review panel to evaluate interdisciplinary doctoral programmes in neuroscience)

RESEARCH INTERESTS: Molecular biology and cellular mechanisms of cell death in CNS ageing, neurodegenerative disorders and neuroinflammation, astrocyte-microglia interactions, pharmacological modulation of oligodendrocyte precursor maturation and demyelinating diseases. Track record of drug discovery project leadership in kinases, ion channels, G-protein-coupled receptors, DNA repair enzymes, growth factors, identification and optimization of tools for target validation studies, utilising RNAi, conditional and viral knockdown\outs\ins, transcriptomics, proteomics and in vitro cell-based disease or mechanism relevant assays in rodent systems.

PUBLICATIONS: OVER 300 publications in the neurosciences, including book chapters and symposia proceedings.

PATENTS: Pharmaceutical compositions containing monosialoganglioside GM1 or derivative thereof suitable for the treatment of Parkinson's disease (Patent No.: US 6,620,792 B1), use of CRF receptor agonists for the treatment or prophylaxis of diseases, for example neurodegenerative diseases (US 2003/0186867 A1), treatment of conditions with a need of GSK-3 inhibition (PCT WO 02/062387 A1), use of CRF receptor agonists for the treatment or prophylaxis of diseases, for example neurodegenerative diseases (PCT WO 01/72326 A1), use of monosialoganglioside GM1 or N-dichloro-acetyl-lyso-GM1 for preventing or reversing neuronal degeneration induced by long term treatment with L-DOPA in the therapy of Parkinson's disease (EP 0 770 389 A1)

REVIEWER FOR JOURNALS: Journal of Neuroscience, PNAS, Nature Reviews, The FASEB Journal, Journal of Neurochemistry, Journal of Neuroinflammation, Neurobiology of Disease, Neurobiology of Aging, Glia, Neuroscience, Apoptosis, PLoS One Biology, Journal of Pharmacology and Experimental Therapeutics, British Journal of Pharmacology, European Journal of Pharmacology, Journal of Neurological Sciences.



JOSEP VALLS-SOLE
SPAIN

67 years old. Senior Consultant in the Neurology Department of the Hospital Clinic of Barcelona, Spain, Professor of Neurology in the University of Barcelona and Head of the Research Group of Neurophysiology of the IDIBAPS. Associate Editor for the journal Clinical Neurophysiology Practice and Deputy Editor for the journal Brain Stimulation. He has published more than 260 manuscripts (current H index 49) and more than 50 book chapters. He has been awarded 3 research prizes and received 18 national/international grants.



JÓZSEF SZÁSZ

ROMANIA

PERSONAL DATA:

- Surname: Szász
- First name: József Attila
- Date and place of birth: 02.APR.1967, Sighisoara, Romania

EDUCATION:

- University of Medicine and Pharmacy (UMPh), Tirgu-Mures, Romania (1986-1992)
- PhD thesis: Motor complications and therapy in advanced Parkinson's Disease (2005)
University of Medicine and Pharmacy, Tirgu-Mures, Romania

WORK EXPERIENCE :

- Resident in Neurology (1992-1998)
- Neurologist (1998-2003)
- Senior neurologist (2003-)
- Assist. Prof. at the Department of Neurology UMPh Tg.Mures (1999-2009)
- Senior Lecturer at the Department of Neurology UMPh Tg.Mures (2009-)

TEACHING ACTIVITY

IN ROMANIAN: clinical practice in neurology for students and resident doctors (1999-)

IN HUNGARIAN: lectures in adult neurology (2005-)

CLINICAL TRIALS

Principal investigator in 10, investigator in 6, phase III, clinical studies

THE MOST IMPORTANT PUBLICATIONS:

1. Kerenyi L, Kardos L, Szász J, Szatmari S, Bereczki D, Hegedus K, Csiba L. Factors influencing hemorrhagic transformation in ischemic stroke: a clinicopathological comparison. European Journal of Neurology 2006 Nov;13(11):1251-1255. ISSN 1351-5101 IF: 2,244
2. Szatmari S, Pascu I, Mihalka L, Mulesa SV, Fekete I, Fulesdi B, Csiba L, Zselyuk G, Szász J, Gebefugi J, Nicolescu S, Vasiesiu D, Smolanka VI, Bereczki D: The Mures-Uzhgorod-Debrecen study: a comparison of hospital stroke services in Central-Eastern Europe. European Journal of Neurology 2002;9:1-4 ISSN 1351-5101 IF: 1,565



3. Rupam Borgohain, Jozsef Szász, P. Stanzione, et al. Randomized trial of safinamide add-on to levodopa in Parkinson's disease with motor fluctuations. *Mov Disord*, 2014, 29:229–237
4. Rupam Borgohain, Jozsef Szász, Paolo Stanzione, et al. Two-Year, Randomized, Controlled Study of Safinamide as Add-on to Levodopa in Mid to Late Parkinson's Disease *Mov Disord*, 2014, 29: 1273–1280
5. Fekete K, Szatmari S, Szőcs I, Szekeres C, Szász J, Mihálka L, Smolanka V, Kardos L, Csiba L, Bereczki D. Prestroke alcohol consumption and smoking are not associated with stroke severity, disability at discharge, and case fatality. *J Stroke Cerebrovasc Dis*. 2014 Jan;23(1):e31-37 IF: 1.984

FIELDS OF INTEREST: movement disorders, dementia, stroke, chronic pain, epilepsy,



CRISTINA TIU
ROMANIA

I always considered myself an optimistic person but still there are certain things which I find depressing, and a CV is one of those things. Suddenly it is not about you anymore, but about a person who had a number of achievements which are rarely the things you find interesting about yourself, and all your life is compressed in half a page.

I have graduated the University of Medicine and Pharmacy “Carol Davila” in Bucharest in 1987 and I started my career in neurology in 1991, as a resident in the Department of Neurology of the University Hospital Bucharest, the same place where now I am Associated Professor and Head of the Stroke Unit. I have two favorite domains: vascular pathology and multiple sclerosis. My main interest is in cerebrovascular diseases, I am coordinating a teaching course for cervical and cerebral ultrasonography and I followed the European Master in Stroke Medicine Programme in Austria.

My involvement in MS field started in year 2000, when the first patients in Romania were treated with DMTs due to a constant effort (read fight) of three people: Prof. Ioan Pascu, Prof. Alexandru Serbanescu and Prof. Ovidiu Băjenaru. Since then, I have followed-up hundreds of patients with MS, and I am now the coordinator of the University Hospital Bucharest Center for the National Programme for treating the Patients with Multiple Sclerosis. I have participated, together with my colleagues in the majority of the main International Clinical Trials in MS in the last decade and we had also several original scientific work related to clinical aspects of MS patients. I am one of the two representatives of the Romanian Society

of Neurology in the Board of ECTRIMS.

In the end of my half page, I am looking forward to future goals: development of basic research in MS in Romania, a National MS Registry, better drugs, a better education for patients and doctors, a better me...



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.

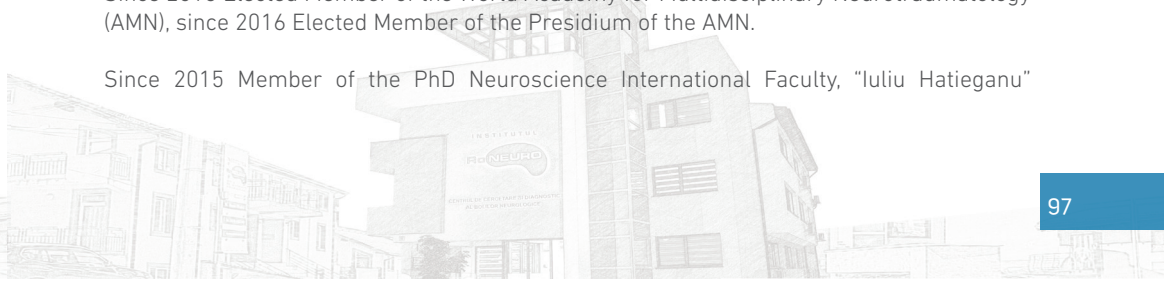
Since 1982 he holds > 100 advanced training courses on biometry for professionals in clinical research as well as teaching courses for university institutions and international societies.

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)





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