Academy for Multidisciplinary Neurotraumatology

FOUNDATION OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

UMF IULIU HAȚIEGANU UNIVERSITY OF MEDICINE AND PHARMACY CLUJ-NAPOCA

Academia de Științe Medicale din România

RoNEURO "RoNeuro" Institute for Neurological Research and Diagnostic

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13TH AMN CONGRESS

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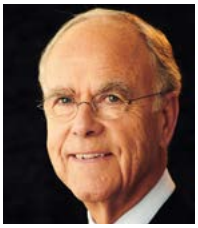

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SCIENTIFIC PROGRAM

OCTOBER 4TH, 2015

08:50 – 09:00 *WELCOME ADDRESS:*
Dafin F. Muresanu (Romania), Volker Hömberg (Germany), A. V. Ciurea (Romania)

SESSION 1, CHAIRPERSONS: Volker Hömberg (Germany), A. V. Ciurea (Romania)

09:00 – 09:30 Dafin F. Muresanu (Romania)
Cognitive and behavioural impairment after TBI

09:30 – 10:00 Volker Hömberg (Germany)
Reinventing neurological rehab: What we have done right-what we have done wrong

10:00 – 10:30 Russell Andrews (USA)
Nanotechniques for neuromonitoring and neurorepair

10:30 – 11:00 Wolf Dieter Heiss (Germany)
PET in coma and in vegetative state

11:00 – 11:10 *DISCUSSIONS*

11:10 – 11:40 *COFFEE BREAK*

SESSION 2, CHAIRPERSONS: Russell Andrews (USA), Kevin K.W. Wang (USA)

11:40 – 12:10 Ignacio Previgliano (Argentina)
Cognitive decline after critical care treatments or how to obtain a brain injury without brain illness: a neurotrophic approach hypothesis

12:10 – 12:40 Anton Alvarez (Spain)
Multimodal drugs for the treatment of neurocognitive deficits and the prevention of dementia after TBI

12:40 – 13:10 Nicole von Steinbüchel (Germany)
Predictors of disease specific (QOLIBRI) and generic (SF-36) health-related quality of life and the instruments' discriminative power

13:10 – 13:20 *DISCUSSIONS*

13:20 – 14:20 *LUNCH*

SESSION 3, CHAIRPERSONS: Ignacio Previgliano (Argentina), Nicole von Steinbüchel (Germany)

14:20 – 14:50	Kevin K.W. Wang (USA) Biomarkers in spinal cord injury: Utilities in research and patient management
14:50 – 15:20	David W. Wright (USA) Traumatic brain injury translational research: shedding light in the darkness
15:20 – 15:50	Christian Matula (Austria) AONeuro – A framework for education, training and science in Neurotrauma
15:50 – 16:20	Hari Shanker Sharma (Sweden) Nanowired delivery of Cerebrolysin enhances neuroprotection in traumatic and concussive brain injuries
16:20 – 16:30	*DISCUSSIONS*
16:30 – 17:00	*COFFEE BREAK*

SESSION 4, CHAIRPERSONS: Christian Matula (Austria), Johannes Vester (Germany)

17:00 – 17:30	Mihaela Baciut (Romania) In quest of the optimum multidisciplinary management protocol for severe cranio-maxillofacial trauma
17:30 – 18:00	Johannes Vester (Germany) The benefit and risks of modern clinical research - RTCs on the way to the titanic effect?
18:00 – 18:30	Nihal Tumer (USA) Overpressure blast injury-induced oxidative stress and neuroinflammation in rat brain
18:30 – 18:40	*DISCUSSIONS*
18:40 – 18:50	*CLOSING REMARKS*
18:50 – 19:50	*AMN BOARD MEETING*

ABSTRACTS

MULTIMODAL DRUGS FOR THE TREATMENT OF NEUROCOGNITIVE DEFICITS AND THE PREVENTION OF DEMENTIA AFTER TBI

ANTON ALVAREZ[1,2]

JESUS FIGUEROA[1,3], *DAFIN F. MURESANU*[4]

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Traumatic Brain Injury (TBI) is more than an acute disorder because it is associated to high rates of lifelong impairments in physical, cognitive and psychosocial functioning. In spite of the clear improvement in survival after TBI achieved over the past decades, the treatment of neurocognitive deficits and the prevention of TBI-related dementia were overlooked until very recently, and even nowadays remain priority issues waiting for an effective drug management. Taking into account that all drugs targeting a single pathogenic pathway failed to demonstrate clinical efficacy and that TBI involves multiple cellular and molecular mechanisms influencing cognitive functioning, recent investigations indicate that multimodal drugs, able to promote brain repair and regeneration by modulating several pathophysiological pathways constitute the most promising therapeutic option to improve the acute outcome and the long-term recovery of cognitive functions after injury.

Neurocognitive deficits are the most common complaints after TBI. Subjects with mild TBI (mTBI) usually experience transient cognitive symptoms, particularly confusion and impairments of verbal and visual memory and attention, and recover cognitive functioning completely within 1-3 months. However, up to 10-15% of the individuals with mTBI show persistent cognitive complaints and difficulties in executive functions such as decreases in cognitive flexibility and in the abilities to maintain attention and to inhibit incorrect responses. Cognitive deficits are also present in almost all patients shortly after moderate and severe TBI (m-sTBI) and include impaired arousal, information processing speed, attention, learning and memory, language, executive functions, and fine motor speed. Cognitive functioning improves during, at least, the first two years after m-sTBI, but more than 50% of these patients endure long-term injury-related disabilities. The investigation of cognitive impairment in TBI patients is a challenging topic because it varies depending on multiple factors such as the severity, type-mechanism and location of the injury, the age of the patient, or the time elapsed since TBI occurred.

Although most of the cases experience an initial recovery (complete or partial) after TBI, some patients show late decline in cognitive functioning, particularly those with advance age and/or with increased levels of depression; and subjects undergoing TBI earlier in life have an increased risk of developing dementia. Several studies showed that a history of m-sTBI anticipates the onset of Alzheimer's disease (AD) at younger ages and that the risk of having AD increases with increasing TBI severity. Similarly, a history of repetitive mTBI was found to be associated with the development of chronic traumatic encephalopathy (CTE), a neurodegenerative condition resembling dementia pugilistica. According to epidemiological studies, the relative risk of dementia in individuals who had a TBI of sufficient severity as to require hospitalization ranges from 1.5- to 3-fold, and the risk of dementia attributable to TBI is in the range of 5% to 15%.

TBI activates endogenous processes of neurorestoration by inducing the expression of neuroprotective genes, which are also responsive to the administration of neurotrophic factors involved in the regulation of the neurovascular unit such as BDNF, IGF-1 and VEGF. Therefore, the modulation of the endogenous repair mechanisms mediated by neurotrophic factors represents an appealing drug target for TBI treatment. Several clinical trials demonstrated improvements of cognitive performance in TBI patients treated with endogenous peptides as well as with the peptidergic drug Cerebrolysin. Results of the available clinical studies indicate that Cerebrolysin induced a faster clinical recovery and a shorter hospitalization time in patients with acute TBI, and improved cognitive performance when administered during either acute or post-acute TBI phases. Thus,

treatment with Cerebrolysin during both acute and rehabilitation periods might contribute to improve more the functional recovery. However, large short-term controlled trials with peptidergic drugs are still needed and long-term efficacy and prevention studies were never conducted with any drug.

NANOTECHNIQUES FOR NEUROMONITORING AND NEUROREPAIR

RUSSELL ANDREWS

Ames Associate (Nanotechnology & Smart Systems), NASA Ames Research Center, Moffett Field, CA, USA

Nervous system trauma occurs in many forms – from massive brain or spinal cord injury to subtle ischemic injury that may go initially unnoticed but result in significant functional impairment. Advances in neuroimaging – CT and MRI – document massive injuries with increasingly exquisite detail. However, changes at the cellular level that can be functionally quite devastating require cellular-level techniques to detect electrical and chemical changes that are the hallmarks of more subtle nervous system injury.

Great progress is being made in monitoring in vivo nervous system function – electrically and chemically – with increasing spatial and temporal precision. Nanoelectrode arrays can record brain electrical activity with orders of magnitude more sensitivity and temporospatial specificity than standard noble metal electrodes. These arrays can also stimulate the brain with equally improved charge transfer – avoiding the electrolysis of brain tissue that limits the effectiveness of standard electrodes such as those used for deep brain stimulation (DBS). Nanoelectrode arrays are proving to offer advances in brain chemical (neurotransmitter) monitoring, with the promise in the near future that multiple neurotransmitters (e.g. dopamine, serotonin, adenosine, glutamate) can be monitored continuously. Similarly, these arrays can monitor the focal tissue oxygen deficits that are essential for detecting small regions of ischemia before irreversible injury occurs.

Nanotechniques promise to open avenues of minimally-invasive nervous system monitoring and modulating as wireless systems are being developed. Several groups have recently reported nanolevel sensors and effectors which can be implanted in the brain, e.g., to transmit focal electrical activity information from multiple sites without wired connections through the skull. The possibilities for understanding both local and remote effects of central nervous system injury are just beginning to be realized.

For neurorepair, nanoscaffolds (composed of self-assembling amino acids) have the remarkable ability to foster axon regrowth (and functional recovery) in animal models of focal nervous system trauma. A very attractive aspect is that these amino acid nanoscaffolds are naturally degraded over time – they do their job and then disappear without a trace (i.e., no scar). A further benefit of nanoscaffolds for neurotrauma (and tissue trauma – surgical or accidental – in general) is their impressive hemostatic properties. The liquid amino acid nanoscaffold can be injected on a region of oozing brain, and – being colorless – can be injected onto the operative field so the surgeon's dream of "bloodless surgery" can be realized.

The last quarter of the 20th century saw incredible advances in imaging the nervous system, with pneumoencephalography and cerebral arteriography being replaced by CT and MRI. The first quarter of the 21st century promises to be a similarly productive time for interacting with the nervous system – thanks to nanotechniques for neuromonitoring and neurorepair.

IN QUEST OF THE OPTIMUM MULTIDISCIPLINARY MANAGEMENT PROTOCOL FOR SEVERE CRANIO-MAXILLOFACIAL TRAUMA

MIHAELA BACIUT
GRIGORE BACIUT, DAFIN MURESANU, CRISTIAN DINU*
Department of Cranio-Maxillofacial Surgery, *Department of Neurosciences, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Severe cranio-maxillofacial trauma is managed in various types of units worldwide, with the outcome depending on the use of a systematic and organized approach, time to therapy onset, extent of injury to vital structures and expertise of a multidisciplinary team.
Evaluation of the CNS should be prioritized and receive equal ranking with respiratory and cardiovascular urgency.
Statistics have shown that success is based on correct case assessment leading to a comprehensive diagnosis, that can reliably sustain the proper selection of treatment. The final goal for maxillofacial trauma care is functional and esthetic rehabilitation at all levels. This represents a tremendous challenge, considering the multitude of specialized functions of organs in the region.
Prioritizing the evaluation of the neurological status is often underestimated, but the question is about intervening early with a precise protocol, instead of contemplating a devastating drama, because every minute matters.
The presentation aims to provide insight to an established management protocol in our Departments of Cranio-Maxillofacial Surgery and of Neurosciences from the "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania. These involve a multidisciplinary team in the approach (maxillofacial surgery, neurology, neurosurgery, ENT surgery, ophthalmology), offering surgical- as well as drug-based therapy.
The adequate use of neurotrophic regulation peptides supports healing through multiple regeneration mechanisms, ensuring the optimum basis for recovery of the patient.

PET IN COMA AND IN VEGETATIVE STATE

WOLF-DIETER HEISS
Max Planck Institute for Metabolism Research, Cologne, Germany

Advances in resuscitation and critical care management have resulted in the survival of many patients despite severe brain damage. These patients may remain in coma or in vegetative state. The probability of recovery of conscious function is dependent on the extent of structural brain damage, which is difficult to assess by clinical, laboratory or functional tests. Positron emission tomography (PET) of 18F-fluordeoxyglucose (FDG) can be used to investigate metabolic and functional impairment of the brain. In acute vegetative state (AVS, duration < 1 month), overall glucose utilization was significantly reduced in comparison with age-matched controls. In a few cases with locked-in syndrome, cortical metabolism was in the normal range. 11C-Flumazenil (FMZ) measures the density of benzodiazepine receptors (BZRs) and thereby furnishes an estimate of neuronal integrity. PET with this tracer demonstrated a considerable reduction in BZRs in cortical areas, but indicated that the cerebellum was spared from neuronal loss. The comparison of FDG- and FMZ-PET findings in AVS demonstrates that alterations of cerebral glucose consumption do not represent mere functional inactivation, but also irreversible structural damage. In some cases with minimally conscious state, auditory stimuli with emotional valence induced more brain activation (investigated by H215O-PET) than meaningless noise; such studies can be used to detect residual cortical function. To improve prognostication of chances for recovery, a combination of functional activation studies and assessment of the extent of neuronal damage might be the optimal procedure and should be tested in larger cohorts of patients with comatose states of different severity.

REINVENTING NEUROLOGICAL REHAB: WHAT WE HAVE DONE RIGHT-WHAT WE HAVE DONE WRONG

VOLKER HÖMBERG
Deptartment of Neurology, Heinrich Heine University, Düsseldorf, Germany

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

In parallel the need for intensive neurorehabilitation to combat resulting impairment and handicap has increased. Fortunately also over the last 20 years neurologic rehabilitation is more and more conceived as appplied neuroscience:

Dramatic progress has been made in the application of evidence based medical principles and the number of well designed randomized con-trolled trials in the field is increasing. Nevertheless there is a remaining epistemological problem in how far the rationales of EBM originally designed for pharmaceutical studies are really suited to as a source of beat evidence :Due to heterogeneity of populations ,usually comparably small sample sizes and hence also difficult to interpret metaanalyses the EBM rationale my sometimes be misleading.

Nevertheless a reasonable approach to design efficient treatment strategies is to follow elementary rules derived from behavioural and neurosciences concerning neuroplasticity and learning mechanisms. This has resulted in the invention of better scientifically founded pro-cedures for neurological treatment of motor ,cognitive and language problems. A good example is the very successful application of the principle of forced use and avoidance of learned non use in con-strained in used movement therapy. This concept now also spreads to non motor fields as language , cognitive and perceptual rehabilita-tion.
Furthermore the use of intelligent mechanical training devices (often loosely called "robots" a has open news therapeutic windows especially in the early stage of treatment in severely impaired patients.

On the other hand pharmaceutical concepts for neuroprotection have more or less failed so fare possibly due to the selection of the wrong mostly monomodal drugs not properly addressing the complexity of the brain´s endogenous defense mechanisms at an early stage after injury. There is however a growing selection of neuromodulatory techniques such as peripheral nerve stimulation , non-invasive brain stimulation and also pharmaceutical interventions with monaminergic drugs and especially antidepressants to facilitate brain recovery within a limited time-window after stroke with the aim to reduce impairment.

In future it will be extremely important to differentiate more clearly treatment elements addressing compensation and task specific learn-ing from those elements addressing impairment reduction especially in the early sensitive period after an insult.

As treatment intensity is likely to be the key element for impairment reduction we certainly have to find clever and affordable ways: to in-crease the daily treatment time of our patients. To day even during inpatient rehabilitation treatment times hardly exceed three hours a day i.e. that we use only a small percentage of waking hours leaving long "idling" time not field by any treatment. In this sense we have to "reinvent" neurorehabilitation within this sensitive post injury period to combat impairment with high frequency treatments combined with neuromodulatory techniques (robot use, peripheral and central stimulation , pharmaceuticals) .

We have to think how our rehabilitation environments should look like and can be "enriched" and how we can generate a high level of motivation and fun in patients to let them successfully participate in such high frequency treatments.
Furthermore prognostic criteria have to be worked out to enable deci-sions when to switch from impairment oriented(massed practice) to compensatory (task specific learning) strategies.

AONeuro – A FRAMEWORK FOR EDUCATION, TRAINING AND SCIENCE IN NEUROTRAUMA

CHRISTIAN MATULA
Neurosurgical Department, Medical University of Vienna, Austria

The AO foundation is a medically guided, global network of people interested in different areas of surgery, in particular trauma. It's the world's leading educational and research organization with more than 10,000 surgeons, in more than 100 countries, and represent one of the most important and extensive networks in medicine. The international faculty consists of over 3,000 experts in different fields of medicine having the overall goal to improve patients care and life! Since 1960, 352'067 surgeons from 124 countries and 146'929 operating room personnel from 73 countries have participated in an AO Course. Every year more than 46,000 surgeons participate in 750 AO education events!

AONeuro is an initiative of the AO Foundation to expand its activities into the area of neurosurgery, particular in Neurotrauma and Skull Base Surgery. AONeuro's mission is to continuously set standards in postgraduate medical education and to foster the sharing of medically guided expertise in a worldwide network of healthcare professionals. To improve patient care means, that we must have a quality approach to developing educational offerings for the multispecialty community. For those reasons, among other activities worldwide, within the last two years international reviewed Curricula in Neurotrauma and Skull Base Surgery has been developed and established. The new curricula provide comprehensive frameworks for our education, training and scientific work in selected areas of practice in neurosurgery, establish a competency-based approach to developing all activities in the areas mentioned before, define learning outcomes that should be achieved by clinicians to improve care based on patient problems and establish quality standards in the named activities –particular in education. To optimize the educational experience, these curricula will be needed to ensure that events are designed to address the patient problems and the needs of the special target audiences. They should address all stages of the career: from training, to early years in practice, to when someone become an expert and integrate the latest science of education for designing, implementing and evaluating quality education. The presented Curricula provide measurable results from an outcome-driven approach proven at special styled meeting within the last two years.

Within the last couple of years AONeuro has proven to be one of the most promising opportunities in terms of education, training and science for all people interested in any kind of neuroscience activities. The ultimate goal is to become the one of the world's leading global "Neuro" community, where information flows freely not only from the organization, but also among peers to affect and improve clinical practices through the sharing of knowledge.

COGNITIVE AND BEHAVIOURAL IMPAIRMENT AFTER TBI

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

TBI is a field with many unmet needs in medicine and public health. It is a major cause of death and disability and also leads to huge direct and indirect costs to society. Currently the incidence of TBI is increasing.

TBI populations are heterogeneous in terms of mechanism of disease, baseline prognostic risk factors, clinical severity and evolution. This heterogeneity generates complex challenges.

Traumatic brain injury (TBI) long-term complications include a wide spectrum of conditions such as physical

disability, endocrine dysfunction, behavioral and emotional changes, cognitive dysfunction, sleep problems, epilepsy, gastrointestinal and genitourinary complications. Cognitive dysfunction represents a common disabling complication, which can be both a direct result of the injury and indirect consequence of most of the conditions mentioned above.

Cognitive dysfunction includes executive dysfunction, attention deficits, memory impairment, lower performance in abstract meaning and processing speed. It represents a consequence of the alteration of all the three levels of organization of the brain: cellular and molecular level, circuitry level and dynamic network level.

Cognitive rehabilitation consists in three main objectives:

1. to enhance those cognitive functions that are impaired;
2. to implement strategies for compensating those functions;
3. to train metacognitive strategies that increase awareness of anticipates difficulties.

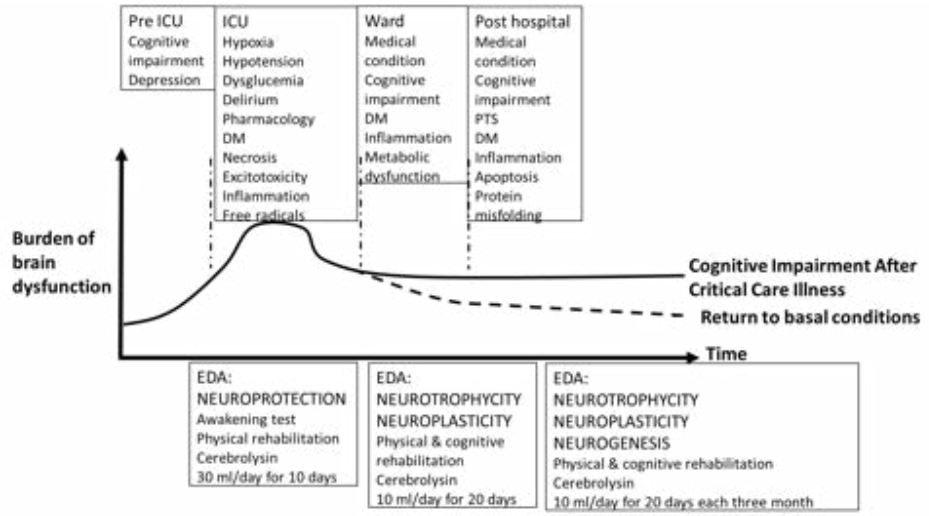
COGNITIVE DECLINE AFTER CRITICAL CARE TREATMENTS OR HOW TO OBTAIN A BRAIN INJURY WITHOUT BRAIN ILLNESS: A NEUROTROPHIC APPROACH HYPOTHESIS

IGNACIO PREVIGLIANO

Head Division of Intensive Care – Hospital Fernandez – Argentina
Neurology Chair – Universidad Maimonides – Argentina

Long term cognitive impairment after critical illness (CIACI) is an emerging entity that affects patients at ICU discharge at one year and probably lifelong. In the largest CIACI's study, on 821 patients 40% of them had global cognition scores that were 1.5 SD below the population means (similar to scores for patients with moderate traumatic brain injury or to patients with mild cognitive impairment (MCI)), and 26% had scores 2 SD below the population means (similar to scores for patients with mild Alzheimer's disease (AD)) after three month and that persisted in 34% and 24% respectively at one year. Deficits occurred in both older and younger patients, and longer duration of delirium was independently associated with worse global cognition at 3 and 12 months.

Neuropathologic studies of the human brain in critical illness demonstrates apoptosis and necrosis. Analyzing the mechanisms of brain cell death and survival in terms of the balance between endogenous defense activity (EDA) and damage mechanism (DM), neurotrophic factors appears as a therapeutic option.



NANOWIRED DELIVERY OF CEREBROLYSIN ENHANCES NEUROPROTECTION IN TRAUMATIC AND CONCUSSIVE BRAIN INJURIES

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Traumatic brain injuries (TBI) or concussive head injury (CHI) is quite prominent in military personnel duirng peacekeeping or combat operations across the World. The pathophysiology of TBI or CHI however is also influenced widely by the ambient temperature range where injury has occurred. Thus, suitable modulation of the therapeutic strategies is needed to contain pathophysiology of brain injuries occurring in either cold or hot environments. In this investigation we present our data on TBI and CHI at thermoneutral ambient temperature range.

Since the pathophysiology of brain injuries are complex, this is unlikely that one single drug could be able to achieve desired neuroprotection over time in various clinical situations accompanied by several other uncontrollable factors such as environmental temperatures, co-morbidity factors like hypertension, diabetes or nanoparticles intoxications. Keeping these views in mind, our laboratory is engaged to find out a suitable multimodal drug e.g., Cerebrolsyin that is a well balanced composition of several neurotrophic factors and active peptide fragments to induce neuroprotection in several animal models fo CNS injury.

In this investigation, we used TBI as well as CHI to evaluate the neuroprotective effects of cerebrolysin at room temperature. These CNS injuries induce profound edema formation and volume swelling in the CNS at 5 h after the insult [1,3]. The microvascular permeability disturbances to protein tracers were prominent in the CNS areas showing neuronal, glial and endothelial cell injuries. Treatment with cerebrolysin (10 µl, 20 µl or 40 µl/min for 10 min) either infused into the left lateral cerebral ventricle 30 min before or 30 min after trauma, or topically applied over the injured brain attenuated brain edema formation, volume swelling and CNS pathology. These neuroprotective effects of cerebrolysin were dose dependent [4,5]. The microvascular permeability disturbances to protein tracers (e.g., Evans blue albumin and radioiodine) at 5 h were also considerably reduced with high dose of the drug. On the other hand, no reduction in brain edema, BBB permeability or brain pathology was seen when cerebrolysin was administered 60 min post-trauma.

Interestingly, TiO2 nanowired cerebrolysin when delivered 60 to 90 min after TBI or CHI, significant neuroprotection was achieved in these models. These novel observations suggest that cerebrolysin administered into the CSF or topically over the traumatized brain in high doses during early phase of CNS injury has pronounced neuroprotective effects. Furthermore nano-drug delivery of cerebrolysin could induce marked neuroprotection even applied longer-time intervals after the primary insults following brain trauma.

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PREDICTORS OF DISEASE SPECIFIC (QOLIBRI) AND GENERIC (SF-36) HEALTH-RELATED QUALITY OF LIFE AND THE INSTRUMENTS' DISCRIMINATIVE POWER

NICOLE von STEINBÜCHEL
and the QOLIBRI Group
Institute of Medical Psychology and Medical Sociology, University Medical Center, Georg-August University, Göttingen, Germany

Psychosocial, cognitive, emotional, and physical problems can emerge after traumatic brain injury (TBI) with potentially major impact on health-related quality of life (HRQOL). Determinants of generic and disease-specific HRQOL have not been compared to date.

In this study, determinants of disease specific (QOLIBRI) and generic (SF-36) HRQOL are investigated in a sample of 795 TBI survivors and compared in detail. Also, the instruments' discriminative power between individuals belonging to a certain group or described by the same health state is analysed. In particular, their absolute informativity is investigated with the Shannon index H'.

The predictors of the Short Form-36 and the QOLIBRI can be distinguished by their contents: those of the SF-36 are characterized by a more physical and the ones of the QOLIBRI by more physiological content. The different determinants also have a significantly differential impact on the absolute informativity of disease-specific as well as generic HRQOL: for recovery (GOSE), anxiety and depression (HADS), e.g., H' indexes of the QOLIBRI are generally higher and more balanced than those of SF-36 subscales: Notably, informativity of Role Physical, Role Emotional and Social Functioning, shows less satisfactory discriminative power compared to all other dimensions and sum scores of both instruments.

Concerning general psychometric criteria in a TBI population, both instruments can be recommended for application. When the focus lies on how a certain subscale or sum score differentiates between individuals in one specific dimension/health state, the QOLIBRI can be suggested as the preferable instrument.

OVERPRESSURE BLAST INJURY-INDUCED OXIDATIVE STRESS AND NEUROINFLAMMATION IN RAT BRAIN

NIHAL TUMER[a,b]
HALE Z. TOKLU[a,b,*], *ZHIHUI YANG*[c], *SEHKAR OKTAY*[b,d], *YASEMIN SAKARYA*[a,b], *NATALIYA KIRICHENKO*[a,b], *MICHAEL K. MATHENY*[b], *JUDY MULLER-DELP*[e], *KEVIN STRANG*[c], *PHILIP J. SCARPACE*[b], *KEVIN K.W. WANG*[c]

[a]Geriatric Research Education & Clinical Center, Malcolm Randall Veterans Affairs Medical Center, Florida, USA; University of Florida Departments of [b]Pharmacology & Therapeutics, [c]Center for Neuroproteomics& Biomarker Research, McKnight Brain Institute Department of Psychiatry and Neuroscience, [d]Marmara University School of Dentistry, Istanbul, Turkey, [e]Florida State University, College of Medicine Department of Biomedical Sciences, Florida, USA

Overpressure blast-wave induced brain injury (OBI) poses significant concerns for military personnel. One deleterious consequence of OBI is impaired cerebral vascular function. We suggest that the cerebral vascular dysfunction impairs oxygenation in the brain resulting in elevated oxidative stress. To test this hypothesis, we examined OBI induced oxidative injury in brain and for comparison, in lung. Rats were divided into 3 groups: Control, OBI (exposed 30 psi peak pressure, 1-2 ms), and Repeated OBI (r-OBI) (three exposures over one week period). Lung and brain tissues (cortex and cerebellum) were collected at 24 h post injury. The neurological examination score worsened in OBI and r-OBI groups (4.2±0.6 and 3.7±0.5, respectively) compared with control (0.7±0.2) and there was lung and brain edema. Malondialdehyde, index of lipid peroxidation, increased in OBI and r-OBI compared with controls in cortex ($p<0.05$) and cerebellum ($p<0.01$-0.001). Glutathione, (endogenous antioxidant), decreased in cortex ($p<0.01$) and cerebellum ($p<0.05$) in r-OBI group compared with control. Myeloperoxidase activity, indicator for neutrophil infiltration, was elevated ($p<0.01$-0.05) in r-OBI. Additionally, tissue thromboplastic activity, coagulation marker, was significantly elevated, indicating a bleeding tendency. Moreover, NGF and NF-κB proteins along with Iba-1 and GFAP immunoreactivity were significantly augmented in frontal cortex, consistent with microglial activation in the frontal cortex. Thus, our data demonstrate that OBI triggers both inflammation and oxidative injury in the brain. These data in conjunction with our previous observations suggests that OBI evokes a cascade of events beginning with impaired cerebral vascular function leading to ischemia and potentially chronic neurological consequences.

THE BENEFIT AND RISKS OF MODERN CLINICAL RESEARCH - RTCS ON THE WAY TO THE TITANIC EFFECT?

JOHANNES VESTER

Department of Biometry and Clinical Research, IDV Data Analysis and Study Planning, Krailling, Germany

Are large randomized clinical trials (RCTs), bound to rigid conventional designs, stifling ingenuity and true progress in clinical research? Increasing costs, tight timelines, pressure for return of investment, inflation of the number of sites with very few subjects in combination with backward-oriented designs create a vicious circle of large RCTs with decreasing precision and increasing sample sizes and risk for study failure. A reversal to smaller, well-controlled clinical trials with innovative and efficient designs may be an important pre-requisite for future breakthrough developments in neurosciences.

Examples from traumatic brain injury, stroke and Alzheimer's disease research are discussed and related to future developments. Innovative, less time- and cost-consuming ways are presented and common traps are revealed. Multidimensional approaches lower the risk of arbitrary endpoint selection and may substantially reduce sample size, risk-based centralized statistical monitoring enhances precision and may reduce total study budget by more than 30%, adaptive trial designs may allow greater flexibility of research process with enhanced risk control. There is time for new concepts bringing research back to innovation and quicker growth of scientific knowledge. The recent FDA and EMA risk-based guidances and the currently launched US 21st Century Cures Act may become important accompanying steps towards a new start in clinical research, especially in domains which suffered from no or very low progress in the past decades.

BIOMARKERS IN SPINAL CORD INJURY: UTILITIES IN RESEARCH AND PATIENT MANAGEMENT

KEVIN K.W. WANG

Program for Neurotrauma, Neuroproteomics & Biomarkers Research, Department of Psychiatry, McKnight Brain Institute, University of Florida, Gainesville, Florida, USA

In the United States, there are approximately 12,000 new cases of spinal cord injury (SCI) each year and some 1.2 million people living with paralysis due to SCI. Seven percent of them are paralyzed due to accident or injury occurring while serving in the military. Military and civilian SCI also cause serious medical complications, presenting significant challenges to the patients recovering or rehabilitating from SCI. Despite that a large amount of SCI research has been conducted, no effective therapy to treat acute SCI is available. In recent years, other researchers and our collaborative team [University of Florida (Zhihui Yang et al.) and University of Miami (W. Dalton Dietrich, Helen M. Bramlett, Michael Y. Wang et al.] have begun to study the potential utilities of biofluid-based biomarkers in the diagnosis, prognosis and management of SCI patients.

In our rat SCI biomarker study, we examined the effects of injury severity and temporal profiling (4, 24 hr, and 7 day post-injury) of a panel of candidate biomarkers in two biofluid types (cerebrospinal fluid (CSF) and serum). Candidate biomarkers included axonal injury markers αII-spectrin breakdown products (SBDP150, SBDP145 & SBDP120), neuronal cell body injury marker UCH-L1, gliosis/glial injury markers S100β, GFAP and GFAP-BDPs, demyelination marker MBP, and neuroinflammation marker IL-6. Our results showed that CSF and/or serum levels of several markers (SBDPs, GFAP, GBDP, UCH-L1 and S100b) were elevated at acute time points (4 - 24 h). CSF GFAP and GBDP levels (4h, 24h), S100β (4h, 24h, 7d) and serum GFAP levels (at 4h) also correlated to SCI severity.

We also conducted a human SCI biomarker study examining the effects of injury severity and temporal profiling of our biomarker panel in both CSF and serum. Serial CSF and serum samples were obtained from 14 SCI patients with initial ASIA score (AIS) of A-B at every 6 hours for up to 6 days. Biomarker levels in SCI biofluid (CSF, serum) were analyzed and compared to normal controls. SBDP150, UCH-L1, GFAP, S100β & IL-6 were found elevated in the acute phase CSF and serum samples from SCI patients. CSF SBDPs, GFAP, GBDP38K, UCH-L1 & IL-6 and serum GFAP, S100β, UCH-L1 & IL-6 also showed SCI severity-correlation (initial AIS). In addition, CSF GFAP, SBDP150 & IL-6 and serum GFAP, S100β, SBDP150 & IL-6 levels showed correlation to AIS improvement at discharge. These results not only allow us to gain important insight into the pathomechanisms of SCI, but our learning from them will directly translate into human SCI studies by examining the role of these biomarkers in monitoring human SCI progression or recovery and guiding personalized therapeutic and rehabilitation strategies.

TRAUMATIC BRAIN INJURY TRANSLATIONAL RESEARCH: SHEDDING LIGHT IN THE DARKNESS

DAVID W. WRIGHT

Emergency Neurosciences, Department of Emergency Medicine at Emory University School of Medicine, USA

Traumatic brain injury (TBI) is a major global health issue, affecting between 1.7 -3.8 million persons in the US alone. Despite decades of research, and many promising therapies, no pharmacological agent has translated into a viable treatment for TBI. The ProTECT III and Synapse trials of progesterone for acute TBI are prime examples of the most recent agonizing failures of the translation process. Preclinical evidence of progesterone's neuroprotective properties were undeniable, with over 200 studies in multiple labs showing robust effects. Yet these findings did not survive the translational process under the classical clinical trial paradigm. A fresh, open and honest examination is needed in order to shed new light on the process and devise the path forward.

CURRICULUM VITAE

ANTON ALVAREZ
SPAIN

Medical Doctor (M.D.), University of Santiago de Compostela (1987)
Diploma of Specialist in Neuroendocrinology, University of Santiago de Compostela (1988)
Graduate in Psychology, University of Santiago de Compostela (1988)
Doctorate in Psychiatry, University of Santiago de Compostela (1988-1990)
Resident Research Fellow of the Ministry of Education and Science (1988-1992)
Department of Psychiatry, Santiago University (1988-1991)
Madrid Complutense University (1992)

Psychiatry Doctor (PhD), Department of Psychiatry, Madrid Complutense University (1997)
Dr. Àlvarez has 22 years experience in Basic and Clinical Research on Alzheimer's disease.
He was involved in more than 150 research projects, including projects funded by Public Institutions, pharmaceutical R&D studies, industrial and R+D+I projects, epidemiological studies and two projects funded by the European Comunity: (1) MimoVax:
Alzheimer's disease treatment targeting truncated AB40/42 by active immunisation (an STREP -Specific Targeted Research Projects- Project approved through the Six Framework Programme of the European Community to develop and test a vaccine for Alzheimer's disease). Period: 2006-2010. (2) BIOMED-PL-950523-European Concerted Action on Pick's Disease. Period: 1995-1998.

As a result of the research activity developed during this period, Dr. Àlvarez published more than 120 scientific articles in national and international journals and books. In addition, Dr. Àlvarez is actively involved in several scientific forums of his specialty (Congresses, Research Groups, Scientific Journals and Associations).

RUSSELL ANDREWS
USA

Appointment: Ames Associate (Smart Systems & Nanotechnology), National Aeronautics and Space Administration (NASA) Ames Research Center, Moffett Field, California, USA 94035

Education: Undergraduate & medical school – Dartmouth College/Medical School, Hanover, NH
Graduate school - Harvard University, Cambridge, MA

Residency: Surgical Internship – Walter Reed Army Medical Center, Washington, DC
Neurosurgery Residency – Stanford University Medical Center, Palo Alto, CA

Professional: Faculty member (Neurosurgery) at the following (1986-2001):
University of California, Davis, Medical Center
Stanford University Medical Center
State University of New York Upstate Medical Center
Texas Tech University Medical Center (Chief, Neurosurgery)
Currently: Since 1998: Ames Associate (Smart Systems & Nanotechnology) at NASA Ames Research Center, Moffett Field, CA, USA. Since 2001: Private practice neurosurgery in Silicon Valley/San Jose, CA.

Major Committees/Memberships:
Aerospace Medical Association
American Association of Neurological Surgeons: Past Chair, International Committee
Asian Congress of Neurological Surgeons – Executive Committee
Bioluminate, Inc. (NASA patent licensee): Scientific Advisory Board
Computer Assisted Radiology and Surgery (CARS): Program Committee
Congress of Neurological Surgeons
Epilepsy Foundation of Northern California: Board Member
European Association of Neurosurgical Societies
European Association for Predictive, Preventive and Personalised Medicine
International Association of Neurorestoratology: VP Neuromodulation
International Conference on Neuroprotective Agents: Co-Director
New York Academy of Sciences (Life Member)
World Federation of Neurosurgical Societies: Education Committee Member

Publications: Editor, Intraoperative Neuroprotection. Williams & Wilkins, 1996
Author: Too Big to Succeed: Profiteering in American Medicine. iUniverse, 2013
Author/co-author of over 35 book chapters
Author/co-author of over 75 peer-reviewed research articles
Presenter/co-presenter of over 200 presentations at
major national/international scientific meetings (many as invited speaker)

Patents: "Multimodality Instrument for Tissue Characterization" US Patent #6,718,196 (April 6, 2004) to NASA on behalf of RW Mah and RJ Andrews.
"Carbon Nanotube-based Nanoelectrode Array for Deep Brain Stimulation" Patent Application by NASA on behalf of J Li, M Meyyappan, R Andrews, March, 2003.

MIHAELA BACIUT
ROMANIA

University studies
- 1990: Faculty of Dental Medicine, „Iuliu Hatieganu" University of Medicine and Pharmacy Cluj-Napoca
- 1999: 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

PhD degree
„Value of ultrasonography in maxillofacial surgery",
University of Medicine and Pharmacy Cluj-Napoca, 2003

Position held
- Professor, Department of Maxillofacial Surgery and Implantology,
  Faculty of Dental Medicine, University of Medicine and Pharmacy Cluj-Napoca since 2007

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

Other positions held
Member in 15 scientific committees

Domains of research and interest
- 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

A.V. CIUREA
ROMANIA

PROFESSIONAL EXPERIENCE

1997-Prezent	Profesor of Neurosurgery University of Medicine and Pharmacy "Carol Davila" Bucuresti Doctorate Coordinator (11 finished PhDs and seven ongoing, unfinished doctorates)
2004-2008	Pro Dean University of Medicine and Pharmacy "Carol Davila" Bucuresti, Decision 15209/07.07.2004 Member of the Board of Professors (2000-2004) (2004-2008) Member of the University Senate (2004-2008)
2009-Prezent	Scientific Researcher First Degree (by national neurosurgical competition)

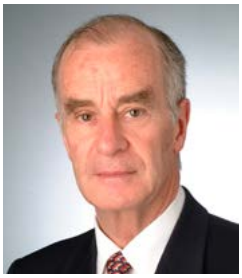
EDUCATION AND TRAINING

1974	Doctorate in Medicine – PhD.
1979-Prezent	MD Neurosurgeon (National neurosurgical competition)
2004-2011 (2011),	International Who's who of intellectuals (2004) & International Who's who of Intelectuals Romanian Dictionary of Personalities (2014)
PUBLICATIONS	90 articles published in Pub. Med. & Thomson ISI and 36 books published in the country and abroad
RESEARCH	18 Research projects
IMPORTANT AWARDS	National Presidential Order " Faithful Service " with the grade of Commander (2000) Romanian Academy Award for the monograph "Neurosurgical Pediatric Pathology" 1981.
DR. HONORIS CAUSA	Nominated at four universities (Oradea , Galati , Chisinau , Iasi)
VISITING PROFESSOR	11 important activities: INI, Hannover, Germany,2014 & Harvard University, Boston, 2005, etc.
EDITORIAL BOARD	12 important speciality Journals : World Neurosurgery (USA) & Neurosurgery (USA)

MEMEBER OF DIFFERENT SCIENTIFIC SOCIETIES 18 memeberships
(WFNS, EANS, ISPN, ESPN, RSN, CNS, ASM, AMN, EMN, SEENS, AMR, AACNS, etc)

SPECIAL SCIENTIFIC CONTRIBUTIONS

Construction of the first tumor tissue banks in Eastern Europe (2003)
Unitube drain – Registered patent at OSIM with no. 00994 / 2005
Coordination of construction of the Center of Excellence in Neurosurgery 2005
(under the Ministry of Health`s patronage)
Author of two Neurosurgical Treaties - Two volumes (Medical Publishing 2010 si 2011)
Hidden Anatomy of Michelangelo (Certificate of Innovation registered at OSIM , 2012)



WOLF-DIETER HEISS
GERMANY

Wolf-Dieter Heiss, born 31.12.1939 in Zell am See, Austria, graduated in medicine from the University of Vienna, Austria, in 1965. He achieved his training in neurology, neurophysiology, psychiatry and nuclear medicine at the University hospital in Vienna and spent research fellowships at the MIT, Cambridge, USA, the Physiological Institute in Stockholm, Sweden, the Department of Physiology of SUNY, Buffalo, NY and the Department of Neurology of

the University of Minnesota, Minneapolis, USA. 1976 he was appointed associate professor at the Department of Neurology of the University of Vienna. In 1978 he became director of the Center for Cerebrovascular Research of the Max Planck Institute for Brain Research and of the Department of Neurology of the City Hospital Cologne-Merheim, Germany. 1981 he was appointed as director at the Max Planck Institute for Neurological Research. 1985 – 2005 he was professor of neurology and chairman of the Department of Neurology of the University of Cologne and director of the Department of General Neurology at the MPI in Cologne. He was president of the International Stroke Society 1992-96, was on the board of directors of the Society for Cerebral Blood Flow and Metabolism, deputy editor of the Journal of Cerebral Blood Flow and Metabolism and at present is associate editor of the Journal of Nuclear Medicine and section editor of Stroke. He was chairman of the program committee of the European Federation of Neurological Societies (EFNS) 1998 - 2001 and was president of the EFNS 2001 – 2005. Since 2005 he is Visiting Professor at the Danube University in Krems, Austria, and since 2009 Adjunct Professor at the McGill University in Montreal, Canada.

His significant portfolio of scientific articles includes 617 papers indexed on Web of Knowledge-ISI, rating a Hirsch index of 63.

In 2013 he became Associated Professor of the Department of Neurosciences, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Romania.

VOLKER HÖMBERG
GERMANY

MEDICAL DIRECTOR
St. Mauritius Therapy Hospital Meerbusch

PERSONAL DATA
Born 25 July 1954
Married to Priv.-Doz. Dr. Kristina Müller, paediatric neurologist

MEDICAL CAREER

1973 - 1980	School, Universities of Düsseldorf and Freiburg; Elective in Neurology at Boston City Hospital, Boston, Mass.; National Hospital for Nervous Diseases, London
since 1975	Junior researcher in the Department of Neuropsychology at the C. & O. Vogt Institute for Brain Research, Düsseldorf and the Department of Neurology, Freiburg (Prof. R. Jung)
1980 - 1981	Research fellow in the Department of Neuropsychology (Prof. G. Grünewald) at the C. & O. Vogt Institute for Brain Research, Düsseldorf
since 1981	Clinical training in the Department of Neurology (Prof. H.-J. Freund), Heinrich- Heine-University Düsseldorf
since 1985	Senior registrar in the Department of Neurology, Heinrich-Heine-

	University Düsseldorf
since 1987	Senior investigator for the German Research Council Special Task Force in Neurology at Heinrich-Heine-University (SFB 200 and SFB 194)
1987-2005	Medical director of the Neurological Therapy Center (NTC), Heinrich-Heine-University Düsseldorf
since 1988	Board examiner for Neurology at the local examination board (Ärztekammer Nordrhein)
1989-1997	Vice president of the German Society for Neurological Rehabilitation
1993	Habilitation in Neurology, Heinrich-Heine-University Düsseldorf
since 1995	Board examiner for physical medicine and rehabilitation (Ärztekammer Nordrhein)
1997-2005	Medical director of the Neurological Therapy Center, Cologne
1998-2004	President of the German Society for Neurological Rehabilitation
since 2000	Medical director and head of neurology, St. Mauritius Therapy Hospital, Meerbusch
since 2003	Secretary General World Federation for NeuroRehabilitation (WFNR)
since 10/2004	Vice president of the German Society for Neurological Rehabilitation
since 2005	Panel-Chairman Neurorehabilitation for European Federation Neurological Societies (EFNS)

CHRISTIAN MATULA
AUSTRIA

Christian W. Matula, MD, PhD is Professor of Neurosurgery at the Neurosurgical Department at the Medical University of Vienna, Austria. He serves as a Director of Skull Base Division and Head of the Neurotrauma subdivision. Furthermore, he is founding member and Neurosurgical Head of AONeuro – a pilot initiative of the AO Foundation-, Chairman of the AONeuro TK Expert Group and permanent member of the AONeuro Steering Committee. He is also the medical director of two private health care centers in Vienna and Lower Austria.
Dr. Matula received his MD degree in 1986 from the University of Vienna, his PhD in Neuroendoscopy in 1996 from the same University, and was appointed Professor in 1997. He completed a fellowship in Neuroanatomy in Würzburg, Germany, a fellowship in skull base surgery in Washington and one in vascular surgery in Phoenix.
Dr. Matula has developed an international reputation in the area of skull base surgery with special focus on new surgical technologies, endoscopic skull base surgery, orbital surgery, but also in Neurotrauma with special focus on skull base trauma, reconstruction and clinical trials. He has been active in many workshops, courses, webinars, and webcasts and has given a high number of invited lectures as visiting professor at numberless congress all over the world. He is the author of more than 250 publications mostly on skull base surgery, microsurgical techniques, neurotrauma, neuroendoscopy and has written several textbooks and atlases. As director of the educational program for neurosurgery at the Medical University of Vienna, he has initiated a variety of well-known seminars and played a major role in developing and enhancing the neurosurgical educational program in Austria in particular at the Department of Neurosurgery, Medical University of Vienna. He is member of several Neurosurgical Societies all over the world and the recipient of countless awards and honors.

DAFIN F. MURESANU

ROMANIA

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, 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 also member of 13 scientific international societies (being member of the American Neurological Association (ANA) - Fellow of ANA (FANA) since 2012) and 7 national ones, being part of the executive board of most. 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 Neurotraumatolgy (AMN) Congresses, Congresses of European Society for Clinical Neuropharmacology, European Congresses of Neurorehabilitation). His activity includes involvement in many national and international clinical studies and research projects, over 300 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (120 papers indexed on Web of Science-ISI, H-index: 14) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dafin F. Muresanu has been honoured with: 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, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy of Medical Sciences "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.

IGNACIO PREVIGLIANO
ARGENTINA

Dr. Ignacio Previgliano is specialist in Critical Care Medicine and Neurology, Professor of Neurology and Associated Professor of Internal Medicine at Maimonides University School of Medicine. His areas of expertise are Neuro Critical Care, Vascular Neurology and Cognitive Impairment. He has won several awards including one of the 2005 9th Congress of the World Federation of Societies of Intensive and Critical Care Medicine. He has published 57 papers in indexed and non-indexed peer review journal. He is reviewer of neurosurgical and critical care journals, collaborated in several books and has his own textbook "Evidence Based Neuro Critical Care".

NICOLE von STEINBÜCHEL
GERMANY

Biography

Since 2004/2005	Director of the Department of Medical Psychology and Medical Sociology, University Medical Center, Georg-August-University of Göttingen
2001-2004	Associate Professor (C4) of Gerontopsychology at Geneva University and Head of the Neurogerontopsychology Unit, Department of Psychogeriatrics, Geneva University Hospital
1999-2000	C3-Research Professor of the Dorothea-Erxleben Foundation, Magdeburg University
1993-1997	C3-Professor of Medical Psychology, Institute of Medical Psychology (IMP), Munich University (LMU)
1997	Postdoctoral thesis ("Habilitation") in „Clinical Psychology and Neuropsychology", Leopold-Franzens University, Innsbruck
1987-1993	Graduation (Dr. rer. biol. hum.) and scientific researcher at the IMP, LMU
1985	Diploma in psychology at the Institute of Psychology, Munich University, studies in philosophy and history of art

Editorship

1998-2012	Editor of the section „Quality of life and disease coping“ of the „Zeitschrift für Medizinische Psychologie“
Since 2004	Editor of the series „Psychomed Compact“, UTB textbooks series

Main areas of work (Selection)
Neuropsychology, cognition, (intercultural) health-related quality of life research, currently outcome work package leader of the CENTER-TBI-Study.

Offices (Selection)

1998-2002	Vice-chairperson of the German Society of Medical Psychology
2001-2005	Member of the board of the Swiss Society of Psychology
Since 2003	Member of the board, vice-treasurer of the Academia, currently Vice President of the Multidisciplinaria Neurotraumatologica (AMN)
2007-2010	Member of the board of the European Brain and Behaviour Society (Scientific Committee)
2008	Founding member of the International Society for Clinical Neuromusicology
2008-2011	President of the QOLIBRI Society

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 potion in the 1st Class. Hari Sharma joined the group of Professor Prasanta Kumar Dey, a neurophysiologist by training in the Department of Physiology, Institute of Medical; Sciences, Banaras Hindu University, Varanasi in 1977 to obtain Doctor of Philosophy Degree (D.Phil.) in Neurosciences and was awarded Ph.D. in 1982 on “Blood-Brain Barrier in Stress.” Hari Sharma after carrying out a series of Government of India funded Research

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

Dr. Sharma on his research on brain pathology and neuroprotection in different models received the prestigious awards from The Laerdal Foundation of Acute Medicine, Stavanger, Norway, in 2005 followed by Distinguished International Scientists Collaboration Award by National Institute on Drug Abuse (NIDA), Baltimore, MD (2006–2008). 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 Annual Meeting of American Association fo Advancement of Science (AAAS) Held in Chicago, IL, USA Feb 13-17, 2014. Hari Sharma has published over 400 research papers, 85 reviews, 14 monographs, and 80 international book chapters and edited 18 book volumes. 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 fo Science, USA (since 1994–); International Academy of Stress, New York (2003–), Swedish Academy of Pharmaceutical Sciences (2010–). Dr. Sharma has served as an expert evaluator and advisor to various Boards, Councils and Institutions for their Research Grants including Wellcome Trust, London, UK (2011–); Catalan Agency for Health Information and Quality, TV3 (2010–), European Commission Projects (2002–), European Nanomed Council (2009–), Ministry of Health Science Foundation; Medical research Council and University Commission of Grants in various countries in Europe, USA, UK, Canada, Hong Kong, Singapore and in Australia. Some of the notable organizations include: Australia and New Zealand Health Council (2000–); University Commission of Grants, Hong Kong (2002–), Singapore Medical Council, Singapore (2003–); UK Charity Organization "Research on Ageing: Help the Aged" (2003–); Euro Nanomed (2010–). Dr. Sharma is designated as ambassador of the City of Uppsala 2007, by Uppsala County administration and Uppsala Tourism for promoting Uppsala, Sweden as International Research Collaboration/Meetings and Conference Destination. Dr. Hari Sharma is married to Aruna Sharma (nee Bajpai) since 23rd April 1979 and has two sons. His political affiliations belong to Swedish Social Democrat Party (Socialdemokraterna, Sverige) where he is associated with the development of Education and Research matters in Sweden actively.

NIHAL TUMER
USA

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Hacettepe University	B.S. M.S	1972	Biology
Hacettepe University	Ph.D.	1980	Biophysics
Medical College of Pennsylvania	Post-doc	1984-88	Pharmacology

Positions and Employment:

2003 - Present, Tenured Professor, Department of Pharmacology and Therapeutics College of Medicine, University of Florida, Gainesville, FL
1989 - Present, Research Pharmacologist, Geriatric Research, Education and Clinical Center. VA Medical Center, Gainesville, FL. .
1994 - Present, Adjunct Professor, Department of Applied Physiology and Kinesiology, University of Florida, Gainesville, FL.
1994-2003 Tenured Associate Professor, Department of Pharmacology and Therapeutics, College of Medicine, University of Florida, Gainesville, FL.
1989-1994 Assistant Professor, Department of Pharmacology and Therapeutics College of Medicine, University of Florida, Gainesville, FL.
1988-1989 Research Assistant Professor, Department of Pharmacology, Medical College of Pennsylvania, Philadelphia, PA.
1984 -1988 Postdoctoral Fellow, Department of Pharmacology, Medical College of Pennsylvania, Philadelphia, PA

Current Professional Memberships
2009 - Present Turkish Pharmacological Society
1994 - Present Society for Neuroscience
1990 - Present American Society for Pharmacology and Experimental Therapeutics
1985 - Present (Fellow) The Gerontological Society of America

Related Peer-reviewed Publications (Selected from 98 total peer-reviewed publications)

1. Toklu HZ, Muller-Delp J, Yang Z, Oktay S, Sakarya Y, Strang K, Ghosh P, Delp MD, Scarpace PJ, Wang KKW, Tümer N. The functional and structural changes in the basilar artery due to overpressure blast injury. J Cerebrovasc Blood Flow Metab. 2015 Jun 24. doi: 10.1038/jcbfm.151. [Epub ahead of print]
2. Tümer, N., Toklu, H.Z., Muller-Delp J.M., Oktay S., Ghosh P., Strang K., Delp MD., Scarpace PJ: The effects of aging on the functional and structural properties of the rat basilar artery. Physiol Rep. 2014 Jun 6;2(6). pii: e12031.
3. Toklu HZ, Kwon OS, Sakarya Y, Powers SK, Llinas K, Kirichenko N, Sollanek KJ, Wiggs MP, Smuder AJ, Talbert EE, Scarpace PJ, Tümer N.: The effects of enalapril and losartan on mechanical ventilation-induced sympathoadrenal activation and oxidative stress in rats. J Surg Res. Feb 6. 188(2):510-6. doi: 10.1016/j.jss.2014.01.054, 2014
4. Kobeissy, F., Mondello, S., Tümer , N., Toklu, HZ., Whidden, MA., Kirichenko , N., Zhang, Z., Prima, V., Yassin, W., Svetlov, S., and Wang, KK: Assessing neuro-systemic and behavioral components in the pathophysiology of blast-related brain injury, Frontiers in Neurology, 21(4):186;1-19, 2013

5. Tümer, N., Svetlov, S., Kirichenko, N., Whidden, M.A, Erdos, B., Prima, V., Sherman, A., Kobeissy, F., Yezierski, B., Scarpace, PJ., Vierck, C and Wang, KK: Overpressure blast-wave induced brain injury elevates oxidative stress in the hypothalamus and catecholamine biosynthesis in rat adrenal medulla , Neuroscience Letters, 544:62-7, 2013
6. Erdös, B., Cudykier, I.,Woods, M., Basgut, B., Whidden, M., Tawil, R., Cardounel, A.R., and Tümer, N: Hypertensive effects of central angiotensin II infusion and restraint stress are reduced with age. J of Hypertension, 28(6):1298-1306, 2010.
7. Erdös, B., Broxson, C.S., Cudykier, I., Basgut, B., Whidden, M., Landa, T., Scarpace, P.J., and Tümer, N: Effect of high-fat diet feeding on hypothalamic redox signaling and central blood pressure regulation. Hypertension Research, 32(11) 983-88, 2009.
8. Erdös, B., Broxson, C.S , Landa , T, Scarpace, P.J, Leeuwenburgh, C, Zhang, Y and Tümer , N: Effect of life-long caloric restriction and voluntary exercise on age-related changes in levels of catecholamine biosynthetic enzymes and angiotensin II receptors in the rat adrenal medulla and hypothalamus. Exp Gerontology, 42(8): 745-52, 2007.
9. Erdös,B., Broxson, C.S., King, M.A, Scarpace, P.J, and Tümer N: Acute pressor effect of central angiotensin II is mediated by NAD(P)H-oxidase-dependent superoxide production in the hypothalamic cardiovascular regulatory nuclei . J of Hypertension, 24(1):109-116, 2006.

Related Chapter (out of 11) : Toklu, H and Tümer, N.: Blood Brain Barrier Permeability and Brain Edema Due To Traumatic Brain Injury. In "Brain Injury Principles: Molecular, Neuropsychological and Rehabilitation Aspects in Brain Injury Models"; Ed; Kobeissy F. Taylor & Francis Group Co. 2014

147 Abstracts and presentations

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 also 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 leading biometrician of the German GUDHIS Study in Traumatic Brain Injury.

Since 1982 has been holding advanced training courses on biometry for professionals in clinical research and university establishments.

Since 1995 he is Senior Consultant for Biometry & Clinical Research. He planned and evaluated about 150 randomized clinical studies worldwide and is member of various international Advisory Boards and Steering Committees including participation as biometric expert in regulatory authority panels and in FDA, EMEA, and BfArM hearings. He is head of the multidimensional section at the institute for Data Analysis and Study Planning and statistical peer reviewer for leading medical journals.

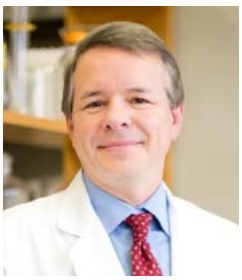
KEVIN K.W. WANG

USA

Dr. Wang He is internationally recognized for his original contributions to the fields of CNS disorders-linked proteolytic enzymes, neuroproteomics and disease biomarker discovery and validation. He obtained his Ph.D. in Pharmaceutical Sciences with Distinction from the University of British Columbia in Vancouver in 1989. He joined Parke-Davis Pharmaceutical Research (Ann Arbor, MI) in 1991, and following the company's merger with Pfizer Inc. (2000), he became Group Leader of CNS Therapeutics/CNS new targets team and co-chaired the Far East Scientific Opportunity Team. In 2002, he moved back to academia to become Associate Professor of Psychiatry at the University of Florida (Gainesville, FL), Associate Director of the Center for Traumatic Brain Injury Studies and Director of the Center of Neuroproteomics and Biomarkers Research. One year after, he co-founded Banyan Biomarkers Inc. (Alachua, Florida). In 2007, he transitioned to Banyan as full-time Chief Scientific & Operations Officer and Director of its Center of Innovative Research. In 2011, he rejoined the University of Florida McKnight Brain Institute as Executive Director of the Center for Neuroproteomics and Biomarkers Research / Chief - Translational Research & Associate Professor of Psychiatry and Neuroscience and continues his basic, applied and translational research. He is also Chair Professor of the Taipei Medical University.

Dr. Wang published more than 250 peer-reviewed papers, reviews and book chapters and co-authored eight US patents. He co-edited four books on proteases, neuroproteomics and biomarkers for CNS disorders. He is Associate Editor of the journals Translational Proteomics and Frontier in Neurotrauma. He also serves on five international journal's Editorial Board. Dr. Wang was Past President and current Council member of the National Neurotrauma Society (USA).

His research interests include neuro-Proteomics, CNS Injury, neurodegeneration, substance abuse research, post-translational modification research, biomarkers, diagnostics and therapeutic development.



DAVID W. WRIGHT

USA

David Wright, MD, is a tenured associate professor of emergency medicine and director, Emergency Neurosciences, Department of Emergency Medicine at Emory University School of Medicine. Dr. Wright is actively involved in both the preclinical and clinical assessment of traumatic brain injury (TBI) and stroke. He is Principal Investigator (PI) of the NIH funded multicenter Phase III clinical trial, ProTECT™ (Progesterone for TBI, experimental clinical treatment) and serves as PI of the Emory hub for the NIH Neurological Emergencies Treatment Trials Network and Co-PI of the Emory hub for the new NIH Stroke Network. Another one of Dr. Wright's goals is to transform healthcare through the development of advanced technologies, especially for neurological diseases. He is an adjunct faculty in the Department of Biomedical Engineering at the Georgia Institute of Technology and works closely with an elite team of engineers at the Georgia Tech Research Institute where he participates in numerous concussion research and technology development endeavors. He is currently one of the top 3 NIH funded emergency medicine researchers in the United States.

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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.

GENERAL INFORMATION

LANGUAGE

The official language is English. Simultaneous translation will not be provided.

CHANGES IN PROGRAM

The organizers cannot assume liability for any changes in the program due to external or unforeseen circumstances.

NAME BADGES

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

FINAL PROGRAM & ABSTRACT BOOK

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

COFFEE BREAKS

Coffee, tea and mineral 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 Mexican currency is Mexican Peso (MXN).

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Electrical power is 120 volts, 60 Hz. Plug Type A (USA) are standard.

TIME

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