



3<sup>rd</sup> Edition of International Conference on

# **NEUROLOGY AND BRAIN DISORDERS**

June 24-26, 2019 | Paris, France

*Theme: Advancements and Challenges in Neuroscience  
& Brain Disorders*

Holiday Inn Paris - Marne La Vallee  
2 boulevard du Levant, 93160 Noisy-le-grand  
Paris, France

*3<sup>rd</sup> Edition of International conference on*

# NEUROLOGY AND BRAIN DISORDERS

*Theme:*

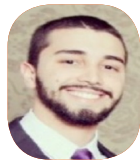
*Advancements and Challenges in Neuroscience  
& Brain Disorders*

JUNE 24-26, 2019  
PARIS, FRANCE



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**Mary Payne**

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**Reidun Stenberg**  
University Hospital Research  
Center, Sweden



**Retno Indrarini**  
Eisai Indonesia  
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**Stephen Grossberg**  
Boston University  
USA



**Susan Hawthorne**  
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**Valida Isanova**  
Kazan State Medical  
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**William S Baek**  
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**Yordian Yahya Bahar**  
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**Young Kyung Seo**  
Daejeon University  
Republic of Korea



**Zdzislaw Chilmoczyk**  
National Medicine Institute  
Poland

Thank You  
All...



# Welcome Message



Dear colleagues,

On behalf of the distinguished members of the Scientific Committee for the 3rd Edition of 'International Conference on Neurology and Brain Disorders and the dynamic organizing team behind this event, it is my pleasure and honour to welcome all attendees to INBC 2019. You are being sincerely thanked for your commitments and efforts in preparing and presenting your innovative and valuable research and findings at this conference. Collectively as researchers, we face an ever growing range of challenges and pressures, as rates of and classifications of neurology and brain disorders are escalating in the bigger, stronger, faster world that we live in today. A very diverse range of distinguished speakers promise to present innovative research, interventions and therapies at this meeting that will assist in providing an antidote to an apparent global physical and mental health crisis and provide each other with opportunities for collaborations.



**Ken Ware**

NeuroPhysics Therapy Institute, Australia

# Welcome Message



Dear conference participants,

It is a great pleasure and honor for me to write this welcome address.

Understanding the activity of a healthy and an altered brain is a vital focus of scientific research. Any change is a motion, and neuronal dynamics are some of the most sophisticated examples of such, positioned between basic biological and social dynamics in their complexity. Making progress in the field of neurology is thus one of the most significant global challenges of our time, with a lot of questions remaining.

How can the field cooperate with fundamental sciences such as physics, mathematics, chemistry?

Are there universal concepts in neuroscience similar to Newton's Second Law? Are modern mathematical tools sufficiently developed to meet the demands of neuroscience? Are there analogous dynamics in mechanics, physics, and chemistry, which we can use to deepen our understanding of mental activity?

I trust that our knowledge of the human brain will continue to evolve as we seek to answer these questions.

*Marat Akhmet*

**Marat Akhmet**  
Middle East Technical University, Turkey




# Welcome Message



Dear colleagues,

It is my pleasure to welcome you all congress participants to the conference. I hope you will have interesting days. It is wide range of neurological issues that we will hear about ranging from children to adults and aspects of the influence of different drugs on the brain. We will hear about the brain development and also about the aging brain. My special interest is gut brain axis where we are beginning of understanding this complex interaction, but we still have much to learn. I hope you will have inspiring days. Very Welcome!



  
**Reidun Stenberg**  
University Hospital Research Center, Sweden

University Hospital Research Center, Sweden

# keynote speakers



***Ken Ware***

NeuroPhysics Therapy  
Institute, Australia



***Marat Akhmet***

Middle East Technical  
University, Turkey



***Margarit Tadevosyan***

Artmed Medical Rehabilitation  
Center, Armenia



***Zdzislaw Chilmonczyk***

National Medicine Institute  
Poland



***Reidun Stenberg***

University Hospital Research  
Center, Sweden

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# About

## MAGNUS GROUP

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Magnus Group (MG) is initiated to meet a need and to pursue collective goals of the scientific community specifically focusing in the field of Sciences, Engineering and technology to endorse exchanging of the ideas & knowledge which facilitate the collaboration between the scientists, academicians and researchers of same field or interdisciplinary research. Magnus group is proficient in organizing conferences, meetings, seminars and workshops with the ingenious and peerless speakers throughout the world providing you and your organization with broad range of networking opportunities to globalize your research and create your own identity. Our conference and workshops can be well titled as 'ocean of knowledge' where you can sail your boat and pick the pearls, leading the way for innovative research and strategies empowering the strength by overwhelming the complications associated with in the respective fields.

Participation from 90 different countries and 1090 different Universities have contributed to the success of our conferences. Our first International Conference was organized on Oncology and Radiology (ICOR) in Dubai, UAE. Our conferences usually run for 2-3 days completely covering Keynote & Oral sessions along with workshops and poster presentations. Our organization runs promptly with dedicated and proficient employees' managing different conferences throughout the world, without compromising service and quality.

# About INBC 2019

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INBC 2019 is designed to bring together top leaders and researchers on one stage acting as a means of disseminating peer reviewed and cutting edge research evidence covering complete field to the neurology community globally. Overall the result will be high quality experience where best content on the most vital topics are presented by leaders with strong discussions, staged in a friendly atmosphere needed to support as much networking and educate as possible. We are excited to continue to grow our international network scientists, researchers, educators, and other scholars in the field of neurology.

Scope of the conference: INBC 2019 Presentations are of top level and wide-ranging spectrum of basic, clinical and translational study with the multidisciplinary tactics to advance and increase the patient care.



DAY 1

# KEYNOTE FORUM

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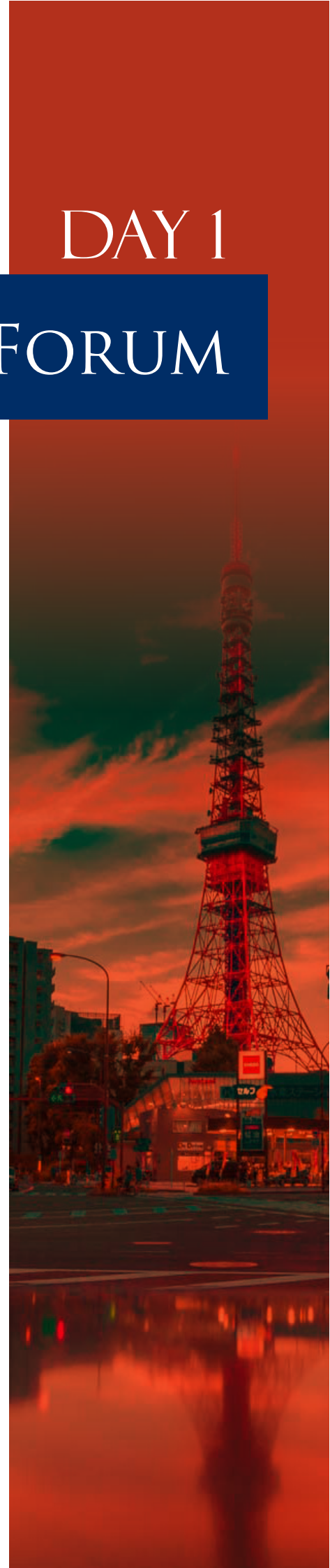
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**Biography**

Ken Ware was founder of Neurotricial Sciences Pty Ltd and NeuroPhysics Therapy and Research and he had been in private practice for almost 30 years, while doing independent and collaborative research. He also presented unique research at 10 major International Science Conferences including neuroscience, Physics, Psychology and Life Sciences, which covers a very broad scientific audience.

He is Former Mr. Universe 1994, National powerlifting and Bodybuilding champion and record holder. He had published relative publications in 'Frontiers in Clinical Physiology' - 'World Journal of Neuroscience' - 'World Journal of Cardiovascular diseases'. He is former Mr. Universe 1994, National powerlifting and Bodybuilding champion and record holder. He is recipient of Her Majesty, Queen Elizabeth's 'Australian Sports Medal' - in 2000, in recognition for personal contributions to the development of the Australian Sporting Culture.

**Hypothesizing the central nervous systems genius to trigger and self-Organize to higher states of complexity as epitomized in the case of Noah Wall the boy born with only 2% of his brain**

**Ken Ware**

NeuroPhysics Therapy Institute and Research Centre, Australia

Noah was born with an estimated 2% of his brain as the result of a cephalic disorder, with the remainder of his cranial cavity being filled with cerebrospinal fluid. This signifies an extreme case of Hydranencephaly. Hydranencephaly is a condition that affects under 1 in 10,000 births worldwide. Infants born with Hydranencephaly may appear quite normal at first but commonly begin to display significant irritable symptoms after a few weeks which develop into a host of physical and intellectual impairments. The prognosis for children with hydranencephaly is generally quite poor, however many children live for several years right into adulthood.

However Noah's brain remarkably redeveloped to an estimated 80% within 3 years, defying all medical predictions for Noah's future. Now at 6 years of age Noah's psychophysical development continues to systematically evolve and he has become an interactive international media personality. Yet the case of Noah Wall challenges us in many ways as there are many questions that beg to be answered scientifically, for well in advance of the required expression of vital regions of the brain historically deemed to be absolutely necessary for sensory motor processing, expression of needs, emotions, associative memory, verbal and non-verbal communication, Noah was able to physically and emotionally respond to environmental cues without the extreme sensory motor deficits that our present scientific wisdom predicted would have left him severely mentally and physically disabled.

While we ponder possible answers to explain such extreme compensatory sensory motor phenomena, we must also determine what inspired Noah's brain to grow. In this presentation I will firstly share what my experiences where in assessing and observing Noah and the rapid transitions which took place under controlled

therapeutic conditions. I will then provide a hypothesis referring to a variety of scientific disciplines and theories attempting to reverse engineer and express the unprecedented growth of Noah's brain from a mere 2% to 80% in 3 years and why he could respond to his environment so well despite the absence of developed brain regions.





### Biography

Dr. Marat Akhmet, (Ph.D.), now is a Professor at the Department of Mathematics, Middle East Technical University, Turkey. He got his B Sc in mathematics at Aktobe State University, Kazakhstan, M Sc and Ph.D. in Differential Equations and Mathematical Physics at Kiev State University, Ukraine. Currently Dr. Marat Akhmet's researches focus on the dynamical models and differential equations. He has published five books and more than a hundred and thirty scientific papers. In the last several years, he has been investigating dynamics of neural networks: periodic and almost periodic motions, stability, synchronization, chaos and its control.

## Synchronization & bifurcations in brain activity

### Marat Akhmet, Ph.D

Middle East Technical University, Turkey

Complexity and synchronization in models are necessary for research in neuroscience. In our talk the complexity will be present through special type of bifurcations - the medusas bifurcations in the Cowan-Wilson model, they have been introduced in our recent papers. Synchronization of biological integrate-and-fire oscillators will be discussed considering the C. Peskin model. The collective behavior of biological and chemical oscillators is a fascinating topic that has attracted a lot of attention in the last 50 years. The integrate-and-fire model of the cardiac pacemaker was developed by C. Peskin to a population of identical pulse-coupled oscillators. The model has been widely adapted for neuroscience. In the present research we give a solution of the second conjecture of Peskin. The talk will consist of main results, simulations and discussion of possible extensions. We will discuss what kind of benefits can be obtained from the study for the artificially intelligent systems, robotics and electronics.



SPECIAL PLENARY TALK

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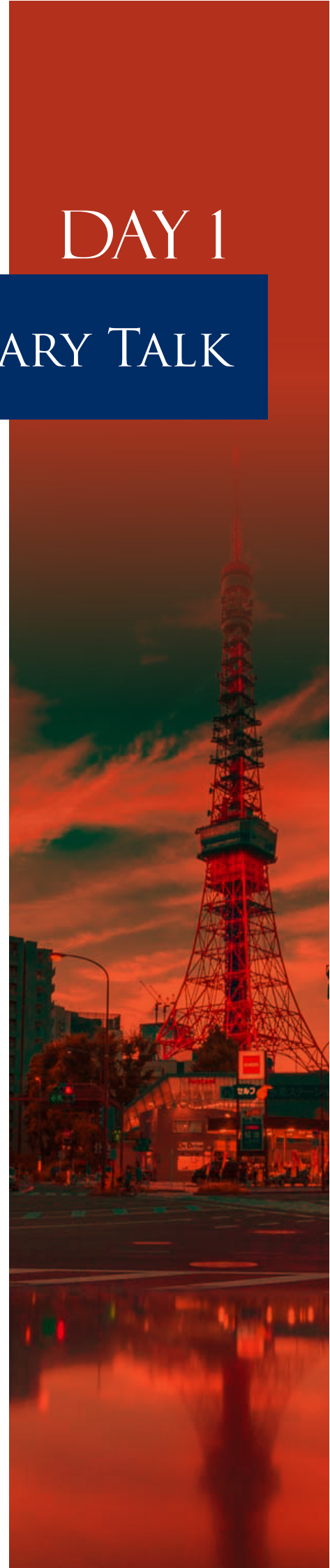
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### Biography

Stephen Grossberg is a principal founder and current research leader in computational neuroscience, computational cognitive science, and biologically-inspired technology. He introduced foundational nonlinear differential equations for short-term memory (STM), medium-term memory (MTM), and long-term memory (LTM). His work focuses upon how individuals, or machines, adapt autonomously in real time to unexpected events. Google Scholar reports more than 73,000 citations and an h-index of 125 of his over 550 publications. He was most recently awarded the 2015 Norman Anderson Lifetime Achievement Award of the Society of Experimental Psychologists (SEP), the 2017 Frank Rosenblatt award of the Institute for Electrical and Electronics Engineers (IEEE), and the 2019 Donald O. Hebb award of the International Neural Network Society (INNS).

## Brain dynamics of normal and abnormal learning and memory consolidation: Multiple hippocampal functions in cognitive, adaptively-Timed cognitive-Emotional, and navigational learning

### Stephen Grossberg

Boston University, USA

This talk provides a self-contained summary of neural models of normal and abnormal learning and memory consolidation in which the hippocampus plays an important role. As heuristically described in the Multiple Trace Theory of Moscovitch and Nadel, the role of the hippocampus in some learning processes is time-limited, but in others more enduring. This theme raises the question of why and how several different kinds of learning processes all include hippocampal resources. The talk will describe neural models of cognitive, adaptively-timed cognitive-emotional, and spatial navigational processes that all involve the hippocampus in learning and memory consolidation processes, but which differ in the extent of hippocampal involvement as memory consolidation proceeds. It hereby provides mechanistic explanations of the differences that have been experimentally reported about hippocampal involvement. Many psychological and neurobiological data are explained in a unified way by these models, including data about clinical disorders like medial temporal amnesia and problems with allocentric navigation.

SPEAKERS

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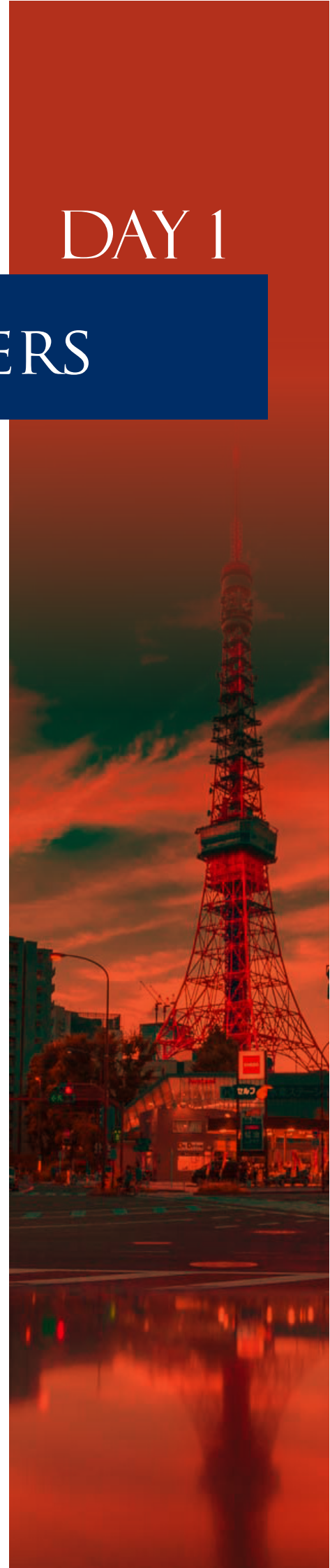
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## Opiate exposure in the developing brain and toxic stress in early childhood: How brain structure and function is altered and impacts life-Long health

Mary Payne, MD

Pediatric Neurology, Marshall University School of Medicine, Department of Neurology, USA

**T**oxins and stressful environments can alter brain structure and function. More importantly, the developing brain in utero is particularly susceptible to exposures to medications and substances of abuse. In my community in rural West Virginia, we have unfortunately experienced a dramatic increase in babies born exposed to opiates, among other drugs. We are approximately 20 times higher than the national average with these exposures. Prenatal brain development has been shown to be negatively affected by toxin exposure, however, many risks of polysubstance abuse are unknown. Furthermore, many of our children live in stressful home situations, whether it be drug use, poverty or inconsistent foster parenting. Persistent stress in early life also effects brain development and can alter long term functioning and adult health. This presentation will provide information on what is known about the developing brain and toxins during the prenatal period and early childhood and the long-term sequela. Also discussed will be current observations from a multidisciplinary neurodevelopmental clinic in Huntington, WV and how the patient findings can be compared to what has been reported from past studies. Neonates, infants, toddlers and older children all have unique findings and issues related to in utero drug exposure and ongoing environmental stress.

### Audience Take Away:

- Understand how substances and toxic stress affect the developing brain.
- Be aware of the unique issues associated with being born drug exposed.
- The audience will have a better understanding of signs of drug withdrawal in a neonate and importance of early intervention to minimize further stress to the brain in the young child's environment.

### Biography

Mary Payne, MD graduated from medical school in 2002 from Louisiana State University. She then continued with a pediatric residency at Tulane University followed by a child neurology fellowship at Children's Hospital of New Orleans. She has been faculty in the department of Neurology at Marshall School of Medicine since 2008. She treats patients with epilepsy, developmental delays, headaches as well as a myriad of pediatric neurology issues. Her research interests include neurodevelopment in infants born exposed to opiates and she coordinates multidisciplinary clinics for children born drug exposed. She also has a quality improvement study at her hospital reducing number of CT scans performed in children in the emergency room setting for mild brain injuries. Improving the developmental needs of children in the state is another area of interest for her, as she sits on the Early Childhood Advisory Council, appointed by the Governor. She has traveled with the CDC to study baby exposed to Zika in utero also. She teaches students and residents in the departments of neurology and pediatrics and supervises students and residents in the outpatient and inpatient settings.

## Evaluation of short term treatment with NAD<sup>+</sup> precursor nicotinamide riboside on cognitive and mitochondrial function in patients with MELAS

Natasa Dragicevic MD PhD<sup>1\*</sup> and Michael Hoffmann MD PhD<sup>2</sup>

<sup>1</sup>University of Connecticut Medical Center, USA

<sup>2</sup>University of South Florida and Orlando VA Hospital, USA

**P**rimarily goal of this study was to measure effectiveness of nicotinamide riboside as direct precursor for coenzyme NAD<sup>+</sup> in patients with mitochondrial DNA mutation 3443 and MELAS (Mitochondrial Encephalopathy, lactic acidosis and stroke like episodes) syndrome. Primary outcome were improved exercise tolerance (motor performance), decreased long term disability and improved cognitive performance. Oxidative stress, mitochondrial biogenesis and to determine bioavailability after oral application. Selection of outcome measures for the future clinical included primary outcomes: exercise tolerance, disability rate and cognitive performance. Oxidative stress, lactate, ATP and sirtuin levels were measured as secondary outcomes. This pilot project succeeded to show improvement in endurance, exercise tolerance and cognitive performance and lower disability scores in patients with MELAS and there is a strong correlation with levels of biomarkers including oxidative stress, lactate ATP levels, nicotinamide and NAD<sup>+</sup> levels and levels of sirtuin 1 without serious and intolerable side effects. This may offer very promising future treatment in patients with MELAS and 3443 mutation but also for patients with other mitochondrial diseases and cognitive dysfunction such as mild cognitive impairment and early dementia.

### Audience Take Away:

- Learn about importance of mitochondria in health and disease
- Discuss novel approach to boosting mitochondrial function in order to improve strength and cognition and decrease oxidative stress and turn down inflammatory response
- Learn about cognitive battery of tests used
- Learn about nicotinamide riboside and its potential wide use in neurodegeneration and ageing
- Learn about side effects and optimal dosing in patients with MELAS and cognitive dysfunction.

### Biography

Dr Natasa Dragicevic is a fellowship trained behavioral neurologist with a PhD in Neurobiology and strong background in basic science. She completed her subspecialty training at Columbia University New York Presbyterian Hospital and New York Neurological Institute, where she became interested in mitochondrial dysfunction and its impact on cognitive function.

Her area of expertise as neurodegenerative diseases including Alzheimer's disease, frontotemporal dementia, Dementia with Lewy bodies as well as mitochondrial diseases and autoimmune encephalitides. She is currently Assistant Professor of Neurology and Director of Behavioral Neurology at University of Connecticut Medical center.

## CB1-Dependent LTD in ventral tegmental area GABA Neurons: A novel target for marijuana

Jeffrey Edwards, PhD\* and Lindsey Friend, PhD, NIH  
Brigham Young University, USA

The ventral tegmental area is necessary for reward behavior where dopamine cells are critical for reward motivated behavior and attaching salience to novel rewarding stimuli. These dopamine cells are regulated by neighboring inhibitory GABA cells. Synaptic modifications known as synaptic plasticity are common in the VTA and thought to be tied to memory of reward and thus behavioral motivation. While dopamine cell plasticity has been thoroughly examined, much less is known regarding GABA cell plasticity. Using whole cell electrophysiology in juvenile/adolescent GAD67-GFP knock-in mice we examined excitatory plasticity in fluorescent VTA GABA neurons. A novel long-term depression (LTD) was induced in GABA cells that was dependent on cannabinoid receptor 1 (CB1) and metabotropic glutamate receptor 5. LTD was absent in CB1 knock-out mice, but preserved in heterozygous littermates. Chronic injections of  $\Delta^9$ -tetrahydrocannabinol (THC), a psychoactive ingredient in marijuana, occluded LTD compared to vehicle injections, however, a single exposure was insufficient to occlude LTD. Bath application of THC induced depression of glutamate synaptic activity and therefore downstream dopamine cells could be disinhibited, which would potentially result in increased reward. As synaptic modifications by drugs of abuse are often tied to addiction, this data also suggests a possible mechanism for the addictive effects of THC, which is most commonly seen in adolescents, by potentially altering reward behavioral outcomes.

### Audience Take Away:

- Brain connections are modifiable based on use-dependency, known as synaptic plasticity. Not only is associative and non-associative memory mediated by plasticity, but also drugs of abuse modify plasticity in the reward circuit, which is thought to mediate addiction. This study illustrates marijuana's ability to modify the plasticity of inhibitory cells in the reward circuit, providing a molecular rationale for marijuana's rewarding/addictive effects.
- Is this research that other faculty could use to expand their research or teaching? Does this provide a practical solution to a problem that could simplify or make a designer's job more efficient? Will it improve the accuracy of a design, or provide new information to assist in a design problem? List all other benefits.

### Biography

Dr. Jeffrey Edwards is a professor in the Physiology and Developmental Biology Department at Brigham Young University. His research focuses on synaptic plasticity of brain circuits including in the hippocampus and ventral tegmental area, the memory and reward centers, respectively. Specifically, his research focuses on neurobiological mechanisms of addiction and exercise/stress effects on memory with an emphasis in endocannabinoids and GABA cells role in synaptic plasticity.



## Epigenetics and Mental Health; Implicating the role of DNA methylation in Rett syndrome

Daniel Kroft<sup>1</sup>, Kimia Sheikholeslami<sup>1,2</sup>, Carl Olson<sup>1</sup>, Marc Del Bigio<sup>3</sup>, Victoria Siu<sup>4</sup>, and Mojgan Rastegar<sup>1\*</sup>

<sup>1</sup>Regenerative Medicine Program, and Department of Biochemistry and Medical Genetics, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, MB, Canada

<sup>2</sup>Faculty of Medicine, University of Toronto, Toronto, ON, Canada

<sup>3</sup>Department of Pathology, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, MB, Canada

<sup>4</sup>Department of Biochemistry, Schulich School of Medicine and Dentistry, Western University, ON, Canada

In this presentation, I will mainly focus on an epigenetic neurological disorder that is caused by a genetic mutation, namely "Rett Syndrome (RTT)". RTT is a neurodevelopmental disease that is caused by MECP2 gene mutations. The X-linked MECP2 gene encodes for MeCP2, an important epigenetic factor in the brain that binds to different types of DNA methylation. RTT patients appear normal at first, without showing any disease-associated symptoms during the first 6-18 months of their life, but by 1-2 years of age they start exhibiting developmental regression, mental disability, speech deficiencies, irregular breathing, seizures, anxiety, and autistic behaviours. Our lab has studied the expression and function of MeCP2 protein variants (E1 and E2) in the murine brain during development and in adult mouse. We have reported the regulation of E1 and E2 by DNA methylation, and their regulation by different types of DNA methylation. In this presentation, I will discuss how the epigenetic mechanisms might be interrupted in the human Rett Syndrome brains. By performing genome-wide DNA methylation on post-mortem human RTT brains in different brain regions that are associated with RTT phenotypes. The global DNA methylation patterns were analyzed by Illumina's Infinium MethylationEPIC BeadChip, in parallel to different types of DNA methylation by dot blot. I will discuss the identified differences in the methylation patterns of gene promoters in different brain regions. Our data indicates the existence of an epigenetic signature for DNA methylation in brain cells and post-mortem brain of RTT patients, providing important insight into the pathobiology of disease in RTT patients.

*This work is supported by funds from International Rett Syndrome Foundation (grant#3212), and Ontario Rett Syndrome Foundation (ORSA). Frozen control tissues and RTT brain regions were obtained through the NIH NeuroBioBank Program (neurobiobank.nih.gov). Additional RTT brain tissues were donated to the Rastegar lab by patient family members with proper consent for research. Research with human brain tissues was reviewed and approved by the University of Manitoba Bannatyne Campus research ethics board.*

### Audience Take Away:

- The presentation will provide an overview on the genetic and epigenetic basis of mental health and neurological disorders, with a clear focus on Rett Syndrome.
- The audience will appreciate the impact of genetics and environmental factors on mental health.
- Currently, Rett Syndrome does not have a cure. In this presentation, I will discuss the results of a genome-wide epigenetic analysis of post-mortem human brain patients, in an effort to identify potential gene targets for future therapeutic applications of Rett Syndrome.

### Biography

Dr. Mojgan Rastegar has completed her PhD at the Université Catholique de Louvain (UCL) and postdoctoral training in US and Canada. In Canada, she conducted postdoctoral training at the McGill University (Montreal) and Hospital for Sick Children (Toronto). Dr. Rastegar is currently an Associate Professor of Biochemistry and Medical Genetics at the University of Manitoba (Canada). She has published more over 40 papers in reputed journals and has been serving as an editorial board member of several Journals including Frontiers in Genetics and Neural Plasticity, among others.

## Reintegration of impaired motor-Cognitive interactions in diseases and injuries of the brain by the author's method of kinesitherapy in the pneumatic suit "Atlant"

**Valida Isanova M.D\* and Aliya Yakubova, M.D**

Dr. Sci., Professor, Department of neurology and neurosurgery Kazan State Medical University, Kazan, Russian Federation  
Kazan Federal University, Kazan, Russian Federation

**T**he nervous system disorders and mental impairments still remain to be among the main causes of children and adults incapacity.

Currently neurorehabilitation has a particular relevance and importance among people suffering from nervous system disorders, incapable of moving independently, self-care, performing socially important work that provides satisfaction and self-esteem, emotional balance and wealth.

However, commonly used schemes of exercise therapy, massage, apparatus physiotherapy are of limited value in rehabilitation of motor and cognitive dysfunctions.

In the rehabilitation context, there has to be an integrated, pathogenetically valid comprehensive rehab method developed for neurological patients.

Following international practices, in Tatarstan (Russian Federation) were developed the unique kinesiotherapeutical method and an antigravitational pneumosuit called "Atlant" for medico-conductive rehabilitation of patients with motor and cognitive impairments. The method is based on higher nervous activity teachings of I.Pavlov, I.Sechenov, V. Bekhterev and C.Sherrington

With the help of straining devices, installed in the pneumosuit "Atlant" along the antagonistic muscles of the body and limbs, the myotatic reflex on extension is triggered in each segment, which activates the motor centres functions in all CNS levels.

There is promoting a restoration of muscle tone, affecting reticular formation, which is the main regulators of vital functions, including motor functions.

Rehabilitational pneumosuit "Atlant" stimulates the hierarchy of movement's organization at all levels of the central nervous system, positively changes the structural and functional reorganization of the nervous system, activates the restoration of the disturbed muscle tone, and creates conditions for the initiation of lost motions and sanogenesis.

The kinesiotherapeutical method in "Atlant" creates the conditions for the patient's active participation in mobility rehabilitation process. The patients gain walking skills and other daily important moving skills, which become possible only with the adequate position of the body and limbs.

Through the available objective trainings with the usage of pneumosuit "Atlant", the patients establish social activity and communication, normal for various functional systems in the motor-cognitive interaction.

### **Audience Take Away:**

- The audience will get acquainted with the unique author technologies of Professor Valida Isanova, accelerating the processes of motor functions' restoration through powerful proprioceptive afferent-efferent stimulation by the method of kinesitherapy in the antigravitational rehabilitation suit "Atlant".
- The author's method of kinesiotherapy in medical-conductive rehabilitation of neurological patients with motor impairments has properties of temporal and spatial summation of impulses. The implementation of motor patterns in three-dimensional space affects the mechanisms of autoregulation of the alpha-gamma motor neuron system at all levels of the CNS to restore the disturbed muscle tone, postural stability and postural control.
- The report will show the pathogenetic basis of the author's kinesiotherapy method and of the antigravitational suit "Atlant".
- The mechanism of action of the rehabilitational suit in the method will be shown.
- The results of years of experience in the application of the author's method and antigravitational suit "Atlant" in Russia will be presented, the effectiveness of which is reliably higher than the commonly used schemes of exercise therapy, massage and apparatus physiotherapy. Thus, the attention of the audience will be drawn to the importance of using pathogenetic methods in the rehabilitation of neurological patients.

## **Biography**

In 2000 Valida Isanova was transferred to a position of professor of department of neurology and neurosurgery of the Kazan State Medical University where continues to work to the present.

Doctor of medical sciences, Professor Valida Isanova personally studied pathogenetic methods of nervous system diseases' rehabilitation in clinics of Germany, England, Switzerland, Austria and China.

One of achievements is developed for restoration of motor and cognitive impairments the author's technology "The method of kinesiotherapy of neurologic patients with impairments of motor functions and rehabilitational pneumosuit (RPS) "Atlant" in the method" (domestic analog of PNF). These technologies in neurorehabilitation were included into an educational program of professional development of neurologists and neurosurgeons in Kazan state medical university.

The techniques developed by professor Isanova were reported in the oral presentations at the international conference "Movement: brain, body, cognition" in Oxford in 2017 and at the international conference "Neurology and brain disorders" in Rome in 2018.

## Neuromodulation – Invasive and noninvasive stimulation in the treatment of orofacial pain

**Richard Rokyta<sup>1\*</sup>, prof., MD. Ph.D. DSc. FCMA, Jitka Fricová<sup>2</sup>, ass. prof., MD. Ph.D.**

<sup>1</sup>Charles University, Third Faculty of Medicine, Department of Physiology, Prague, Czech Republic

<sup>2</sup>Charles University, First Faculty of Medicine, General University Hospital, Department of Anaesthesiology, Resuscitation and Intensive Medicine, Management of Pain, Prague, Czech Republic

**I**t will be described the contemporary neuromodulatory methods – e.i. both invasive and noninvasive ones. As a as stimulation were used electrical current (both alternative and constant current) and magnetic field stimulation. Also the noninvasive stimulation using the electrical and magnetic stimuli will be mentioned. Especially indications and also advantages and disadvantages will be mentioned.

Invasive methods: PNS, PFNS, SCS, MCS, DBS, ES.

Noninvasive methods: TENS, rTMS, tDCS

### Audience Take Away:

- The understanding of principles of invasive and noninvasive neuromodulatory methods and their possible using in the treatment of chronic pain
- The description of orofacial pain from the point of view of basic research and the clinical signs
- The understanding of main advantages and disadvantages of described methods.
- The clinical possibilities of neurostimulatory methods in the treatment of orofacial pain.
- The most frequent etiological factors of orofacial pain

### Biography

Prof. Rokyta was for 27 years Head of Department of Normal, Pathophysiology and Clinical Physiology, 3rd Faculty of Medicine, Charles University in Prague. He taught and still teaching the Physiology and Pathophysiology. He founded and directed special one week course about the pain from the different points of view – pathophysiology, pharmacology, biochemistry, psychology, psychiatry, neurology, neurosurgery, general surgery, orthopaedic and traumatology, burn medicine podiatry, rehabilitation medicine.

He participates in the postgraduate education of medical doctors for the specialisation (attestation) in pain which in Czech Republic the independent medical specialisation.

### Pain research

Prof. Rokyta started with pain research in the Laboratory of prof. Denise Albe-Fessard in Paris.

He has 760 publications and scientific communications, 10 lecture notes for Czech and foreign students, - co-author of Textbook of Medical Physiology (1987,1991) and Textbook of Pathophysiology (1998).

SCI 897, H-index 18, 480 scientific lectures in Czech Republic and abroad

He was the chairman and coordinator two Research goals:

### Pain management

He organised:

1. Congress of EFIC Pain in Europe IV. ,
2. Topical Seminars in Istanbul in the V.th Pain EFIC Congress
3. Topical Seminars in Hamburg in the VII.th Pain EFIC Congress
4. Since 1997 he is the member of the Board of Czech Pain Society
5. From 2009 he is the president of Czech Pain Society
6. From 2009 he is the Councillor of EFIC
7. Every year from 2010 he is organising the Czech- Slovak Dialogues on Pain in different the positions – chairman of Scientific Committee or the President of Congress.
8. He organised many other international and national congresses in physiology and pathophysiology.

He founded the Czech Journal of Pain (Bolest) in 1997 and up to now he is the Editor in chief of this journal

He is involvement and service to IASP is clear from above mentioned activities. He is also the other of very important books especially he is the main editor textbook of algesiology (Pain – Bolest) in two editions (2006, 2012). This textbook in the basic source of knowledge for the Czech algesiologist. He published several other books about the defferent sort of pain (Back pain, Opioids the pain in the old each, Neuromodulation, How to treat the pain). He was also the co-author of the chapters of pain in the different monografies (The child and the pain, Analgesia and anaesthesia during the labor, Clinical pharmacy). He translated the book Douleur from Albe Fessard from French to Czech language.

**Membership and function in scientific societies:** In many Czech and international companies, a member of scientific councils of academic and scientific institutions, member of editorial boards of several international and national journals, international companies and their representative for the Czech Republic.

**He received many scientific and social awards.**

He was awarded for his contribution to the development of french culture by Prime Minister of Republic of France - Chevalier des Palmes Academiques. Honorary member of the Czechoslovak and Czech Physiological Society, Honorary Member of the Czech Medical Association JE Purkyně, Laufberger Medal, Gold Medal 3rd Faculty of Medicine, Charles University in Prague, Gold Medal of Charles University in Prague, Gold Medal of the Institute of Experimental Medicine AS CR, Gold Purkyně Medal of Czech Medical Association JE Purkyně, Award of the Czech Physiological Society for scientific publications, Prochaska price, Charvat price from Paul Janssen Foundation for the popularization of science, Paul Janssen Foundation Award for pain management, Charles University Rector's Award for best scientific publication, the monography Pain (Bolest).



## Typical benzene poisoning on brain magnetic resonance imaging

**Yan Wang**

Chengdu Fifth People's Hospital Chengdu, China

**B**enzene poisoning is rare; acute and chronic benzene poisoning mainly result in damage to the central nervous system. Here we report a patient with benzene poisoning who is mainly affected by central nervous system damage.

### Case report

A 38-year-old man who had been exposed to benzene 2 months ago presented with headache and dizziness. His cerebrospinal fluid and blood tests were normal; his cerebrospinal fluid pressure was 230mm H<sub>2</sub>O. Brain magnetic resonance imaging revealed bilaterally symmetrical abnormal signals in the cerebellar tonsils, basal ganglia, thalamus, subcortical region, and parts of the white matter. Benzene poisoning is rare; acute and chronic benzene poisoning mainly result in damage to the central nervous system and hematopoietic system, respectively<sup>1</sup>.

Axial brain magnetic resonance image reveals widely symmetric long T1 signals (a,b) and long T2 signals(c,d) in the cerebellar tonsils, basal ganglia, thalamus, cerebral hemisphere, subcortical region, and parts of the white matter bilaterally.

Fluid attenuated inversion recovery shows widely symmetrical higher signals in the cerebellar tonsils, basal ganglia, thalamus, cerebral hemispheres, subcortical regions, and parts of the white matter bilaterally(a,b); diffuse lesions are significantly restricted.

### Biography

Yan Wang is the chief physician department of neurology, the Fifth People's Hospital of Chengdu. He major in neurological intervention. He also is the young member of the Interventional Branch of the Chinese Stroke Association, member of the Carotid Artery Group of the Chinese Society of Microcirculation Peripheral Vascular Diseases Committee. And he is the Graduate Responsible Tutor of West China Hospital of Sichuan University; Adjunct professor at Chengdu University of Traditional Chinese Medicine.

## Surgical treatment of severe brain injury

**Csóka András MD, PhD**

Military Hosp. Chief of Neurosurgery Department, Hungary

One of the largest mistakes of the modern science may be the analyzing of the efficacy of the medical treatment by the rule of the evidence-based medicine in the state around the death. What are the most important bioethical rules in the lifethreatening extreme emergency or hopeless status? It is a very important topic as the scientific world has often forgotten the rule of bioethics which says, “In life threatening illness the scientific rationale for the treatment must be sufficiently strong that a positive result would be widely accepted.” (Warren T. Reich, Encyclopedia of Bioethics, page 2276) In these cases, it is a mistake to insist on the method of evidence-based medicine, which is the prospective randomized study. We must not neglect bioethics.

What is the rationale base of the aforementioned rule in the treatment of emergency or hopeless status around the death? The status around the death is such a hundred or thousand? unknown equation that we must not fix only one or two constant criteria in analyzing the results as we probably make a lot of mistakes in our consequence. This is the reason why bioethics uses the “scientific rationale” which could be better in the treatment than applying the results of the prospective randomized study fixing some constant. The history of decompressive craniectomy (DC) in the course of severe brain injury is a very good example. We took some steps backward during the debate of more than 100 years (first described in 1905 by Cushing [1]). The evidence proved by Decompressive Craniectomy in Diffuse Traumatic Brain Injury (DECRA; issued in 2011 NEJM) [2], which mixed the analysis of the status of far away from death and the status around the death in its conclusion. Mixing life threatening and curative characteristics, it was obvious that the conclusion of DECRA was false.

The results of Rescue ICP (2016 NEJM) has corrected the false results of DECRA but we had to wait 6 years. During this period a lot of patients should not have died if the science had not accepted the results of studies around the death automatically. We have not insurrection against the results of possible new study of DC, which can decrease the effect of last study. We have to give up to perform studies around the death. We have to hear the voice of scientific rationale as bioethics advise to us. Probably we are going to operate many times in vain, but we can avoid the mindless death of the child caused by a reversible curative pathological process called brain edema. We have to know that in emergency care around death, we have to make 10 times unnecessary efforts while it is worth doing the DC. The nine DC causes less damage for the patients than only one fatal death.

### Audience Take Away:

- It is a good example to be careful in making decision to give up the medical treatment or not in lifethreatening situation.
- The situation is quite similar to the situation of emergency coniotomy or reanimation or nursing of comatose patients. We should continue the debate not about the performance of treatment, but on how to increase the efficacy of treatment. Nobody has done any randomized study about the coniotomy. It was discovered, described, and everybody does it often in vain. It does not cause great damage as compared to its benefit. In the course of the rehabilitation of long term comatose patients the situation is the same. There are no one patients who wake up after many years. This congress helps to drive the debate in the right direction.

### Biography

1983-89 Semmelweis Medical School, Budapest  
 1994 National Board Examination (neurosurgery)  
 89-93 National Institute of Neurosurgery (resident)  
 93-03 National Institute of Traumatology from 1994 consultant neurosurgeon  
 03-07 Markusovszky hosp. Chief of Dept. of Neurosurgery Szombathely  
 07-09 Szt. Johns Hosp. Chief of Dept. of Neurosurgery Budapest  
 10-13 BAZ County Hosp. Chief of Dept. of Neurosurgery Miskolc  
 13-present Military Hosp. Budapest Chief of Dept. Neurosurgery Cs. Ph.D  
 2002 Topic: Neurotrauma  
 Special Interest: Decompressive Craniectomy, By pass

## Misfolded Proteins in the Retina

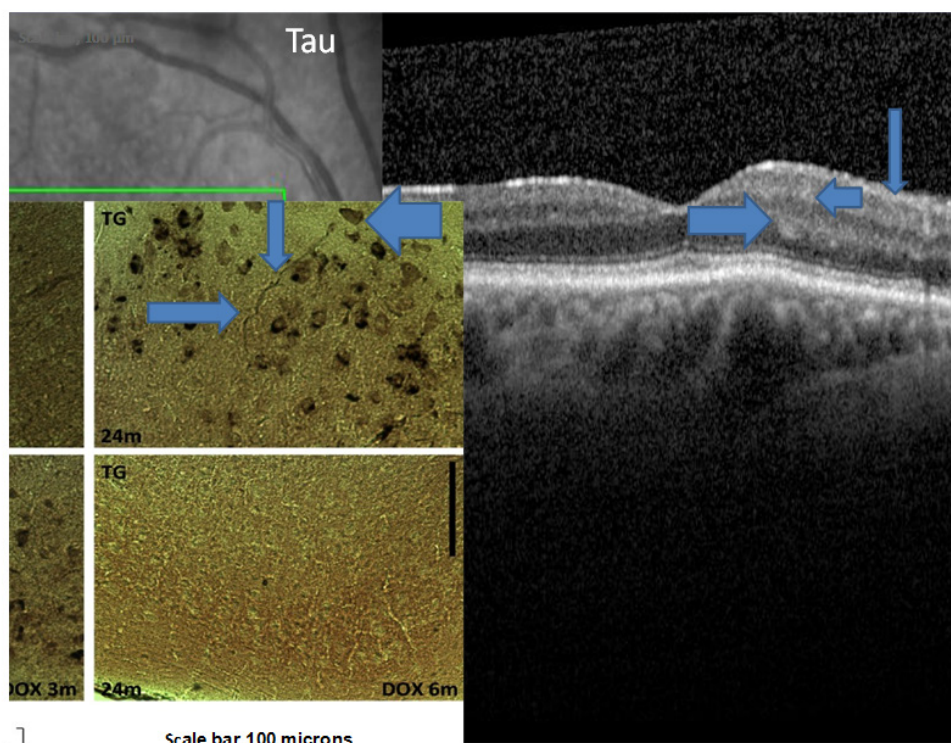
Umur Kayabasi, MD  
Bahcesehir University, Turkey

**Background:** Recent research suggests that Tau is the culprit lesion along with neuroinflammation in the etiology of Alzheimer's Disease ( AD ). Retina is the extension of the brain and is the most easily approachable part of the central nervous system. Detection of the pathological protein accumulations may be possible by using spectral domain optical coherescent tomography ( SD-OCT ) and fundus autofluorescein ( FAF ). There is evidence showing that retinal plaques start accumulating even earlier than the ones in the brain. Most recent Tau protein images in the brain consist of normal or reverse C-shaped paired hellical filaments.

**Methods:** 30 patients with PET proven AD were examined by SD-OCT and FAF. Mean age was 72. Hypo or hyperfluorescent retinal lesions on FAF were scanned by SD-OCT and neurofibrillary tangles ( NFT ) and other accumulations were observed in a masked fashion. The researchers agreed on the shape of the lesions. Both C-shaped ( normal or reverse ) NFTs and thinner fibrillary structures were taken into consideration. Also 10 age-matched healthy controls were examined.

**Results:** In all the patients, NFTs that exactly corresponded with the histopathologic and cryo-EM images of Tau in terms of shape and dimension were detected along with thin fibrils and lesions similar to amyloid beta. The number of the retinal filaments and other abnormal proteins was in concordance with the severity of the disease process. The advanced NFT lesions had normal or reverse paired C shapes and thin fibrils had the shape of histopathologic images seen in early developmental stages of the disease. Healthy patients did not have NFTs, but only had rare thin filamentous shapes.

**Conclusions:** Retinal images of Tau were disclosed for the first time in live AD patients. Retinal neuroimaging is a trustable biomarker and tool for monitoring the disease.



### Biography

Umur Kayabasi is a graduate of Istanbul Medical Faculty. After working as a resident in Ophthalmology, he completed his clinical fellowship program of Neuroophthalmology and electrophysiology at Michigan State University in 1995. After working as a consultant neuro ophthalmologist in Istanbul, he worked at Wills Eye Hospital for 3 months as an observer. He has been working at World Eye Hospital since 2000. He has chapters in different neuro- ophthalmology books, arranged international symposiums, attended TV programs to advertise the neuro- ophthalmology subspecialty. He has also given lectures at local and international meetings, plus published papers in neuro-ophthalmology. He became an assistant professor at Uskudar University- Istanbul in 2015.

KEYNOTE FORUM

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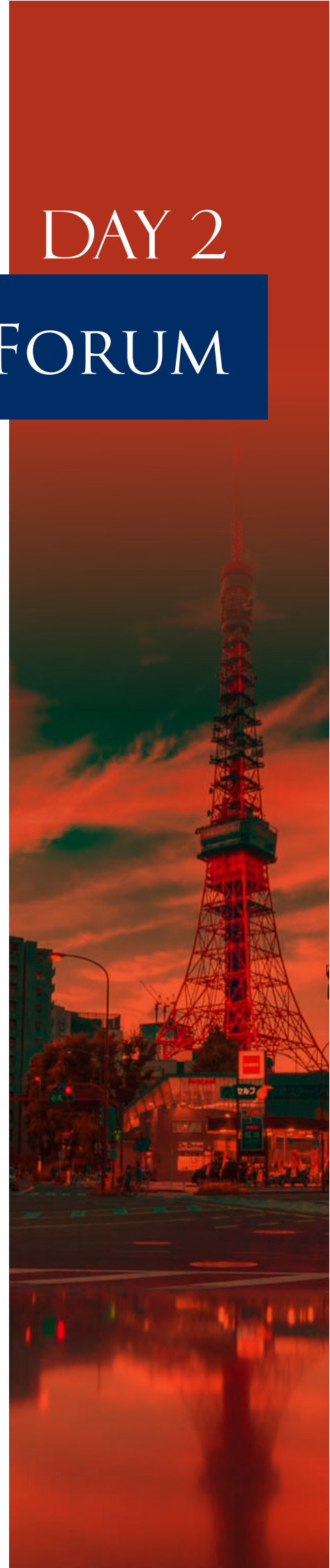
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### Biography

Zdzisław Chilmonczyk worked as a research associate in Warsaw University in Chemistry Department during the period of 1969-1983. During 1983-2000 he acted as Pharmaceutical Research Institute, Warsaw as senior researcher, group leader, and research director. He also acted as Professor and head of Cell Biology from 2000 to 2017.

His Research activities include 107 original papers in international journals, 30 patents and patent applications with 8 implementations of pharmaceutical technologies in industry majorly 5 books and chapters interacted with 32 lectures at Polish and international conferences also chaired 9 sessions at Polish and international conferences. He is also President of 2 international conferences. Research topics include Medicinal chemistry, neuropsychopharmacology, new antidepressant and anxiolytic drugs search, apoptosis mechanisms.

### Prizes and Awards

- Ministry of Science and Higher Education and Technics, III grade Award
- Rector of Warsaw University Award, II grade, collective
- Main Technical Organization of Poland Award, I grade, Master of Technique
- Scientific Award of Polish Pharmaceutical Society, collective
- Stanislaw Biniecki's Medal for substantial achievements in the field of medicinal chemistry and pharmacy
- Polish Academy of Sciences Committee of Analytical Chemistry Medal

## Cytotoxic and neuroprotective activity of serotonin transporter inhibitors and serotonin receptor ligands with antidepressant activity

**Zdzisław Chilmonczyk PhD, D Sc**

National Medicine Institute, Poland

Serotonin exhibits multiple non-neural functions involved in essential hypertension, early embryogenesis, follicle maturation and behaviour. Growth stimulatory effects of the neurotransmitter have been described for a variety cell types. 5-HT was found to induce migration of the human prostate cancer cell lines - PC-3 and Du145 - and several 5-HT<sub>1A</sub> antagonists and serotonin reuptake inhibitors were reported to inhibit the growth of different tumor cell lines in vitro. SSRIs are among the most commonly used antidepressant drugs. It has been shown that some antidepressant drugs and some serotonin 5-HT<sub>1A</sub> receptor ligands may exhibit neuroprotective activity, which could be connected to their antidepressant activity. On the other hand, it was reported that the very same group of compounds may induce apoptosis in some cancer cell lines. This activity could be connected to the compounds serotonergic activity since it was found that 5-HT induced proliferation and migration of PC-3 and DU-145 cells (but not androgen-dependent LNCaP cells). The action of 5-HT was inhibited to varying degrees by the inhibition of MAPK and PI3K as well as by a 5-HT<sub>1A</sub> receptor antagonist.

In the present paper the literature available data concerning the cytoprotective and proapoptotic activity of several SERT inhibitors and serotonin receptor ligands will be summarized and discussed. Additionally, the cytotoxic activity of several SERT inhibitors and 5-HT<sub>1A</sub> receptor ligands in some neuroblastoma and prostate cancer cell lines as well as their propensity to influence cAMP, ERK1/2 and Akt biochemical transduction pathways will be discussed. It is suggested that one should not expect a straightforward relationship between the activation of particular serotonergic pathways by the examined compounds (SSRIs and 5-HT<sub>1A</sub> receptor ligands) and their cytotoxic or cytoprotective activity.

### Audience Take Away:

The audience will learn that antidepressants may also exhibit the neuroprotective or proapoptotic like activity.

- The same compounds may influence different transduction pathways (cAMP, ERK1/2, Akt) in a different way.
- It is suggested that one should not expect a straightforward relationship between the activation of particular serotonergic pathways by SSRIs and 5-HT<sub>1A</sub> receptor ligands and their cytotoxic or cytoprotective activity.
- It should help in a search for new antidepressant and antitumor drugs.
- It should help physicians to understand that antidepressant drugs should be carefully administered for patients with different cancer types.





### Biography

Reidun Stenberg is a Swedish pediatric neurologist working at Örebro University hospital and Örebro University doing research on the gut health and undernutrition/underweight in children with cerebral palsy and autism with focus on gut-brain axis. Member of the Swedish Neuropediatric society and neuropediatric representative to the Cerebral Palsy follow up program register, CPUP. Teacher at Örebro University in Pediatric Medicine and Neurology, since many years, for medical students, nurses, medical personnel and occupational therapists. Teacher in scientific program for future physician's specialists at the University Hospital in Örebro. Scientific publications of original peer reviewed articles and reviewer for suitable scientific journals.

## Gut-Brain axis in children with cerebral Palsy or Autism

### Reidun Stenberg MD, PhD

University Hospital Research Center, Sweden

**U**ndernutrition with poor weight and height gain is frequently seen in patients with cerebral palsy (CP) and is a consequence of feeding and gastrointestinal problems that are poorly understood and investigated and therefore difficult to treat properly. Children with autism also have gastrointestinal problems with symptoms that can be difficult to interpret since they have problems to communicate.

The overall goal of the research is to study gut health (gut biomarkers in relation to clinical data, the intestinal permeability and the gut microflora) and it's impact of the brain.

Undernutrition/underweight has a great negative impact on a person's life quality and can lead to disturbances in the gut, the brain and the bone density. In our previous studies of CP- children we found a high frequency of antibodies against food in children with the lowest weight. Our hypothesis is that they have increased permeability in the gut allowing entrance of undigested proteins in the circulatory system that could stimulate the immune system and interfere with other transport mechanism over the gut barrier such as uptake of vitamins, nutrients and water, leading to difficulties for weight gain. The clinical significance of the dietary antibodies is subject of a collaborative research at Celiac Disease Center at Columbia University, New York. We do not know anything of the microbiota in these patients but have ongoing studies.

Research has shown that probiotics that can be a promising therapy on altered gut flora and that it can improve the immune system, reinforcing the colonic defense barrier, and protects the body against pathogens. The gut microbiota and probiotics treatment relating to the brain will also be discussed.

#### Audience Take Away:

- Knowledge about underweight and gut health in persons and especially in disabled persons is poor. More research on this topic is essential since undernutrition/underweight is treatable and should be done, especially early in life, to avoid sequele in the gut and the brain. The importance of a normal microflora has according to recent research been highlighted and its impact on our health and the function of the brain. Dietary antibodies especially gluten has also been discussed to have negative impact on the brain for example on behavior in autism and mood in patients with celiac disease.



### Biography

Margarit Tadevosyan working experience 28 years, more than 36 articles and abstracts. Born on 29.05.1964. Graduated from Yerevan State Medical University after Mkhitar Heratsi in 1988, Republic of Armenia. Works at “Artmed” Medical Rehabilitation Center, Mental health rehabilitation center “STRESS”. The major task of the center is the therapy of patients with borderline mental disorders. Also works as lecturer in Armenian Medical Institute, Department of psychiatry and clinical psychology. Member of “Armenia psychiatric association” since 2009, member of “World federation of medical biology” since 2009.

## CAPS as an instrument of verification of PTSD diagnosis in combatants with PTSD

### Margarit Tadevosyan PhD

“Artmed” Medical Rehabilitation Center, Armenia

The aim of this study was to investigate the dynamics of clinical manifestations of posttraumatic stress disorders (PTSD) among combatants. We conducted a comparative study of two groups of patients: 1) with mental disorders due to brain damage and dysfunction (F06-F07) as a result of combat traumatic brain injury (TBI), 2) with combat PTSD (F43.1) and enduring personality change after catastrophic experience (F62.0). The patients with PTSD had mild TBI without or with brief loss of consciousness and the patients of second group endured moderate TBI with long loss of consciousness.

We used the methods of clinical interview and clinical research, standard method in PTSD assessment; Clinician-Administered PTSD Scale (CAPS) and the Mississippi Scale for combat-related PTSD. Groups of patients were formed according to the ICD-10 criteria. They were comparable according to the age, sex, long term of disease, many social-psychological features.

The obtained data allow us to suppose that at the certain stage of development of these disease the reapprochement of their clinical manifestation takes place, though specific etiopathogenetic mechanisms occurs. These as well as a number of other clinical and biochemical data testify the current transformation of combat PTSD into organic brain disease.

#### Audience Take Away:

- They will be able to research dynamic of clinical manifestations of PTSD.
- Get information about CAPS and Mississippi as gold standard in PTSD assessment.
- Get information about PTSD clinical manifestations.

SPECIAL PLENARY TALK

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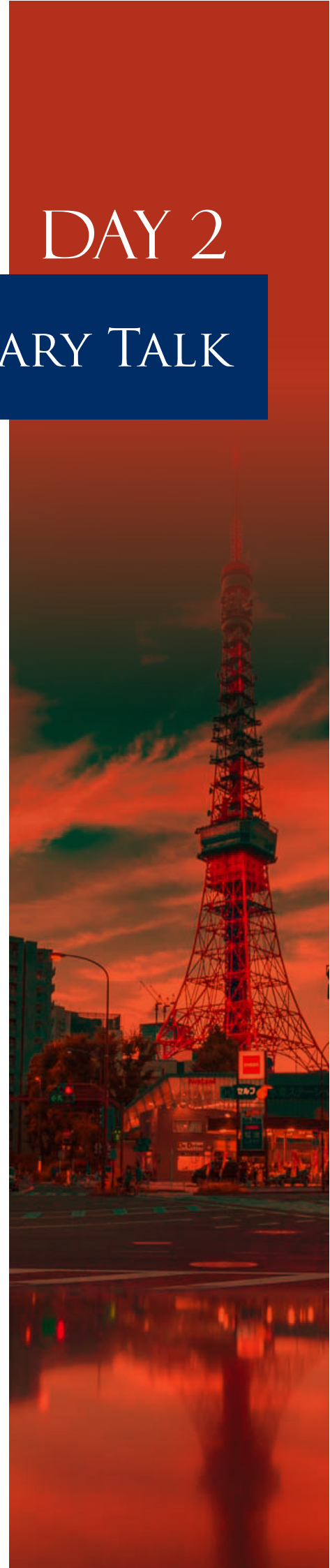
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### Biography

William S Baek is a triple board-certified neurologist, Clinical Associate Professor of UC Riverside, Faculty member of the AAN, and singer/songwriter. Born in NYC, he graduated from Seoul National University College of Medicine and completed his Neurology residency at the University of Chicago and a fellowship in Clinical Neurophysiology at UC San Diego. He also completed an NIH postdoctorate research fellowship at the Children's Hospital of Philadelphia.

He has served as the Primary Stroke Center Medical Director, Internal Medical Residency Program Faculty Member, Neurology Clerkship Director, EMR champion, and QI/Peer Review Committee member at Kaiser Fontana Medical Center. He also serves on the Clerkship Directors Consortium, Ethics Section of the AAN and is a member of the AANEM.

He was the official bilingual moderator for the 2009 AOCCN, IFCN, in Seoul, Korea. He is on the Editorial Board for the Journal of Neurology and Neuroscience and JSM Alzheimer's Disease and Related Dementia. He has over 35 publications, almost all as sole author.

He is a certified medical interpreter for Korean, Japanese, and Spanish and has done TV shows in Korean, English and Spanish. Baek's research interests include not only neurological disorders but also Neurogenetics, language-concordance, ethics, professionalism, and music therapy.

## Musicalization of neurological disorders: Songs of love and hope to heal our patients

### William S Baek, MD FAAN

Parkside Medical Group, USA

The presenter will give an oral presentation on his music album he released in 2018 which was inspired by patients with neurological disorders to raise patient awareness and heal patients through music.

#### Audience Take Away:

- The audience will learn how music can be used to describe an illness and its impact to raise patient awareness and promote music therapy.
- The songs can help patients and families understand the illness and its impact which is otherwise difficult to address during an office visit due to time constraints. Music can convey the emotional, social and ethical challenges the patient must face.

# SPEAKERS

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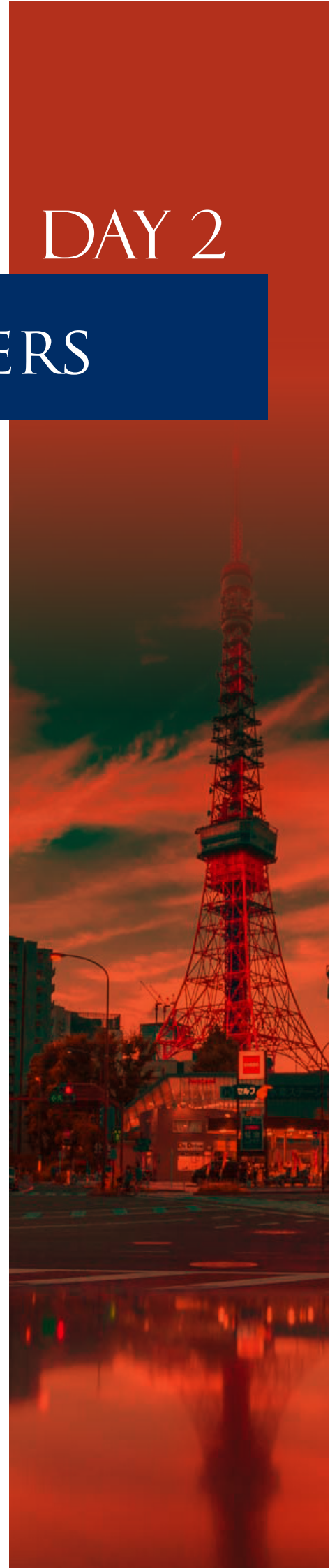
# NEUROLOGY AND BRAIN DISORDERS

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## Perturbing and detraining fear and avoidance associated with pathological anxiety disorders in adults

**Ken Ware**

NeuroPhysics Therapy Institute, Australia

It is understood that long-term elevation of fear and avoidance gives rise to anxiety disorders, including PTSD and OCD. Conditioned fear stimuli and associated conditioned fear responses are widely understood factors. Behavioral conditioning methods have included fear extinction and memory consolidation, detraining, exercise, tai chi, and pharmaceuticals. Evidence indicates it is difficult to remove fear in the adult system, and interventions largely cannot resolve chronic anxiety disorders. The medical field's use of hormetic dose response is fairly well-established now, and sports medicine works with non-medicinal doses of stress to provide stimulation in the hormetic low dose zone, followed by an inhibitory response at higher doses: classic Hormesis. The benefit of eliciting hormetic dynamics in the human system has been observed with NeuroPhysics Therapy in countless people whose anxiety disorders resolved without medicine. The use of this nonlinear approach addresses stimulus-response conditioning that gives rise to chronic anxiety. This presentation focuses first on the nonlinear dynamics in the neurobiology of fear and anxiety, then describes requirements to hormetically perturb the anxious system under controlled conditions. In that setting, individuals are prone to successfully escape the previously non-controllable behaviors of rogue attractor landscapes embedded within neural nets that give rise to the emergence of the individual's disorders. This is accomplished by using novel, controlled doses of psychophysical stress directly correlated with everything the client experiences; environmentally enriching stimuli are the integral core of the therapy. The presentation then explains and exemplifies how the hormetically informed use of sensitively prescribed mild resistance super slow movements performed on specialized resistance equipment by the individual appears to be a powerful way to account for consistent success of evaluating deterministic reactions to the environment by the individual and addressing anxiety disorders. It sets initial conditions for success because the controlled dose dependent perturbations of the psychophysical system are the dose individuals' hormetically need to break the rogue symmetry of the system.

### Biography

Ken Ware was founder of Neurotricial Sciences Pty Ltd and NeuroPhysics Therapy and Research and he had been in private practice for almost 30 years, while doing independent and collaborative research. He also presented unique research at 10 major International Science Conferences including neuroscience, Physics, Psychology and Life Sciences, which covers a very broad scientific audience.

He is Former Mr. Universe 1994, National powerlifting and Bodybuilding champion and record holder. He had published relative publications in 'Frontiers in Clinical Physiology' - 'World Journal of Neuroscience' - 'World Journal of Cardiovascular diseases'. He is former Mr. Universe 1994, National powerlifting and Bodybuilding champion and record holder. He is recipient of Her Majesty, Queen Elizabeth's 'Australian Sports Medal' - in 2000, in recognition for personal contributions to the development of the Australian Sporting Culture.



## What is new in neuroscience

**Aage R. Møller, Ph.D. (D. Med. Sci.)**

Founders Professor of Neuroscience, The University of Texas at Dallas School of Behavioral and Brain Sciences, USA

The brain is a *distributed system* where many functions involve several different parts of the brain. Activation of *neuroplasticity* can alter many features but some such as long-term memory, sexual preference and handedness seem to be “hard-wired.” *Maladaptive plasticity* plays a vital role in many common diseases such as chronic neuropathic pain, spasticity, and probably also conditions such as fibromyalgia. Modern technology has made it possible to study *functional connection* in the brain and determine the strength of the connections. Recent studies have shown how the *strength* of many connections in the brain varies rapidly and widely. Other studies have found that changes in *connectivity* are related to the symptoms and signs of many diseases such as chronic neuropathic pain, severe tinnitus and some age-related symptoms. Mood disorders such as depression, fibromyalgia, and chronic neuropathic pain have similar systems consequences. The risk of giving birth to a child with autism spectrum disorder or spina bifida is lowered if the mother takes *folic acid* before and during pregnancy indicating that the root cause of these diseases is errors in the brain at the early stages of pregnancy. Activity in the vagus nerve facilitates activation of neuroplasticity.

Studies have shown that electrical stimulation of the *vagus nerve* may facilitate reversal of maladaptive plasticity and thereby it may become a way of managing disorders such as chronic neuropathic pain that now has few effective treatments. The immune system affects neural function, and the nervous system controls the immune system. Other studies have shown that *oxytocin* is involved in bonding similar to that of *dopamine* and *arginine vasopressin*.

The recent discoveries in neuroscience have importance for *the treatment* of neurological diseases, and perhaps more important these studies show clearly that it is possible to *reduce the risk* of many diseases that now lack effective therapies by a change in lifestyle. Many studies have agreed that physical exercise and proper nutrition including *supplements* of vitamins such as especially *vitamin D3*, *B-vitamins* and *omega 3* can substantially reduce the risk of many serious diseases that now lack effective treatment, including several forms of cancer and dementia including Alzheimer’s disease.

In the future, *prevention* might be the prime objective of health care professionals and the primary task might be to reduce the risk of acquiring diseases leaving treatments as a last resort. It would be a formidable task, however, to convince people that preventive means are potent means for reducing the risks of illness, perhaps best illustrated by the low compliance with vaccinations such as for influenza, which causes an average of 20,000 lives annually in the USA. Vaccination is very effective in reducing the death from influenza, but compliance with vaccinations is low (for adults in the USA it has been approximately 40% for many years).

### Biography

Dr. Aage R. Møller, graduated as Doctor of Medicine from the Karolinska Institut, Stockholm, Sweden, 1965. After 12 years of research and teaching in at the Karolinska Institut, he immigrated to the USA and became Associate Professor of Otolaryngology at the University of Pittsburgh School of Medicine, later Professor of Neurosurgery at the same institution. He moved 1998 to The University of Texas at Dallas School of Behavioral and Brain Sciences as Professor in Cognition and Neuroscience and later Founders Professor and Distinguished Lecture. Dr. Møller is the author of more than 200 articles in refereed journals, the single author of 17 professional books, most recently: “Neuroplasticity and its Dark Sides,” 403 pages, 2014. He is co-editor of 9 books, most recently “Textbook of Tinnitus” by Springer 2010, 785 page, translated to the Chinese language. Dr. Møller has received many honors for teaching, research and leadership.

## Gap junction channels and hemichannels as a therapeutic target in stroke

Christian C. Naus\*, M. Freitas-Andrade PhD, N. Wang PhD, J. Bechberger MSc, M. DeBock PhD, P. Lampe PhD, L. Leybaert MD, PhD, and C.C. Naus PhD.

University of British Columbia, Canada

Connexin and pannexin membrane channel proteins for gap junctions which are conduits that allow neuronal, glial, and vascular tissues interactions. In the brain, this interaction is highly critical for homeostasis and brain repair after injury. The main gap junction protein in the brain, Connexin43 (Cx43), is mainly present in astrocytes; its function is influenced by kinases that phosphorylate specific serine sites located near its C-terminus. Stroke is a powerful inducer of kinase activity, but its effect on Cx43 is unknown. We investigated the impact of a permanent middle cerebral artery occlusion (MCAO) stroke model in mice that were wild-type (WT) or knock-in of Cx43 with serine to alanine mutations at the protein kinase-C site Cx43<sup>S368A</sup> (PKC), the casein kinase-1 sites Cx43<sup>S325A/328Y/330A</sup> (CK1) and the mitogen-activated protein kinase sites Cx43<sup>S255/262/279/282A</sup> (MK4). We demonstrate that MK4 transgenic animals exhibit a significant decrease in infarct volume which was associated with significant behavioral improvement. An increase in astrocyte reactivity with a concomitant decrease in microglial reactivity was observed in MK4 mice. In contrast to WT, MK4 astrocytes displayed reduced Cx43 hemichannel activity. To further validate the potential of targeting Cx43 hemichannels in stroke, pharmacological blockade of Cx43 hemichannels with TAT-Gap19 significantly decreased infarct volume in WT animals. This study provides novel molecular insights and charts new avenues for therapeutic intervention associated with Cx43 function. Understanding the molecular mechanisms by which these membrane channels function, in health and disease, might be particularly influential in establishing conceptual frameworks to develop new therapeutics against connexin and pannexin channels.

### Audience Take Away:

- An understanding of how the gap junction proteins, connexins and pannexins, contribute to the unique pathways of direct intercellular communication in the brain.
- How gap junction channels contribute to neuroprotection in stroke.
- How connexin hemichannels enhance neuronal injury in stroke.
- How both gap junction channels and hemichannels can be specifically targeted to enhance neuroprotection in stroke and other neurodegenerative diseases.

### Biography

Dr. Christian Naus received a PhD in Anatomy (1985) from Western University, followed by postdoctoral studies at the Scripps Clinic in La Jolla, CA. He started his academic career as an MRC Scholar in the Faculty of Medicine at Western University in 1987. He was recruited to the Faculty of Medicine at the University of British Columbia in 2002 to Head the Departments of Anatomy & Cell Biology, and Physiology, and merged them into the current Department of Cellular & Physiological Sciences. He became Director of the Life Sciences Institute from 2009-2013, promoting interdisciplinary discovery research in biomedical and health sciences. Dr. Naus was recipient of a Canada Research Chair in Gap Junctions in Neurological Disorders, and is an elected Fellow of the Canadian Academy of Health Sciences. His research program explores the role of gap junction channels and their proteins (connexins and pannexins) in disease, including consequences of mutations on gap junction structure and function, and the role of these intercellular channels in diagnosis of disease and development of novel therapeutic strategies. He has conducted over 25 years of research in neurobiology and cancer, focused on cellular and molecular studies to characterize the role of gap junctions in proliferation, differentiation, transgenic mouse models of neurological disorders, and preclinical therapeutic studies for stroke, cancer and Alzheimer's disease.

## MicroRNA: A new tool for Natalizumab therapy in Multiple Sclerosis?

André Eduardo de Almeida Franzoi<sup>1</sup>, Fernanda Subtil Machado<sup>2</sup>, Isabelle Pastor Bandeira<sup>3</sup>, Washigton Luiz Gomes de Medeiros Junior<sup>4</sup>, Wesley Nogueira Brandão<sup>5</sup>, Marcus Vinicius Magno Gonçalves<sup>6</sup>  
University of the Region of Joinville, Brazil

**W**e will discuss about: 1) What are microRNAs; 2) How microRNAs are currently being studied in Multiple Sclerosis; 3) The relevance and demand of microRNAs as biomarkers in the disease; 4) The particularity of the effect on lymphocytes of Natalizumab therapy in the disease; 5) The changes described in microRNAs with the therapy with this drug; and 6) Future perspectives of the use of microRNAs as biomarkers of therapeutic response with this drug.

### Audience Take Away:

- The main goal is to inspire listeners' curiosity about the study of microRNAs in Multiple Sclerosis. The perspective of the future with these molecules being possible biomarkers in different stages of the disease, may stimulate more and more researchers to study microRNAs.
- The possibility of using microRNAs as biomarkers of therapeutic response in Multiple Sclerosis is of major clinical interest. Many researchers and doctors may benefit in the future by discussing the topic. After all, the quality of the evaluation of the clinical response of each patient may be more precise, precocious and individualized.
- The discussion may benefit many patients with Multiple Sclerosis in the future. Our focus should always be to provide higher quality of life and more effective therapies for our patients.

### Biography

He is in the department of Medicine at the University of the Region of Joinville, SC, Brazil During medical school, he performed scientific research in the areas of: Atrial Fibrillation and Stroke; Neurological Disorders in Hyperargininemia; Alzheimer's disease and the Main Aspects; Deep Brain Stimulation in Patients with Parkinson's Disease; Intestinal Dysbiosis and Multiple Sclerosis; and MicroRNAs and Multiple Sclerosis. With medical colleagues, he described case reports on: Neuromodulation in a patient with quadriplegia; Cerebral Histoplasmosis; Temporalis Muscle Hypertrophy as a cause of Facial Pain; Wolfram Syndrome as a cause of Progressive Cerebellar Ataxia; and Pseudo-Athetosis in a patient with Multiple Sclerosis.

## Wildtype TDP-43 functions in DNA repair but this process is perturbed in amyotrophic lateral sclerosis (ALS)

Anna Konopka<sup>\*1</sup>, Donna R. Whelan<sup>4</sup>, Md Shafi Jamali<sup>1</sup>, Prachi Mehta<sup>1</sup>, Toby D. M. Bell<sup>5</sup>, Adam Walker<sup>1,3</sup>, Julie D. Atkin<sup>1</sup>

<sup>1</sup>Centre for MND Research, Department of Biomedical Sciences, Faculty of Medicine & Health Sciences, Macquarie University, NSW, Australia

<sup>2</sup>Department of Biochemistry and Genetics, La Trobe Institute for Molecular Science, VIC, Australia

<sup>3</sup>Queensland Brain Institute, The University of Queensland, St Lucia, Queensland, Australia,

<sup>4</sup>Department of Pharmacy and Applied Science, La Trobe Institute for Molecular Science, La Trobe University, Bendigo, VIC, Australia

<sup>5</sup>School of Chemistry, Monash University, Wellington Road, VIC, Australia

**P**athological forms of TAR DNA-binding protein 43 (TDP-43) are present in motor neurons of almost all amyotrophic lateral sclerosis (ALS) patients, and mutations in TDP-43 are present in familial ALS. Loss and gain of TDP-43 functions are implicated in pathogenesis but the mechanisms are unclear. Here we demonstrate that wildtype TDP-43 is recruited to sites of DNA damage where it participates in non-homologous end joining (NHEJ) DNA repair. However, ALS-associated TDP-43 mutants lose this activity, which induces DNA damage. Furthermore, DNA damage is present in mice displaying TDP-43 pathology prior to disease, implying an active role in neurodegeneration. Additionally, DNA damage triggers features of TDP-43 pathology; cytoplasmic mislocalisation and stress granule formation. This study reveals that TDP-43 functions in DNA damage/DNA repair, but loss of this function triggers DNA damage and associates with key pathological features of ALS.

### Audience Take Away:

- New knowledge about neurodegeneration; they will look at the disease from new perspective, what can accelerate also their research; potentially familiarize them with a new research technique; it will give an opportunity for collaboration.

### Biography

Dr Anna Konopka obtained her PhD degree in 2015 from the Nencki Institute of Experimental Biology, Polish Academy of Science in Warsaw, Poland. Her research resulted in two first author papers and six co-authored papers. Since January 2017 Dr Konopka have been employed as a postdoctoral research fellow at Macquarie University, Sydney, Australia working within Prof Atkin's group on DNA damage in neurodegeneration in ALS. Since joining Prof Atkin's laboratory Dr Konopka have published four journal articles. Her publications reflect her research interests in neurodegeneration in ALS, particularly interests in DNA damage in neurodegeneration.

## **Depression as a risk for Alzheimer's disease: What is the evidence**

### **Joe Herbert**

John van Geest centre for Brain Repair, Department of Clinical Neurosciences, University of Cambridge, UK

**I** will review the risk for subsequent Alzheimer's disease for those diagnosed with major depressive disorder, and discuss the genetic, endocrine and immunological factors that increase or reduce the link between these two conditions.

### **Biography**

Joe Herbert interested in the role of the brain in adaptive responses, with particular reference to the reciprocal interaction between hormones and the brain. His experimental work is focussed on the way that neural factors, such as serotonin and glucocorticoids, regulate the formation of new neurons in the adult hippocampus, and the role these play in responses to stress. I have a large parallel clinical programme, focussed on determining the risk factors (genetic, environmental, psychosocial and endocrine) that predispose to depression in collaboration with Prof Goodyer (Psychiatry). I also work on the role of hormones in financial decision-making and risk perception.

## **Baby brain: Examining the link between sleep, information processing speed and executive functioning during late stage pregnancy**

**Kate Connelly<sup>1</sup>, Janet Leatham<sup>2\*</sup>, PhD**

<sup>1</sup>Doctoral Student, Massey University, Wellington, New Zealand

<sup>2</sup>Massey University, Wellington, New Zealand

**B**aby brain' is a term given to the phenomenon experienced by many pregnant women who feel that pregnancy has induced cognitive impairment. Investigation of cognitive deficits during pregnancy has focussed on subtypes of memory, but more recently has included the domains of information processing speed and executive functioning with inconsistent results being found.

Using a larger sample and different measures than previous studies, the current study sought to clarify these inconsistencies and examine the relationship between information processing speed and the planning component of executive function. Could the perceived impairments in executive functioning can be more accurately understood as secondary consequences of impairments in processing speed?

Participants were 133 New Zealand women, 68 in the late stages of pregnancy with their first child, and a control group of 65 who were not (and had never been) pregnant.

Results showed significant impairment in simple reaction times for pregnant women compared to controls and a trend towards significance impairment on more complex choice reaction time measure. There was no difference between the groups in the planning component of executive functioning.

Deficits in sleep quality and altered mood during pregnancy were considered as potential moderating variables on results. While pregnant women had significantly poorer self-reported sleep quality than controls, this did not correlate with cognitive scores. However, anxiety was shown to impact on planning time during the executive functioning task, and on performance during that task.

The results of this research clarify current inconsistencies in results published in extant literature and reveal areas for further research regarding cognition during pregnancy.

### **Biography**

Dr. Janet Leatham working as a Professor of Neuropsychology in School of Psychology at Massey University, New Zealand.



## Anti- $\beta$ 2-Glycoprotein I autoantibody expression as a potential biomarker for strokes in patients with anti-Phospholipid syndrome

Husham Y. M. Ali\* & Zainalabideen A. Abdullah

College of Medicine, University of Zakho, Iraq

**A**nti-phospholipid syndrome (APS) is an autoimmune disease. Cerebral ischemia associated with APS occurs at a younger age than typical atherothrombotic cerebrovascular disease, is often recurrent, and is associated with high positive IgG anti-phospholipid (GPL) unit levels. This study sought to determine the frequency rates of anti-cardiolipin (aCL) dependent on the presence of  $\beta$ 2-GPI, anti- $\beta$ 2-glycoprotein I (a $\beta$ 2-GPI), and anti-phosphatidyl serine (aPS) IgG autoantibodies among stroke patients, and thus demonstrate the importance of testing for a $\beta$ 2-GPI autoantibodies. For these study, stroke patients and control subjects recruited from Mosul, Erbil, and Dohuk provinces in Northern Iraq were evaluated. All cases were under 50 years-of-age and had no recognizable risk factors. Using ELISA to evaluate the presence of IgG isotype of aCL, a $\beta$ 2-GPI, and aPS autoantibodies in their blood, the results indicated that the frequency of a $\beta$ 2-GPI was 14/50 (28%), aCL was 11/50 (22%), and aPS was 9/50 (18%) among stroke patients. In contrast, aCL was detected in 2/30 (6.7%) of control subjects; each of the other anti-phospholipid antibodies (APLA) was never observed. Of all the a $\beta$ 2-GPI<sup>+</sup> cases, the incidence of stroke patients having the combined profile of a $\beta$ 2-GPI + aCL was 11/14 (78.6%) and of a $\beta$ 2-GPI + aPS was 9/14 (64.3%). Only 2/14 (14.3%) of these a $\beta$ 2-GPI<sup>+</sup> patients also expressed aCL in the absence of aPS. The frequency of patients expressing all three markers was only 9/14 (64.3 %). In none of the APS/stroke patients were aCL or aPS expressed in the absence of the a $\beta$ 2-GPI. Conversely, a $\beta$ 2-GPI as a sole marker was seen in 3/14 (21.4%) of these patients (i.e., in absence of either other marker). It can be concluded from these studies that among the three major forms of APLA examined, the presence of a $\beta$ 2-GPI IgG autoantibodies appeared to correlate best with stroke in patients who were concurrently suffering APS.

### Biography

Husham Bayazed has completed his PhD at University of Mosul, College of Medicine. He is now a Consultant at the Scientific Research Center, University of Zakho/Kurdistan Region, Iraq. He is a Specialist and Consultant in Microbiology and Immunology and has published more than 25 papers in reputed journals and has been serving as a Scientific Reviewer for many local and international medical journals. In addition, he has a Fellowship of ISC, Infection, Cancer, Immunology Advisory Board Member (EUROMDnet) Belgium, Membership of World Stroke Organization, Membership of Metabolomics, USA, and Membership of American Association of Science & Technology with more than 20 participations in international scientific meetings all over the world.

## The klotho protein and Alzheimer's interrelation

Valentina Barkhanskaya<sup>1\*</sup>, Yekaterina Blok<sup>2</sup>, Yelena Pozdnyakova Ph.D<sup>3</sup>., Gulshat Kemelova MD, PhD<sup>4</sup>, Valida Isanova MD<sup>5</sup>

<sup>1</sup>Student of Karaganda Medical University, Karaganda, Kazakhstan

<sup>2</sup>Student of Karaganda Medical University, Karaganda, Kazakhstan

<sup>3</sup>Associate Professor, Karaganda Medical University, Karaganda, Kazakhstan

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<sup>5</sup>Dr. Sci., Professor, Department of neurology and neurosurgery Kazan State Medical University, Kazan, Russian Federation

Nowadays Klotho protein (KP) is actively researched by scientists but in the textbooks. There is a strong proof of KP biological functions in protection of the myelin sheath from damages and the reduction in synthesis of KP during the age. In the medical literature, there is a lot of information about KP functions, however relatively a few found about Alzheimer's disease (AD) and KP. We want to make an assumption about the correlation of KP and AD based on the relevant information.

This study included articles from Cochrane library, PubMed, NIH, etc. In order to find out appropriate publications and for the conceptualization of theory keywords such as "Klotho protein", "Alzheimer", "neurodegenerative process", "age-related diseases" were used.

81 articles were studied and 6 (7 percent) of them were selected. Most of them were about klotho protein related to renal and cardiovascular diseases. It means that interaction the KP and AD were studied not well.

In order to be confident that KP influences on the myelin sheath, we need more evidence with human biological materials. We consider that KP could be a biomarker of neuron defects and useful in Alzheimer's therapy. Therefore, there is a necessity of the more detailed research of KP on the genetic, molecular, cellular and clinical levels.

### Audience Take Away:

The audience will get acquainted with the latest research on the strategic importance of Klotho protein in neurology (Alzheimer's disease). From this presentation, the audience will learn about the role of Klotho protein in the protection of hippocampal neurons from amyloid activity. The audience learns about the role of Klotho protein in the maturation and protection of myelin. The congress participants will know the possible role of Klotho as a biomarker with neuron defects and the role of Klotho as a component under redox stress. We will show the audience the latest research in the field of Alzheimer's disease prevention using the combination of Klotho protein and drugs. It will expand the audience's outlook in the field of promising areas for the prevention and treatment of Alzheimer's disease.

### Biography

Student of General Medicine faculty of Karaganda Medical University, Karaganda, Bachelor. Kazakhstan Lore of The International Federation of Medical Students Associations (IFMSA). Took the 3rd place on the International Student Meeting "The New Generation-New energy-New Era" (2017) with the work "Application of the effective vocabulary-building methods in Karaganda State Medical University" Presented a thesis "Физиологические основы влияния рекламы на человека" on 76th International Pirogov scientific medical conference for students and young scientists (2017). Wrote the article "Systematic Research of the Forecasting Stroke" with PhD professor I.A. Kadyrova (2017)

Took an Exchange Program in Department of Medical Genetics in Palacký University Olomouc (Czech Republic)(2018) where studied an unusual case of chimerism in the patient and worked in laboratory

Working on the project "Research the activity of the cerebral cortex with ordinary memorization and memorization with the Memory Palace method on EEG"

Wrote the thesis "The influence of advertising of the physiological processes in the brain" in LIMSC – Leiden International Bio Medical Student Conference (15/03/2019)

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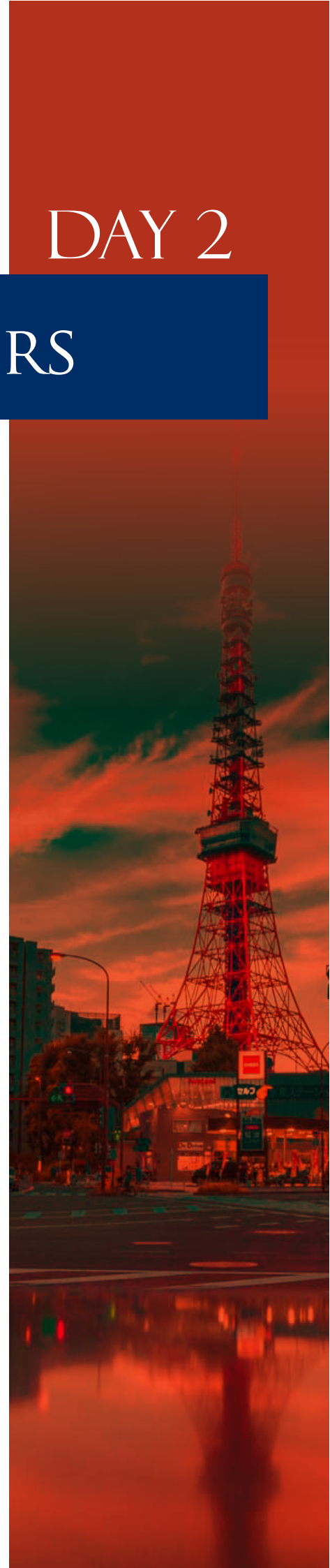
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BRAIN DISORDERS

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## Development of a targeted drug delivery system for the CNS using a novel *in vitro* blood brain barrier model

Susan Hawthorne, MSc PhD FHEA SRPharmS<sup>1\*</sup>, Ms Rachel Huey, MPharm MPSNI<sup>1</sup>, Professor Paul McCarron, PhD<sup>1</sup>, Dr Dan Rathbone, PhD<sup>2</sup>

<sup>1</sup>School of Pharmacy and Pharmaceutical Sciences, Ulster University, United Kingdom

<sup>2</sup>School of Life and Health Sciences, Aston University, United Kingdom

Efficient delivery of therapeutics to the central nervous system (CNS) is extensively limited by the blood brain barrier (BBB). Cell penetrating peptides (CPP) have gained recognition for enhancing the uptake of conjugated payloads into various cell types, however, the non-specific manner of cellular uptake is not suitable for toxic or expensive drugs such as proteinaceous growth factors. Nanoparticles, depending on their chemical composition, can be formulated to entrap a variety of drugs within their core, releasing their payload over a time period. For biological applications, nanoparticles composed of poly(D,L-lactide-co-glycolide) (PLGA) can be surface modified with a targeting peptide to facilitate specific delivery of a therapeutic payload to certain areas of the body, achieving controlled and targeted delivery.

Rabies virus-derived peptide (RDP) has shown promise as a targeting peptide for drug delivery to the brain. This derivative of rabies virus glycoprotein (RVG) may potentially facilitate drug targeting to the CNS for the treatment of neurodegenerative disorders such as Parkinson's disease. Previously, we have shown that RDP action in SH-SY5Y neuroblastoma cells is dependent on the nicotinic acetylcholine receptor (nAChR). However, due to the size of RDP (39 residues) it may be prone to proteolytic degradation *in vivo* thereby limiting its targeting capabilities.

In light of this, we subsequently modelled a new peptide on the RDP/nAChR interaction and designed a novel targeting ligand, which we termed DAS. The serum stability and neural cell-specific targeting properties of the novel RDP-derivative, DAS, were investigated to assess its potential as a neural cell-targeting ligand. DAS peptide demonstrated greatly enhanced serum stability *in vitro* compared to RDP. Furthermore, DAS-labelled PLGA nanoparticles (with a drug payload) demonstrated neural cell-specific targeting abilities.

To investigate the ability of this new peptide to carry a conjugated payload into the CNS, we have developed a human cell line *in vitro* BBB model. This triple-layer co-culture composed of brain microvascular endothelial cells, pericytes and astrocytes exhibited both excellent *in vitro* TEER values and expression levels of ZO-1 and claudin-5 tight junction proteins, all measures of BBB integrity. Our results clearly demonstrate that DAS can effectively and efficiently deliver conjugated drug-loaded NP across a BBB model and release drug payload on the basolateral (brain) side of the model. TEER values were unaffected by targeted drug delivery signifying that BBB integrity was not compromised by the new targeted delivery system. Although inter-species BBB models have been used previously in drug transport studies, it is advantageous to have an all human-derived model. The differences between interspecies BBB cells is not well known and use of human cells may more accurately predict human *in vivo* responses to drugs and their delivery vehicles.

RDP derivatives such as DAS may prove beneficial in the pursuit of effective regenerative treatments for various neurodegenerative diseases such as Parkinson's disease, providing a means of targeted delivery for new therapeutics with curative potential by providing a means of overcoming the restrictions of the BBB.

### Audience Take Away:

- We have developed a human-derived BBB model that can be used for drug transport studies.
- This model can be used to develop lead compounds before expensive animal models are employed.
- This model can be used for the development of therapeutics for a range of neurodegenerative disorders.
- These targeted nanoparticles can be loaded with a range of compounds including growth factors and antibody-based drugs that normally demonstrate difficulty in overcoming the BBB.

### Biography

Dr Susan Hawthorne is a lecturer in the School of Pharmacy and Pharmaceutical Science at Ulster University, United Kingdom. Her career began in the field of protease/peptide chemistry and she has been involved in research into breast and prostate cancer, the role of proteases in parasitic disease and, subsequently, the use of peptides as selective targeting agents for drug delivery. Her recent work has involved drug delivery for topical wound management, delivery of RNAi to breast cancer cells as an anti-proliferative and anti-invasive strategy, formulation of combined cancer chemotherapy polymersomes and development of CNS targeted drug delivery strategies.

## Addition associated engram cells as therapeutic targets of addiction

Yida Wang, Bin Li MD

Georgetown University Medical Center and Washington Institute for Health Sciences, USA

**N**orman M. White employed the theory of learning and memory to explain the mechanism of drug addiction. Base on his theory, we can understand addiction as a kind of memory that associates a feeling of euphoria with the use of a substance or a certain behavior. Memory engram cells are a group of intermediate neurons that associate with different events and represent a percept, memory, or concept in brains. Memory engram technology can label and manipulate the specific memory engram cells. Cocaine addiction associated engram cells have been found in the mice brains. When these engram cells were abolished or suppressed, the addictive behavior was significantly relieved. Thus, selectively eliminating the memory engram associated with addiction, i.e. eliminating the association between euphoric sensation and drug use, may be an effective treatment of addiction.

Synaptic pruning plays an important role to remove unnecessary neuronal connection from the developing and mature brains. The process of synaptic pruning implicates activation of pro-apoptotic caspases, the proteasome-ubiquitin pathway, repulsive guidance cue signaling, and growth-promoting signaling, etc. Elimination of addiction associated memory may be achieved by activating the synaptic pruning process in the addiction associated engram cells. Hereon, a gene therapy framework is proposed to achieve this goal.

Step 1. The design of the gene transfer system: firstly, this system should be able to identify the engram cells under a “turn on” situation. Secondly, the system can initiate synaptic pruning process in the target engram cells. Temporal specificity of labeling is achieved by the exogenously controlled gene regulation systems (turn on), such as tetracycline, rapamycin, RU486. Memory engram technology which is based on the experimental fusion of immediate early gene, such as c-fos, arc, that can be used to identify the engram cells. The transcription factor CREB and  $\Delta$ FosB are also related to addiction associated memory, they could be used to identify the engram cells, too.

Step 2. Location of the gene delivery sites: It has been reported that the hippocampus mediates contextual control of drug self-administration, the dorsal striatum mediates stimulus–response habitual responding for drug reinforcement, and the amygdala mediates conditioned drug seeking. Regarding to different situations of addictive patients, it is necessary to determine the appropriate sites of brain for gene therapy.

Step 3. Identification of the special mental state: to identify the engram cells associated with addiction, the subjects must be in a particular mental state, such as the onset of drug addiction or a euphoric state after drug use. In this particular mental state, the targeted immediate early gene shall be expressed in the engram cells that is associated with addiction. Meanwhile, the exogenously controlled gene regulation system is turned on, so that these engram cells are recognized and future pruning mechanism is activated to erase the addiction associated memory.

In summary, this proposal suggests that the addition associated engram cells could be used as therapeutic targets for addiction, and the gene therapy techniques that combine memory engram technology and synaptic pruning will be used to erase the addiction associated memory.

### Audience Take Away:

- According to White’s theory, addiction can be understood as a kind of memory that associates a feeling of euphoria with the use of a substance or a certain behavior.
- Memory engram cells are the neurobiological basis of addictive memory.
- Addition associated engram cells could be used as therapeutic targets for addiction.
- Elimination of addiction associated memory may be achieved by activating the synaptic pruning process in the addiction associated engram cells.

### Biography

Yida Wang is a research intern in Georgetown University Medical Center and Washington Institute for Health Sciences located at Washington metropolitan area of United States. Under the guidance of mentor, Bin Li, MD., who is a research specialist in Georgetown University Medical Center and Washington Institute for Health Sciences, he proposed a framework for gene therapy of addiction that the addition associated engram cells could be used as therapeutic targets of addiction and the gene therapy techniques that combines memory engram technology and synaptic pruning could be used to erase the addiction associated memory.

## Although cognitive tests still in normal limits, Tau and amyloid- $\beta$ is high in APOE $\epsilon$ 4 carriers in cases with subjective memory complaints

Nilgun Cinar<sup>1\*</sup>, Sevki Sahin<sup>1</sup>, Fusun Er<sup>2</sup>, Baris Topcular<sup>3</sup>, Miruna Florentina Ates<sup>1</sup>, Sibel Karsidag<sup>1</sup>

<sup>1</sup>Department of Neurology, Faculty of Medicine, Maltepe University, Istanbul, Turkey.

<sup>2</sup>Department of Computer Engineering, Okan University, Istanbul, Turkey.

<sup>3</sup>Department of Neurology, Faculty of Medicine, Bilim University, Istanbul, Turkey.

<sup>4</sup>Alzheimer's Disease Neuroimaging Initiative (ADNI)

**Background:** Subjective memory complaints (SMC) are often detected in the elderly. APOE $\epsilon$ 4 genotype has been identified as the most important risk factor for late onset Alzheimer Disease (AD). We aimed to evaluate temporal change of Tau and Amyloid Beta (A $\beta$ ) in SMC with APOE- $\epsilon$ 4 carriers (C) and non-carriers (NC) based on cognitive tests.

**Method:** In order to find cognitive changes from baseline to 1 year follow up of AD patients, Assessment Scale (ADAS)-13 scores were evaluated according to APOE- $\epsilon$ 4 status in SMC cases from Alzheimer's Disease Neuroimaging Initiative (ADNI) data. SMC cases were divided into two groups as NC and C according to APOE- $\epsilon$ 4 genotypes. Phosphorylated Tau (PTau) and A $\beta$  were compared among the groups.

**Results:** Total 87 SMC cases (n:33 C, 54 NC, female/male: %51/49, mean age of NC group was 72 $\pm$  5.5 and C group was 70 $\pm$ 5.2 years) were enrolled to the study from ADNI. PTau levels were 28.5 $\pm$  12, 35.8 $\pm$  18, 20.1 $\pm$  6, 20.8 $\pm$  7 pg/ml in C and NC group at baseline and 24 months later, respectively. In C group, PTau levels were significantly high since the beginning. A $\beta$  levels were 961 $\pm$  378, 799 $\pm$  274, 1180 $\pm$  347, 1097.8 $\pm$  355 pg/ml in C and NC group at baseline and 24 months later respectively. In C group, A $\beta$  levels were significantly low since the beginning. There were no significant difference between two groups of ADAS-13 scores at the beginning or 24 months later.

### Conclusion:

APOE $\epsilon$ 4 carriage may be associated with cognitive impairment in SMC as well as AD patients despite the accumulation of Tau and A $\beta$  where cognitive dysfunction cannot be measured by objective tests. Long-term follow-up studies are needed.

### Biography

Nilgun Cinar graduated from the Cumhuriyet University School of Medicine. She worked as practician doctor in Sinop and Ankara between 1996 and 2001. She completed her residency in neurology in Eskisehir Osmangazi University School of Medicine. She worked in different instituitons, including Sanliurfa Siverek State Hospital and Aksaray Training and Research Hospital Neurology Services between 2006-2008. She became Assistant Professor in 2009 and associate Professor in 2013 at Maltepe University School of Medicine. She published many articles to both national and international journals. Dr. Cinar generally works in multidisciplinary areas, including cognitive neurology, stroke, headache, electrophysiology and movement disorders. She is an active member of cognitive neurology and quality of life working study group of Turkish Neurological Society. She currently works as Associate Professor of Neurology in Maltepe University, Department of Neurology.



## RSK3 mediates necroptosis by regulating RIP3 activity in retinal ganglion cells

Mi Wang, Limin Guo, Shuchao Wang, Lvshuang Liao, Yanxia Huang, Fengxia Liu, Yun Zhang, Jufang Huang, Dan Chen  
Kun Xiong\*

Department of Anatomy and Neurobiology, School of Basic Medical Science, Central South University, China

**R**eceptor-interacting protein 3 (RIP3) plays an important role in the necroptosis signalling pathway. Our previous studies have shown that RIP3/mixed lineage kinase domain-like protein (MLKL)-mediated necroptosis occurred in retinal ganglion cell line 5 (RGC-5) cells during oxygen-glucose deprivation (OGD) injury. However, the upstream regulating pathways of RIP3 have yet to be uncovered. The purpose of the current study was to investigate the role of ribosomal protein S6 kinase 3 (RSK3) in the phosphorylation of RIP3 in RGC-5 cells during necroptosis following OGD injury. First, we found that the expression of RSK3, RIP3/p-RIP3, and MLKL/p-MLKL was upregulated and that the necroptosis of RGC-5 cells was elevated after OGD injury. Then, we performed a preliminary computer simulation to evaluate whether RSK3 could interact with RIP3, and later confirmed this interaction by co-immunoprecipitation. Furthermore, we found that the application of a specific RSK3 inhibitor, LJH685, or rsk3-siRNA decreased the phosphorylation of RIP3, while over-expressing rip3 did not affect the expression of RSK3, which indicates that RSK3 is an upstream regulator of RIP3 during the necroptosis induced by OGD in RGC-5 cells. Finally, in vivo studies with rats showed that pretreatment with LJH685 before acute high intraocular pressure episodes reduced the necroptosis of retinal neurons and improved the recovery of impaired visual function. Taken together, our findings suggested that RSK3 is one of the key upstream regulatory molecules in RIP3 phosphorylation during RGC-5 necroptosis.

### Audience Take Away:

- Our study will further enhance our understanding of the RIP3 regulatory mechanism in neuronal necroptosis and provide a theoretical and experimental basis to validate potential intervention targets for clinical treatment of conditions such as acute glaucoma.

### Biography

Kun Xiong, MD, PhD, Professor, Department of Anatomy and Neurobiology, School of Basic Medical Science, Central South University, China. Field of Specialization: Neurobiology of neural injury/regeneration; he is the academic editor of Editorial Board of Medicine and Neural Regeneration Research. He has supported by 3 grants from National Natural Science Foundation of China, and published more than 30 articles about neuroscience in International academic journal.

## Korean medicinal herbs inhibit MPP<sup>+</sup>-induced mitochondrial dysfunction in SH-SY5Y human neuroblastoma cells

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<sup>1</sup>Korean Medicine Research Center for Healthy Aging, Pusan National University, Yangsan, Republic of Korea

<sup>2</sup>Department of Korean Medical Science, School of Korean Medicine, Pusan National University, Yangsan, Republic of Korea

These days, interplay between brain and gut is important role in brain related disorders. Immune system and tight junctions in gut are thought that there is a correlation with Central nerve system and brain. Two kinds of medicinal herbs, *Rumex japonicus* Houutt. (RJ) and *Atractylodes macrocephala* Koidz. (AM), has been used to treat various digestive disease and inflammation in Korea. Also, RJ and AM has anti-oxidative and anti-inflammatory effect. Therefore, RJ and AM are expected to improve not only digestive disease but also brain disorders such as Parkinson's disease (PD). In the present study, we evaluated the protective effect of RJ and AM against neurotoxin 1-methyl-4-phenylpyridinium ion (MPP<sup>+</sup>)-induced mitochondrial dysfunction in SH-SY5Y human neuroblastoma cells, an *in vitro* PD model. SH-SY5Y cells were incubated with SF for 24 h, after which they were treated with MPP<sup>+</sup>. MPP<sup>+</sup>-induced cytotoxicity and apoptosis were confirmed by 3-(4,5-dimethyl-thiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay and terminal deoxynucleotidyl transferase-mediated biotinylated UTP nick end labeling assay. Immunofluorescent staining is conducted to confirm the PD related factors (Parkin, PINK1 and DJ-1), reactive oxidative species (ROS), and permeability in mitochondria. Also, ATP assay and western blot was performed to evaluate mitochondrial function-related factors (Parkin, PINK1 and DJ-1) and apoptosis factors (caspase-3 and cytochrome c, Bcl-2 and Bax,). Methanol extracts (0.01 mg/mL of RJ; 0.01 mg/mL of AM) suppressed MPP<sup>+</sup>-induced cytotoxicity and apoptosis. Also, RJ and AM effectively inhibited collapse of mitochondrial membrane potential and increase of ROS. In the result of western blot, RJ and AM regulated the expressions of apoptosis (caspase-3 and cytochrome c, Bcl-2 and Bax,) and PD (Parkin, PINK1 and DJ-1) related proteins. The SH-SY5Y cells treated with RJ or AM showed higher ATP activity than MPP<sup>+</sup> only treated group. Therefore, RJ and AM effectively suppressed MPP<sup>+</sup>-induced cytotoxicity, apoptosis and mitochondrial dysfunction, and loss or mutation of mitochondria-related PD markers.

### Audience Take Away:

- This study presents importance of mitochondrial dysfunction and experimental ways to confirm the effect of medicinal herb extracts *in vitro* model of PD.
- Treatment of Korean medicinal herbs including RJ and AM are expected a kind of way to alleviate PD.
- Further, a study is needed to prove the effects of RJ and AM in digestive system and brain, and correlative mechanism.

### Biography

Hee-Young Kim has completed her Ph.D from Pusan National University in Republic of Korea. At present, she is conducting postdoctoral studies in Korean Medicine Research Center for Healthy Aging of Pusan National University. She is studying the effects of Korean traditional medicines in digestive disease and Parkinson's disease.

## An experimental study on the antidepressant effect of gami-jigyultang

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Depressive disorder results in enormous social loss like treatment cost, family burden and workplace inefficiency.

Depression is explained by various mechanisms, but among them, the lack of monoamine-based neurotransmitters such as serotonin and epinephrine is considered to be important mechanism.

Several antidepressants like TCAs, SSRIs, and MAOIs have been marketed and used but they have side effects such as nausea, vomiting, insomnia, anxiety, and sexual dysfunction.

Therefore, there is a growing need to develop a new therapeutic agent with fewer side effects.

In this study, we investigated the antidepressant effect of Gami-Jigyultang, the herbal extract known to treat depression in Korean medicine.

We used C57BL/6 mice and randomly divided into several groups according to the dose of induced drug. Except for normal, depression was induced by applying restraint stress like trapped in a narrow space during 2 weeks. The stressed mice were taken Gami-Jigyultang or Antidepressants or saline in oral administration 2 hours before the stress situation. After that, they were exposed to forced swimming test(FST) and open field test(OFT) and the serum corticosterone, BDNF mRNA, protein, and serotonin mRNA levels were measured and compared.

The mice taking Gami-Jigyultang showed more active behaviors in the FST than saline or amitriptyline induced mice.

In OFT, Gami-Jigyultang-fed mice showed a significant increase in the number of movements in contrast to amitriptyline and saline.

It can be concluded that Gami-Jigyultang inhibited the release of corticosterone without significant difference in the concentration, and through this, it had an antidepressant effect and was more effective than amitriptyline.

### Audience Take Away:

- An anti-depressive effect of Gami-Jigyultang which is more effective than amitriptyline.
- A possibility of developing antidepressants using Gami-Jigyultang in the future with additional research.
- Refer to the study of other antidepressant effects using herbs.
- A preliminary data of various Korean clinical studies on depression.

### Biography

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09/2017 A Survey of the Recognition on the Practice Pattern, Diagnosis, and Treatment of Korean Medicine of Dementia and Mild Cognitive Impairment - Focusing on the Differences between Neuropsychiatrists of Korean Medicine and General Physicians – Co-1st author. J of Oriental Neuropsychiatry

03/2018 A Research to Evaluate the Safety and Efficacy of Yukwool-tang (Liuyu-tang) for Major Depression in Women: A Study Protocol for a Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Clinical Trial. Co-1st author. J of Oriental Neuropsychiatry

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## Expression profiles of microRNA and mRNA in the rat spinal cord under inflammatory pain

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**Backgrounds:** Several recent studies demonstrated that microRNAs (miRNAs) are involved in pain processing pathways by using microarray-based approaches. However, a significant proportion of the computational predictions of miRNA targets are false-positive interactions. To increase the chance of identifying biologically relevant targets, an integrated analysis of both miRNA and mRNA expression profiles were done in the rat spinal cord under complete Freund's adjuvant (CFA)-induced inflammatory pain.

**Methods:** We analyzed miRNA and mRNA in the same spinal cord with microarrays on Days 5 and 14 after CFA injection. The rats were randomly assigned to different groups. CFA 5d group, Day 5 after CFA injection; CFA 14d group, Day 14 after CFA injection; Control group, without CFA injection. After behavioral tests, the ipsilateral lumbar (L4-L5) spinal cords were quickly dissected for microarray analysis of miRNA and mRNA (n = 3 each group).

**Results:** Five miRNAs and 1096 mRNAs in the CFA 5d group and 16 miRNAs and 647 mRNAs in the CFA 14d group were differentially expressed filtered with at least a 1.5-fold change in either direction. The integrated analysis revealed 54 mRNA targets with an inverse correlation to the expression patterns of 3 miRNAs in the CFA 5d group. Seventy-five targets were inversely correlated to 6 miRNAs in the CFA 14d group. The miRNA-mRNA interaction networks revealed significant changes of miR-124, miR-149, miR-3584 and their target gene of IL6R, ADAM19, LAMC1 and CERS2 in the CFA 5d group. In the CFA 14d group, significant changes of miR-124, miR-29, miR-34, miR-30, miR-338 and their target gene of TIMP2, CREB5 and EFNB1 were noted. Interaction analysis between miR-124 and IL6R showed miR-124-3p could attenuate inflammatory pain and decrease IL6R expression in the spinal cord.

**Conclusions:** These specific miRNAs and their target genes provide novel biomarkers for the diagnosis and treatment of inflammatory pain.

### Biography

Ping-Heng Tan received the M.D. degree from National Defense Medical Center, Taipei in 1989, and the Ph.D. degree from the National Sun Yat-Sen University, Kaohsiung, Taiwan in 2004, respectively. In 2006, he was a Research Fellow at the Pain Research Center, Brigham & Women Hospital, Harvard University. Dr. Tan was the chief of Department of Anesthesiology in E-Da Hospital/I-Shou University, Kaohsiung, Taiwan from 2009 to 2017. Dr. Tan is a P.I. of Pain Research Lab and a Professor and Chief of Department of General Anesthesia in Chi Mei Medical Center, Tainan, Taiwan now. He is interested in research in pain medicine mainly in the role of microRNA in pain medicine.

## Utility of ultrasonography in assessing dysphagia in patients with Parkinson's disease

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**Objective:** Dysphagia is a common bulbar dysfunction in Parkinson's disease. Recently efforts have been made to evaluate dysphagia using ultrasonography. Laryngeal elevation could be measured by identification of the hyoid bone and the thyroid cartilage. The aim of this study was to compare the shortest hyoid-thyroid distance, tongue thickness, and the time interval between the initiation of tongue movement and the shortest hyoid-thyroid approximation using ultrasonography in elderly Parkinson's disease patients.

**Methods:** Healthy controls and Parkinson's disease patients with dysphagia were compared. Ultrasonography was performed 3 times for evaluating tongue thickness, the shortest hyoid-thyroid approximation, and the time between the initiation of tongue movement and the shortest hyoid-thyroid approximation. This study was also tried to evaluate these parameters of elderly Parkinson's disease patients based on H-Y grade.

**Results:** A total of 10 healthy controls and 13 Parkinson's disease patients with dysphagia were enrolled. No significant differences were demonstrated between the 2 groups for the shortest hyoid-thyroid approximation (controls,  $1.29 \pm 0.37$  cm; Parkinson's disease patients,  $1.55 \pm 0.39$  cm,  $p=0.11$ ), tongue thickness (controls,  $4.48 \pm 0.49$  cm; Parkinson's disease patients,  $4.37 \pm 0.59$  cm,  $p=0.64$ ), and the time to the shortest hyoid-thyroid approximation (controls,  $1.78 \pm 1.29$  ms; Parkinson's disease patients,  $2.88 \pm 1.72$  ms,  $p=0.11$ ). However, the time to the shortest hyoid-thyroid approximation was significantly prolonged in patients above H-Y grade 3 ( $1.45 \pm 0.32$  ;  $3.96 \pm 1.70$  ms,  $p=0.004$ )

**Conclusion:** Ultrasonography can be useful method for evaluating dysphagia in patients with Parkinson's disease by direct visualization and measurement of the hyoid bone. Moreover, ultrasonography might contribute to understanding the pathophysiology of dysphagia in Parkinson's disease.

### Audience Take Away:

- Dysphagia is a common bulbar dysfunction in Parkinson's disease.
- Ultrasonography can be useful method for evaluating dysphagia in patients with Parkinson's disease.
- Ultrasonography might contribute to understanding the pathophysiology of dysphagia in Parkinson's disease.

### Biography

2007 - Licensed to Practice Medicine in Korea  
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## Age-related Dysphagia in the Elderly Population

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**Objective:** Dysphagia is an important issue in an aging society. Stroke is the most common cause, but dysphagia can occur without a stroke or underlying disease. Aging itself can cause or aggravate dysphagia and there have been many studies that describe the effect of aging on swallowing physiology. We are already living in an aging society and furthermore population of oldest old, defined as age of 80 or older, is rapidly growing. Among the elderly population, there is a need to examine how the dysphagia in oldest old people differs from others.

**Methods:** From January 1, 2017 to December 31, 2017, patients with aged 60 years or older who underwent VFSS due to dysphagia were included. The WHO and the UN defined the older/elderly criteria as 60 to 79 years old and the oldest old as 80 or older patients. Based on this, a total of 206 patients were divided into two groups. : Group I (60~79 years old, n=135), group II (80~96 years old, n=71). General characteristics were compared between the groups. Among the objective indicators that can be evaluated through VFSS, widely used penetration aspiration scale (PAS) and videofluoroscopic dysphagia scale (VDS) scores were evaluated and compared between the groups. VDS evaluates oral phase and pharyngeal phase separately and each score was added to obtain a total score. The etiologies of dysphagia were classified into two categories: neurologic disorders and non-neurologic disorders. Neurologic disorders included CNS disorders (stroke, brain tumor, neurodegenerative disease, traumatic brain injury, other brain disorders, spinal cord injury) and PNS disorders (NMJ disorders, myopathy and peripheral neuropathy). Non-neurologic disorders included local structural lesions involving the head and neck, poor general medical condition, and unknown etiology.

**Result:** The male ratio was significantly higher in both groups; the ratio was statistically significantly lower in Group II than Group I. MMSE was significantly lower in group II than in group I. The duration of dysphagia was shorter in group II. (Table 1)

Table 1. General characteristics

Characteristics	Group I (n=135)	Group I (n=71)	p-value
Sex	Male 124 (919%)	Male 56 (78.9%)	0.008*
Age (years)	71.53±3.76	86.13±3.50	0.000*
MMSE	17.85±9.89	12.61±9.08	0.000*
Durarian of dysphagia (months)	17.78±20.04	11.96±17.73	0.047*

Values are presented as mean±standard deviation, MMSE, Mini-Mental State Examination, \*p<0.05

PAS was statistically significantly higher, meaning more severe dysphagia, in group II than in group I (p value = 0.004). Oral VDS score, pharyngeal VDS score, and total VDS score also showed higher value, meaning more severe dysphagia, in group II. (Table 2)

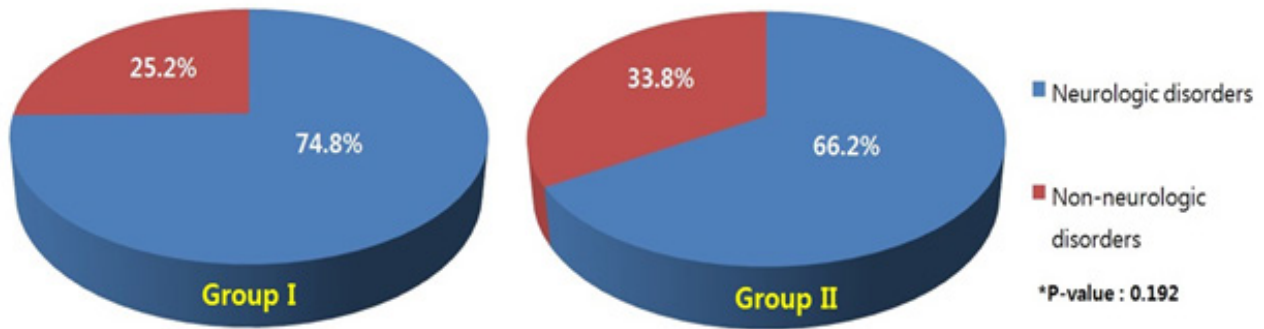
Table 2. VFSS findings

Scale	Group I (n=135)	Group I (n=71)	p-value
PAS	4.26±2.88	5.60±2.71	0.004*
Oral VDS score	6.37±6.56	8.77±7.22	0.009*
Pharyngel VDS score	23.23±14.19	30.59±14.54	0.001*
Total VDS score	29.60±18.12	39.36±18.62	0.001*

Values are presented as mean±standard deviation, PAS, penetration aspiration scale VDS, videofluoroscopic , dysphagia scale, \*p<0.05

In an etiology, the ratio of non-neurologic disorders was higher in group II than group I, but there was no statistical significance (p value=0.192).(Fig 1)

Fig 1. Etiology of Dysphagia



**Audience Take Away:**

- Dysphagia of elderly population should be monitored closely.
- Among the elderly population, dysphagia in the oldest old population has a tendency to be more severe with shorter duration of onset compared to the elderly population.
- If oldest old patients present with swallowing difficulty, immediate evaluation and therapeutic intervention should be carried out regardless of the etiology.

**Biography**

2007 - Licensed to Practice Medicine in Korea  
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## Normal MRI in patients with acute stroke is the best predictor of 90-day outcome

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**T**he aim of our study was to evaluate the usefulness of MRI in patients presenting with a suspected diagnosis of acute stroke. We admitted 4400 patients with the diagnosis of acute stroke between Jan 2014 and June 2017 at Hamad Medical Corporation. A total of 2880 patients underwent 3T MRI within 48 hours of admission. Patients were assessed for demographics, risk factors, clinical features, severity of stroke and outcome. We found that Ischemic stroke was diagnosed in 65.4% (1885/2880) including lacunar strokes 44.1% (831), cortical strokes 26.6% (502), and posterior circulation stroke 29.3% (552). Normal MRI was found in 5.4% (n=101) in patients with confirmed ischemic stroke. Normal MRI was more frequent in lacunar strokes compared to posterior circulation or cortical strokes (62.4%, 24.8% and 12.9%,  $p < 0.0001$ ). Abnormal MRI was significantly higher patients with diabetes (55.5% vs 43.6%,  $p = 0.019$ ), dyslipidemia (54.9% vs 43.6%,  $p = 0.026$ ), higher systolic blood pressure at arrival (157.8 vs 151.7 mmHg,  $p = 0.047$ ), higher admitting NIHSS (5.21 vs 3.43,  $p < 0.0001$ ), higher HbA1c on (7.5% vs 6.9%,  $p = 0.021$ ) and higher serum cholesterol (5.06 vs 4.62,  $p = 0.002$ ). Patients with normal MRI were found to have better 90-day prognosis (mRS 0-2) as compared to patients with abnormal MRI on admission (68.3% vs 53.0%,  $p = 0.003$ ). After excluding mimics and TIAs, 5.4 % of patients with acute ischemic stroke have normal MRI. These patients have lower NIHSS, are more likely to have lacunar stroke and have a significantly better prognosis.

### Audience Take Away:

- Normal MRI should be expected more frequently in lacunar strokes compared to posterior circulation or cortical strokes.
- Abnormalities in MRI and ischemic injury is more evident in patients with diabetes, dyslipidemia, hypertension and higher NIHSS at admission.
- Patients with normal MRI after acute ischemic stroke have a possibility of better prognosis as compared to abnormal imaging after stroke.

### Biography

Dr. Pooja George is a lead clinical researcher in the Department of Neuroscience at Hamad Medical Corporation. She completed her undergraduate medical training at Government College of Cochin, India. Her recent endeavors are finalizing an international project on Multiple Sclerosis in collaboration with Weil Cornell Medical College. She has led major research projects in the department of neuroscience that include Multiple Sclerosis, Stroke, Corneal confocal microscopy and Wall motion abnormalities with stroke. Her research interest primarily focuses on imaging in stroke patients and Wall Motion Abnormality.

## Epidemiological profile of patients with spinal muscular atrophy in a tertiary hospital of the south of Brazil

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**Introduction:** Spinal muscular atrophies (SMA), prevalence of 1.5:100.000, recessive inheritance, neuromuscular diseases with anterior medullary horn degeneration, are caused by mutations in the survival of motor neuron protein, represented by SMN1 and SMN2 genes, supporting the motor neurons in the medulla and brainstem. They're classified according to symptomatic onset age and maximum motor function acquired. Actually, the only approved pharmacological treatment is intrathecal nusinersena.

**Method:** The research objective – observational, transversal and retrospective – objective is to trace the epidemiological profile of the patients, correlating to risk and protective factors for morbimortality and patients using nusinersena. The selected children have a clinical and genetic diagnosis (n = 36), the data collected refer to the period from January 2010 to December 2018, 2 children who died during the period and 1 without genetic confirmation were excluded. The statistical strategy used was through Excel and SPSS v.22.O program, using chi-square test with values of p <0.05. The variables collected were onset age, identification, family history, health plan type, school life, diagnosis, urgent and elective hospitalizations, surgeries and other information of clinical follow-up.

**Results:** The mean age is 7.5 years (range 1-21.9), 48.5% female and 51.5% male. SMA type 1, 2 and 3 presented 21.2%, 66.7% and 12.2%, respectively, and there were not patients with type 0 and IV. The diagnosis occurred in the first life year in 45%, 42.4% between the 1-4 and 12.1% from 4-15y. Family history was present at 21.2%. The initial symptoms were hypotonia (33.3%), muscle weakness (42.4%) and delayed neuropsychomotor development (51.5%), the latter reported by parents (54.5%), muscle weakness (88%), frequent hospitalizations (18%), orthoses (18%), gastrointestinal symptoms (9%), pain (18%) and difficulty gaining weight (18%). The need of hospital admission is 80% and 45.5% needed ICU. 15% remained more than 30 days (30% with more than 30 days of ICU). The most prevalent emergencies are pulmonary infections (66.7%), respiratory insufficiency (27.3%), extrapulmonary infections (24.2%) and feeding difficulties (48.5%). Elective hospitalizations for surgeries (51.5%): gastrostomy (24.2%), tracheostomy (15.2%) and orthopedic surgeries (20%). The feeding is oral (66.7%), gastrostomy (30%), nasoenteric (3%), and only 60.6% with adequate weight. Only 21% under treatment, 3 patients took 6m-1y to start treatment and 2 patients waited more than 1y. The reasons of small plot with nusinersena are very advanced disease (6%), study with oral drug (3%), judicial waiting for approval (57.6%) and 12.1% had previous surgery for spinal arthrodesis. A neurologist and a physiotherapist (100%), orthopedist (54%), pulmonologist (27%), occupational therapist (24%), nutritionist (15%), gastroenterologist 12%) and pediatric surgeon (9%) were the professionals of multidisciplinary team. Patients enrolled in education were 57.5%, the majority (45.5%) being in a special school.

**Discussion:** In our study, the most prevalent SMA was type II. They have 2 SMN2 copies (63.5%), 3 (33.3%) or 4 (3%) related to the prognosis. Those with 2 copies have hypotonia as the first symptom (63%), hospitalizations (37%), pneumonia (54%), respiratory failure (45.5%), respirator use (72%), tracheostomy (45.5%), gastrostomy (64%) and GMFSC V (54.5%).

**Conclusion:** These data confirm, as a disease of high morbimortality, the ensurance of performing adequate genetic tests and have the copies of the SMN 2 counted for prognostic purposes.

### Audience Take Away:

- Our research aims to demonstrate the richness of details of an epidemiological profile of spinal muscular atrophy of the biggest pediatric hospital in Latin America - Hospital Pequeno Príncipe - in addition to demonstrating the scarce Brazilian reality of multicentric research, our work being an attempt to really consider the SMA patient as respected and duly assisted in the public health service. The current research considers several aspects in its design as relations of genetic exams with urgent and elective hospitalizations, interurrences and complications, schooling, parents' opinion regarding the establishment of the disease, data regarding patients with or without pharmacological treatment, reasons for not receiving the nusinersena beyond the types of rehabilitation used by patients and access to them.

- Regarding this, there is much to learn from the profile of the patient with SMA, the reality of Brazilian research in neuropediatrics, the possibility of expanding the work to a multicenter level. This profile is a great possibility to invest resources in rehabilitation, research, management of the disease, parental guidance and access to treatment with Nursinersena, a drug approved only a few months ago for all SUS patients.
- Finally, our research aims to raise epidemiological data in the attempt of a representative regional and future national sample, to raise awareness of more and more professionals about the disease and consequently to have more parents oriented about the pathology of their children. Thus, professionals and specialists from various areas can establish a multi and interdisciplinary guideline for the adequate management of the patient with SMA.

### **Biography**

Dra. Fernanda Bonilla Colomé is a Brazilian doctor living in Curitiba in the south of Brazil. Certified in Medicine in Porto Alegre by Brazilian Lutheran University. She is certified as a Pediatrician from Mackenzie Evangelical University Hospital and in Neuropediatrics from Little Prince Hospital, both localized in the city of Curitiba. During the two years of the residency program in Neuropediatrics she studied with Dr. Adriana Banzatto Ortega about Neuromuscular diseases, especially Spinal Muscular Atrophy. She is currently taking Masters Degree in Health Sciences Teaching and teaching residents and graduation students in Mackenzie Evangelical University. She is currently attending her office at the Neurokids clinic and at the Pediatric Specialties Center in the cities of Colombo and Curitiba respectively.

## **Focal dystonia - A presenting feature of an acute stroke – A clinician's challenge**

**Moncy Thomas MD\*, Bartlomiej Piechowski Jozwiak MD, Seby John MD**  
Cleveland Clinic Abu Dhabi, UAE

### **Aim:**

This case illustrates exact clinico-radiological match with hyperacute left sided cephalo-brachial dystonia and right sided putaminal infarct. AMD symptoms resolved after thrombolysis and patient's outcome was positive.

### **Discussion:**

Though not uncommon it takes a combination thorough clinical examination and detailed history taking along with imaging to detect this unusual presentation and act immediately for better outcome of the patient.

- Movement disorders occur uncommonly in association with stroke in adults and tend to resolve over time.
- The lesions can be due to middle or posterior cerebral artery territories.
- After hemiballism-hemichorea, dystonia is the second most common movement disorder after stroke
- Post-stroke dystonia has been attributed to lesions of the putamen (the most common site of isolated lesions causing dystonia) > caudate > pallidum > thalamus > midbrain.

### **Audience Take Away:**

- Stroke and dystonia are sudden onset problems faced by patients
- A clinician as we say in old school is inclined towards history and examination and not fully dependent on imaging
- With this case we wish to enforce the need for not forgetting the old school teachings and how the case shows the exact clinico-radiological match with hyperacute left sided cephalo-brachial dystonia and right sided putaminal infarct

### **Biography**

Moncy Thomas, MD, DM, is an Associate Staff Physician in the Neurological Institute of Cleveland Clinic Abu Dhabi. Dr. Thomas associates with the first fully integrated Neurological Institute in the Middle East which provides treatment for a broad spectrum of neurological disorders. Prior to joining Cleveland Clinic Abu Dhabi, Dr. Thomas served as Head of the Division of Neurology at St James Hospital in India, where the division focused on Stroke, Epilepsy, Movement Disorders, Headaches, Peripheral Neuropathies, Dementia, Multiple Sclerosis, Spine Sleep, Neuromuscular, and Neuro Rehabilitation. During this period, he established the stroke unit and headed the thrombolytic therapy team. He initiated therapy with newer thrombolytic therapy with Tenecteplase in his stroke unit with successful outcomes. A native of India, Dr. Moncy received a Master's Degree in General Medicine, and a Doctorate in Medicine in Neurology from the Bharath University of India. He has significant experience in the field of Neurology Neurophysiology and Neuropsychiatry. Dr. Moncy's primary field of expertise is in neurology, with special interest in Strokes, Movement Disorders, Headaches, Peripheral Neuropathies, Epilepsies and Dementia.



## The approach of non-traumatic congenital unilateral facial paralysis through two cases reports and literature review

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**Introduction:** The incidence of facial paralysis in children is 0,2%, trauma and infection includes the majority, and it can be diagnosed as a part of a syndrome or sole. However, non-traumatic congenital facial paralysis (NCFP) is quite rare. Developmental abnormality due to interruption of blood supply occurring during nerve embryogenesis results in peripheral facial paralysis. First presentation of this comprises Moebius Syndrome (MS) which includes other malformations. Two conditions that might enter in discussion are hereditary congenital facial paresis (HCFP) and unilateral facial nerve agenesis (UFNA).

**Method:** The objective is to give a peer review about congenital facial paralysis and report 2 cases, approaching the possible differential diagnosis.

### Results:

**Case1:** A female 4-month-old infant referred to the neuropediatrician after the mother's perception that the child has asynchrony in blinking the eyes, with deficiency of this movement in the right eye. The child, without previous hospitalizations, nor previous complaints of health, was born of caesarean delivery, term and normal follow-up in the developmental milestone without interurrences. There isn't family history of consanguinity or neurological diseases. She has adequate tone and strength. In MRI, the seventh right cranial nerve was not found in the intra-meatal tract, but branches of the right and left vestibular and cochlear nerves (thickness and preserved signs) were found. On the left side we also observed the seventh cranial nerve with caliber and present and normal signs. The initial approach adopted included follow-up with ophthalmologist and physiotherapist.

**Case 2:** A female, 3 years, natural term delivery, with left facial paralysis and jaundice. She was transferred to neonatal ICU. She was diagnosed with MS with an adequate neuropsychomotor development. In February 2017, she underwent surgery to correct strabismus. She is being followed up by an otolaryngologist for a nasal obstruction. Nowadays, she has dysphagia, choking with water sometimes. On physical exam, she has right peripheral facial paralysis, bilateral patellofemoral hyperreflexia nor other alterations. She has a normal echocardiogram, CT with paranasal sinus veins; on MRI, there's hypodensity area in sickle and tent. The ophthalmologic evaluation suggests Moebius Syndrome, even being unilateral facial paralysis, due to having fixed bilateral convergent strabismus and laryngomalacia with indication of supraglottoplasty and bilateral tympanotomy. The actual MRI and otologic evaluation are normal.

**Discussion:** Both cases are unilateral congenital facial palsy, the first has an isolated NCFP, which moves away from incomplete MS or other causes of complex NCFP, and clinical suspicions go further between HCFP and UFNA. However, her MRI confirms facial nerve agenesis, tapering to congenital right facial nerve agenesis. The second case has unilateral facial palsy, otolaryngological abnormalities, strabismus and dysphagia, which takes us to the diagnosis of incomplete MS.

**Conclusion:** The neuropathology of the three conditions most approached on our research are quite different between themselves, and clinically the diagnosis of incomplete MS is confused given to cases of HCNP or UFNA. Therefore, all of the causes above (isolated or complex) might have be considered in the painel of differential diagnosis.

### Audience Take Away:

- The initial optimal assessment of the neonate born with unilateral facial paralysis should be performed as soon after birth as possible by a multidisciplinary team with the goal being to distinguish between a traumatic or developmental etiology.
- Our research with those two cases exemplify really rare conditions and non-widespread in neuropediatrics science, which leads to a huge learning on science community. The cases in question report a non-routine condition of the pediatricians and neurologists practice and a very rare and contradicional situation. Therefore, it is really relevant for the identification of children. Whom enter in the difficult differential diagnosis of congenital facial paralysis.

## **Biography**

Dra. Fernanda Bonilla Colomé is a Brazilian doctor living in Curitiba. In the south of Brazil. Certified in Medicine in Porto Alegre by Brazilian Lutheran University. She is certified as a Pediatrician from Mackenzie Evangelical University Hospital and in Neuropediatrics from Little Prince Hospital, both localized in the city of Curitiba. During the two years of the residency program in Neuropediatrics, she studied with Dr. Adriana Banzatto Ortega about Neuromuscular diseases, especially Spinal Muscular Atrophy. She is currently taking Masters Degree in Health Sciences Teaching and teaching residents and graduation students in Mackenzie Evangelical University. She is currently attending her office at the Neurokids clinic and at the Pediatric Specialties Center in the cities of Colombo and Curitiba respectively.

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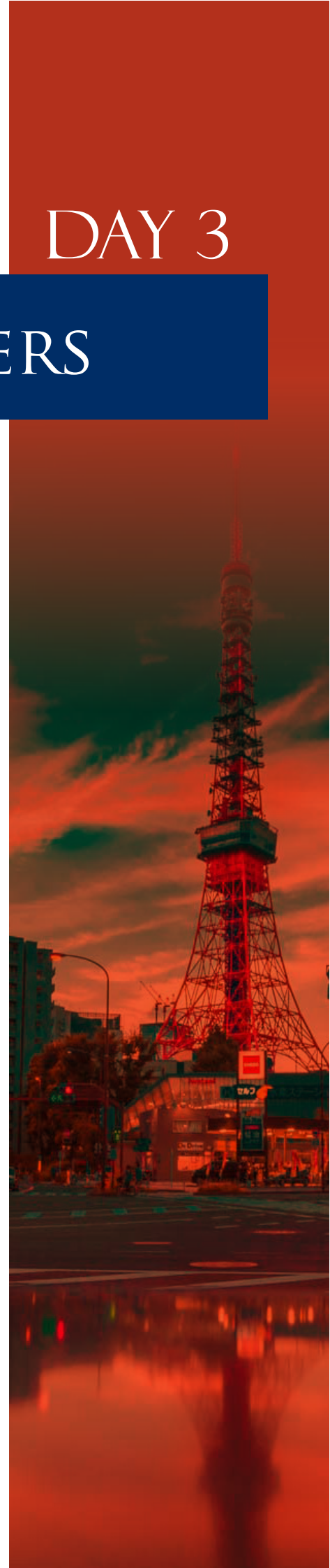
NEUROLOGY AND  
BRAIN DISORDERS

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## Obstructive sleep apnea in various cognitive disorders

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Various research studies suggested an association between Obstructive Sleep Apnea (OSA) and various cognitive disorders, including Alzheimer disease. The degree of OSA has been directly correlated with the severity of cognitive impairment. Stroke and vascular diseases are significant comorbidities in these patients. We report the occurrence of OSA in patients with various cognitive disorders on the Island of Guam and correlate the severity of OSA with the results of the neuropsychological testing and neuroimaging studies.

**Methodology:** A retrospective review of medical records of patients evaluated in The Neurology Clinic with the diagnosis of OSA in patients with various cognitive impairments from July 2016 to July 2018 was conducted. These include patients with Alzheimer disease, vascular dementia, unspecified dementia, and Mild Cognitive Impairment.

**Results:** There were 375 patients with various cognitive impairments and 16% have been diagnosed with OSA. Among patients with OSA, 46% have severe OSA, 38% have moderate OSA, and 16% have mild OSA. Severe impairment on Global Cognitive Scores (GCS) was seen in 60% of patients with severe OSA, 44% of moderate OSA, and 20% of mild OSA. Moderate GCS were seen in 29% of patients with severe OSA, 39% of patients with moderate OSA and 30% of patients with mild OSA. Evidences of silent stroke were seen in 25% of patients and another 31% have leukoaraiosis on their neuroimaging studies. The occurrences of vascular diseases including hypertension, diabetes mellitus, hyperlipidemia and cardiac disorders were higher in those with severe and moderate OSA compared to those with mild OSA and without OSA.

**Conclusions:** Obstructive Sleep Apnea is a common comorbidity of patients with various forms of cognitive impairment. The severity of OSA correlates with the degree of impairment on neuropsychiatric testing. Neuroimaging studies demonstrated evidences of Silent stroke and leukoaraiosis among these patients.

### Audience Take Away:

- The audience will heighten their understanding and awareness on the significance of diagnosing and treating OSA in patients with dementia. They will learn that the severity of OSA correlates with the degree of cognitive impairment. The audience will realize that various vascular diseases, silent strokes and leukoaraiosis are common in patients with OSA. The results of this research will also facilitate further studies to be conducted in order to determine if the treatment of OSA and vascular diseases, may prevent progression of cognitive impairment in dementia.

### Biography

Dr. Ramel A. Carlos is a board certified neurologist working on the Island of Guam for the past 16 years. He is currently working at The Neurology Clinic in Tamuning, Guam. He completed his residency and fellowship training in Wake Forest University, Winston-Salem, North Carolina, USA. He has presented his clinical research in various neurology conferences including the Asean Neuroscience Conference in Singapore, World Congress of Neurology in London, U.K, Int. Conf. on Vascular dementia in Amsterdam, Int. Conf. of Alzheimer disease in Kyoto, Japan, and recently during the Advances in AD and PD Therapies in Torino, Italy.

## Neuropsychiatric disorders and stroke in cancer pain patients

Jinfeng Yang, MD, PhD<sup>\*1</sup>, Ge Huang, MD<sup>2</sup>, Jiali Shao, MD, PhD<sup>3</sup>, Chen Su, MD, PhD<sup>4</sup>

<sup>1,2,3,4</sup>Hunan Cancer Hospital/ the Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, Hunan, China.

**T**here are all kinds of physical and psychosocial symptoms in advanced patients diagnosed with cancer, some patients suffered a sudden stroke. The management of patients is very difficult for physicians, nurses and family of the patient. The following is what the presentation includes:

- (1) All the factors will be discussed, which include older age, progressive cancer disease, malnutrition resulted in cachexia, autonomic failure, cognitive disorders, side effects from drugs such as opioids, tricyclic anti-depressants, chemotherapeutics, water electrolytes and acid base disturbances including hypokalemia, hyponatremia, dehydration and multiple organ failure, etc.
- (2) The tools, measurements and mechanism will be analyzed.
- (3) Therapeutic and prevention will be discussed.
- (4) A few cases experience will be shared.

### Audience Take Away:

- (1) Understand all the neuropsychiatric symptoms and syndromes from advanced patients diagnosed with cancer;
- (2) Work out the measurements and mechanism of neuropsychiatric disorders;
- (3) Promotion of intervention studies utilizing pharmacologic and nonpharmacologic treatments for depressive disorders and cognitive disorders in advanced cancer patients;
- (4) Encouragement expansion of the focus of such research to other neuropsychiatric disorders.

### Biography

Jinfeng Yang MD, PhD is Chairman of Anesthesiology Department of Hunan Cancer Hospital/the Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University (Division of Anesthesiology Department, Pain Ward, OR and PACU). Chairman, Anesthesia and Analgesia for Cancer Patients Association of Hunan Province, China. Chairman, Perioperative Management Committee of Hunan Province, China. Vice-chairman, Society of Anesthesiology of Hunan Province, China. Vice-chairman, Pain Association of Hunan Province, China.

## Epilepsy in the MENA (Middle East and North Africa) region

**Boulouar Mesraoua<sup>1,2\*</sup>, Musab Ali<sup>1</sup>, Lubna Elsheikh<sup>1</sup>, Dirk Deleu<sup>1,2</sup>, Hassan Jasim Al Hail<sup>1,2</sup>, Gayane Melikyan<sup>1,2</sup>, Semmar Nada<sup>3</sup>, Zouheir Souirti<sup>3</sup>, Reda Ouazzani<sup>4</sup>, Najib Kissani<sup>3</sup>**

<sup>1</sup>Hamad Hospital, Qatar,

<sup>2</sup>Weill Cornell Medical College-Qatar,

<sup>3</sup>University Hospital Mohamed VI, Marrakech, Morocco and

<sup>4</sup>University hospital of Specialities, Rabat, Morocco

**Background:** MENA (Middle East and North Africa) region extends from Morocco to Iran; in MENA, studies on epilepsy are lacking ; only 2 surveys examined epidemiology and neurology training programs in this vast geographic area.

**Objective :** 1) Describe the available data on Epilepsy in the Mena 2) compare those findings to similar data from neighboring ,and advanced countries and 3) give recommendations on future research on epilepsy in MENA

**Materials and Methods:** This study was made possible through a 1) literature search to identify articles published from 1980 to December 2017 on epidemiology, Causes ,treatment modalities of epilepsy , as well as epilepsy research in Mena and 2) Additionnel data from surveys ,emails and phone interviews of leading neurologists/epileptologists in the Area.

**Results:** More than 2 millions people with epilepsy(PWE)live in MENA ,with a population estimated at 355 millions; number of neurologists varies from 0.05/100.000 to 2,3/100.000 ;Most of neurologists based in large cities ;significant shortages of trained healthcare physicians, especially at primary care level(lack of knowledge about epilepsy );Nine countries out of 20 have prevalence data on Epilepsy (from 0.9/1000 in Sudan to 11/1000 in Morocco) ; epilepsy incidence is reported only from 3 countries. Five countries out of 20 have data on the causes of epilepsy: high proportion of epilepsies of genetic origin (high consanguinity 30 to 54%); Neurocysticercosis in eastern part of the MENA and Onchocerciasis in Sudan (Nodding Syndrome) are also important causes of Epilepsy .Use of AEDs are reported from 5 countries. Surgical treatment of Epilepsy is uncommon in MENA;6 countries provide data on traditional practice in Epilepsy .Finally there is only one recent Indexed Epilepsy Journal generated in MENA (Nameej , North African and Middle East Epilepsy journal ,from Morocco)

**Conclusion:** There is still an insufficient number of neurologists in the MENA, and an urgent need for further epilepsy research ,particularly epidemiological research ,in order to have an accurate idea about the burden of epilepsy in this vast Region

### Biography

Dr Boulouar Mesraoua is Consultant Neurologist at Hamad General Hospital and Associate Pr of Clinical Neurology at Weill Cornell Medical College –Qatar; After a Medical Graduation from the University of Oran in Algeria, Dr Mesraoua moved to Belgium, the City of Liege, for a Residency in Internal Medicine and Neurology; after getting the Belgian Board of Neurology (with high marks), he went to the National Hospital for Nervous Diseases, Queen Square, London, UK, for a fellowship in Clinical Neurophysiology, under Pr Willison ; Dr Mesraoua had also further training in Epilepsy and Continuous EEG Monitoring for two years in the Neurophysiology department of Zurich ,Switzerland ,under Pr HG Wieser ,an internationally known clinical epileptologist .

Dr Mesraoua is actually Director of the Neurology Fellowship Program and Director of the Comprehensive Epilepsy Program at Hamad General Hospital, Doha, Qatar.He is also Assistant Director of the Residency Program at Qatar Medical School.

His main interests are Epilepsy ,clinical neurophysiology ,Clinical Neurology AND Multiple Sclerosis ; He is the Chairman and the Organizer of the well known Qatar Epilepsy Symposium, he is running yearly for the past 12 years and which is considered a landmark in the region; He has also started THIS year (November 2018), together with other epileptologists from the region and elsewhere, a yearly EEG Course, Internationally, Dr Mesraoua is an active and elected member of the Commission on Eastern Mediterranean affairs (CEMA ), a branch of the International League Against Epilepsy (ILAE) ,where he represents the Middle East and North Africa(MENA ) and where he hold the position of chief of the epilepsy epidemiology section; Dr Mesraoua is a member of the American Academy of Neurology (AAN), the European Academy of Neurology (EAN) and the American Epilepsy Society (AES).

Dr Mesraoua main objectives are to encourage frequent gathering of the epileptologists/neurologists from the MENA region, promote Epilepsy Teaching in the MENA Region, and encourage multicenter studies involving neurologists and epileptologists in the MENA region, particularly epilepsy epidemiological studies.

Dr Mesraoua is the recipient of two research Grants, as the Lead Principal Investigator, (750.000 USD and 250.000 USD) from the Qatar National Research Fund (QNRF) and the Hamad Hospital Internal Research Grant (IRGC) on “Continuous EEG Monitoring in the ICU “and on “Alpha-lacto-albumin , proof of concept in the treatment of epilepsy”.

Dr Mesraoua is the author and co-author of many peer reviewed publications and two book chapters in the field of Epilepsy and Clinical Neurology.



## **Lithium to prevent dementia: A review and call to action**

**Neil Jeyasingam**

Sydney University, Australia

**L**ithium is an agent with established neuroprotective qualities, considerable epidemiological evidence supporting its use as a dementia prophylactic, and was strongly debated to be part of the UK's national dementia strategy. Yet it has failed to enter regular clinical use for this purpose – not for lack of evidence, but rather arguably for saturation of poor quality evidence and aborted peripheral clinical trials. This presentation presents a review of the story of lithium's almost rise to fame, and argues for a fresh approach.

### **Biography**

Dr Neil Jeyasingam is a psychogeriatrician and former Maudsley Research Scholar. He holds dual masters in health administration and psychiatry, and has a special interest in electroconvulsive therapy. A senior clinical lecturer with Sydney University, He has 42 published papers. His areas of interest are phenomenology, philosophy, psychotherapy, personality disorders.

## Infant – Parent interactions of reflexive and voluntary gaze and sensory responsiveness

**Bengt Sivberg, PhD**

Professor, Faculty of Medicine, Lund University, Sweden, and Professor at Sebastian Kolowa Memorial University, Lushoto, Tanga Province, Tanzania

Screening studies of an infant population (n = 4329; 9 months of age) in primary health care with the aim to describe observed atypical behaviors that might be associated with autism spectrum disorders are sparsely reported. An observational tool, named SEEK developed for child health care, was adopted focusing on social interaction, communication, motor skills, and an interview with parents. Infants scoring highly positive on the SEEK were observed a second time by psychologists and judged to have a delayed reaction to stimuli and preverbal language development, deficits in communication skills, the latter more often among boys than girls. Twenty-three infants (AT) of those with most positive atypical performance were compared with 22 typically developing infants (TD) having no positive scores on the SEEK during spontaneous play with mother and father to challenge different play styles. 135 videos, each of five minutes, were used in the comparison and analyzed with the Observer 11.5, Noldus Information Technology. Inter-reliability of the scoring of behaviors was good. Frequency and duration of infants' orientation towards the parents' eye zone was significantly higher among TD than AT, indicating a stronger social gaze behavior. Findings may indicate an equal competence at reacting to reflexive stimuli but a significant difference on voluntarily responses to parents' social invitation. The brains intentional network is highly involved in the competency of sensory responses. Already in the 1950-ties, research proposed that the general alertness (tonic - general wakefulness and arousal) did not differ between individuals with autism or not. However, those studies did not differ between tonic and phasic alertness, the latter refers to changes in response readiness to a target or activity. Filthy years later research has proposed that children with autism possess a normal ability to sustain attention and that this is not the primary impairment but may be due to developmental delay or motivational reasons. Our results support earlier research reporting of an equal competence to respond on non-social (reflexive) stimuli at this very young age. Maybe the situation would be very much the different at the ages of three or four due to developmental reasons and the delayed learning process. On the contrary, our results support a genuine difference in the early competency to respond on social stimuli during play with parent, especially the voluntarily gaze (orientation and executive competencies) interaction with the parent. The infants' sensory responsiveness during the play were analyzed for frequency and duration measured in seconds. Responsiveness as reaching for toys (objects), grabbing and holding toys, dropping toys, facial expressions as response of stimuli, oral sounds, imitative responses, and playtime with a toy were analyzed as well as body posture. The presentation will discuss differences between the two groups of infants, and present hypo-and hyper-responsiveness as well as sensory seeking behaviors in relation to possible neurological structures. At this very early age hypo responsiveness and sensory seeking behaviors seems to be dominant in the AT group in comparison with the TD group.

### Audience Take Away:

- The main clinical implications of this research is the importance of observing the voluntarily gaze interactions between infant and parent at visits at child health care centers or home visits during the 18 first months. The gaze needs to be observed also concerning the duration of gaze contact since the infant is learning and generalizing competencies at best in the end of the duration. Also, the different deviations of sensory responsiveness help health care professionals and parents to be alert to notice very early precursors of that a young child/infant is in need of supportive intervention with the aim to speed up their development. One example of this can be a very neutral face expression over long time despite amusing activities are going on in the room.
- Many studies have used experimental designs as for example the eye tracking technique. This is very efficient for many purposes but not useful in the study of spontaneous behaviors without restrictions. Social interaction is a very complicated activity, which needs to be taken into account of its full richness in observation of interactions. Further observational studies of natural play activities need to be performed with even more sophisticated observational tools. The use of the Observer tool for analysis was very helpful, but in the development of the observational schedule it is very important to have a simple and efficient structure for the observation and additionally to develop a manual for the scoring of behaviors or what the study concern. For the future, it would be ideal to develop more flexible research tool with use of high computer technology with are able to take into account the observation of the complex human interactional world. That would advance rigorousness in science and save time and efforts of the researchers.

## **Biography**

Dr. Bengt Sivberg is directed on autism spectrum disorders or conditions since several decades. My research interest is focused on finding early precursors of atypical development associated to later diagnosis of ASD. During the period, I have been active in research I have seen a change to a more positive view of the possibility to find signs of early atypical development associated with ASD, not only in risk-siblings studies but also in community samples. For many years, I have been the research group manager for Integrative Health, and supervised PhDs to their dissertation. Additionally I have researched families having a child with autism because family members are very important to improve early support.

## Optogenetic manipulation of slow oscillations in an Alzheimer's animal model

Ksenia Kastanenka, PhD\*, Steven S. Hou, Ph.D., Amanda Lariviere, Michal Arbel, Ph.D., Alex Kim, Jonathan M. Hawkes, Brian J Bacskai, Ph.D.

Massachusetts General Hospital, Harvard Medical School, USA

Slow oscillations are important for consolidation of memory during sleep, and Alzheimer's disease (AD) patients experience memory disturbances. Thus, we sought to examine slow wave activity using the voltage-sensitive dye RH1691 in an animal model of AD (APP mice). The power of slow oscillations at 0.6Hz was decreased starting at 3 months of age. Soluble amyloid-beta was sufficient to disrupt the slow waves. Cortical GABA levels were low in APP mice and application of exogenous GABA restored the slow oscillations, indicating that aberrant excitatory activity within the cortical circuit was responsible for slow oscillation dysfunction. Next we sought to manipulate slow waves in APP mice with optogenetics. Driving slow oscillations at normal frequency with light activation of channelrhodopsin-2 (ChR2) expressed in excitatory cortical neurons restored slow wave power by synchronizing neuronal activity. Using multiphoton microscopy, we performed longitudinal imaging of senile plaques and monitored intracellular calcium. Cytosolic calcium is a surrogate marker of neuronal activity and is normally tightly regulated. We had previously demonstrated that resting calcium levels measured with the genetically encoded calcium sensor YC3.6 were elevated in a subset of neurons in APP transgenics, and hypothesized that an effective treatment would restore calcium to control levels. Driving slow oscillation activity with optogenetics halted amyloid plaque deposition and prevented calcium overload associated with this pathology. On the other hand, driving slow oscillation activity at twice the normal frequency (1.2Hz) resulted in increased amyloid production, increased amyloid plaque deposition, disruptions in neuronal calcium homeostasis, and loss of synaptic spines. Therefore, while restoration of physiological circuit dynamics is sufficient to abrogate the progression of Alzheimer's disease pathology and should be considered an avenue for clinical treatment of patients with sleep disorders, pathophysiological stimulation of neuronal circuits leads to activity dependent acceleration of amyloid production, aggregation and downstream neuronal dysfunction.

### Audience Take Away:

- The audience will learn about neuronal activity aberrations associated with Alzheimer's disease.
- The audience will also learn how optogenetics can be used to manipulate oscillatory activity in animal models of disease.
- The audience will appreciate that Alzheimer's disease is a circuit disorder and not a simple proteinopathy.

### Biography

Dr. Ksenia Kastanenka is an independent investigator at Massachusetts General Hospital and Harvard Medical School in Boston, MA. Ksenia received her Doctorate of Philosophy in Neuroscience from Case Western Reserve University under the mentorship of Dr. Lynn Landmesser. During doctorate training, Ksenia has developed her expertise in optogenetic control of neuronal circuits by studying and manipulating motoneuron pathfinding during development. Subsequently, Ksenia has joined the laboratory of Drs. Brian Bacskai and Brad Hyman in the Neurology Department at Massachusetts General Hospital and Harvard Medical School to apply optogenetics and multiphoton microscopy in order to dissect the role neural activity plays in onset and development of Alzheimer's disease (AD). Ksenia's work has identified perturbations in neuronal activity stemming from overexcitation within cortical circuits. In an attempt to prevent and/or reverse the disorder, Ksenia has studied the effects and mechanisms of action of AD therapeutics, such as anti-Abeta immunotherapy, aducanumab, and the novel multimodal botanical extract DA-9803. Ksenia strongly believes that these translational studies are important for getting effective therapies to patients.

## Neurologic Disorders in the Geriatric Psychiatry Context: An Anatomy of Care

**Howard H. Fenn, MD**  
Stanford University, USA

**T**he geriatric patient's neurological disease is often accompanied by psychiatric and behavioral symptoms which confound the diagnostic process and complicate medical treatment and its delivery. An aged patient is often at the nexus of systemic medical, psychiatric, psychosocial problems which contribute to symptoms that are often difficult, if not impossible, to parse and to address. Conditions such as major neurocognitive disorders with behavioral disturbance, chronic pain, sleep disorders, depressive disorders, anxiety and legal/capacity issues are common. Physiological aging, acute and chronic medical conditions, onset of psychiatric symptomatology, and/or exacerbation of chronic psychiatric conditions may interact with neuropathology to instigate the exacerbation and intractability of neurological disease.

### **Audience Take Away:**

- This presentation will review some of the common psychiatric conditions whose symptomatology overlaps and/or exacerbates the neurological symptomatology, and offer strategies to help delineate and treat the psychiatric aspects. The evidence base to assess and manage the intertwined medical/neurological/psychiatric problems in the geriatric population is not robust. Flowcharts will be offered which review available evidence which can help with clinical decision-making.

### **Biography**

Dr. Howard Fenn is a senior consultant at the Stanford/VA California Alzheimer's Disease Center. He has extensive experience in Geriatric Psychiatry and currently supervises the Stanford Geriatric Psychiatry and Geriatric Medicine fellows. Dr. Fenn also evaluates patients in the VA Compensation and Pension unit.

## Analysis of the influence of various factors on the quality of life of patients with epilepsy in Kyrgyz Republic

Elnura Eralieva<sup>\*1,2</sup>, Bolot Kulov<sup>3</sup> M.D.

<sup>1</sup> Department of Neurosurgery, Osh City Clinical Hospital, Kyrgyzstan.

<sup>2</sup> Department of Neurology, Neurosurgery and Psychology, Graduate School, Osh State University.

<sup>3</sup> Kyrgyz Scientific Research Institute of Balneology and Rehabilitation, Kyrgyzstan

Epilepsy is a disease characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition. Approximately 50 million people currently live with epilepsy worldwide. Close to 80% of people with epilepsy (PWE) live in low- and middle-income countries. Despite the major impact of epilepsy on quality of life (QoL) in PWE and family members, this aspect has not been studied much in Kyrgyz Republic.

The aim of the study was to assess the QoL in PWE and to determine the clinical, demographic and socioeconomic factors which are associated with the QoL in such patients in Kyrgyz Republic. According to the official data obtained by the authors in different countries, the *Quality of Life in Epilepsy Inventory – 31* (QOLIE-31) prevalence rate is between 42.13-76.23.

The study was performed on 51 patients with epilepsy with different etiology, including 24 women (47.06%) and 27 men (52.94%). The mean age of respondents was 35.64 (range: 15-68 years). As regards the employment status, 25.49% of patients were employed, 50.98% were unemployed, 5.88% studied and 17.65% didn't study. The mean age at onset of epilepsy was 27.8 (range: 3-53 years). Duration of the disease was classified into one of the two categories: duration of epilepsy ≤5 years (50.98%) and >5 years (49.02%) (An average duration of epilepsy was 7.8 years, ranging from 0.3-29 years). Patients were divided into two groups by seizure type, in which 98.04% reported having generalized motor onset seizures, 1.96% reported having generalized non motor onset seizures. The frequency of seizures ≤ 2-3times per month was 21.57% and >2-3 times per month was 78.43%. The medication analysis revealed that 80.39% of the participants were on monotherapy, whereas 19.61% were on polytherapy. The mean total score of the QoL in PWE measured by QOLIE-31 scale was 40.13 (range: 7.75-69.85), with the lowest subscale score being 27.96 for Seizure Worry and the highest subscale score - 55.43 - for Medication Effects.

**Conclusions:** The most important clinical, demographic and social factors affecting QoL in PWE were duration of the disease, frequency of seizures, the age of onset and occupation. The worst scores were attained in the seizure worry domain. The QoL in PWE in our country is lower than the other countries' statistics.

### Audience Take Away:

- This presentation shows for the first time the quality of life in people with epilepsy in Kyrgyzstan at the international level, which is an advantage of this work. In addition, audience will have an idea of the situation of QoL in PWE in developing countries on the example of Kyrgyzstan and compare with global data.
- Knowledge of factors significantly affecting QoL in PWE allows to plan and coordinate the treatment, nursing care, and rehabilitation procedures more effectively.

### Biography

Eralieva Elnura is a young scientist. She works as a neurologist and neurophysiologist (EEG) at Osh City Clinical Hospital in Department of Neurosurgery in Kyrgyzstan. Also, she is a third-year graduate student at Osh State University. Now she is working on her PhD thesis on "Clinical and epidemiological features of cognitive impairment in patients with post-traumatic epilepsy in Kyrgyzstan". She is the author of 3 articles and 1 book.



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