

Scholars World Congress on

NEUROSCIENCE AND BRAIN DISORDERS FORUM

27-28 March 2023 | London, UK



Hosted By:

Kevin Peter

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09:00-09:45 Registrations
09:45-10:00 Opening Ceremony

Keynote Forum



Andras Csokay
MHEK, Hungary

Title: Jesus Prayers Applied in Separation of Craniopagus Twins

Biography: András Csókay born on 16 February 1956 and he is a Hungarian neurosurgeon with international recognition in the field of neurosurgery for his development of a technique to enhance microsurgical precision in the vascular tunnel and for the separation of a pair of Bangladeshi (Islam) Craniopagus Twins.

10:00-10:40



Gradimir Dimitrijevic
University Vojvodina, Serbia

Title: Biochaga and Biodihydroquercetin, two Siberian supplements, very good in Brain disorders Cardiovascular Rehabilitation and prevention, than in Oncology and like Nutrition supplement

Biography: Gradimir Dimitrijevic has 30 years' experience in transfusion medicine, most of the time as expert in clinical transfusion but with very good experience in therapeutic apheresis and donor apheresis, as well as, blood component therapy.

10:40-11:20

Networking and Refreshments Break @ 11:20-11:40



Um Albaneen Yusuf Jamali
Deena Institute of Technology, Bahrain

Title: Fostering Creativity using AI Robotics in Curriculum

Biography: Specialist in the Education of Gifted and Talented students for 17 years. The Kingdom of Bahrain's delegate at the World Council for Gifted and Talented students WC-GTC. Board member of The Arabian Council for Gifted and Talented.

11:40-12:20

Group Photo

Speaker Sessions:
Session Chair: Gradimir Dimitrijevic, University Vojvodina, Serbia



Christina Masri
Aleppo University, Germany

Title: Primary Cerebral Venous Thrombosis in a Patient with Immune Thrombocytopenic Purpura

Biography: Christina Masri, 27 year old, graduated from Aleppo University, faculty of medicine 2014-2019, former resident Doctor in Aleppo university Hospital, department of Internal medicine-2021.

12:20-12:50



Fatima Jamali

Deena Institute of Technology, Bahrain

Title: Educational Neuroscience and Dyslexia

Biography: Fatima Jamali is a Science teacher since (2008) International school of Choeifat. She Completed Postgraduate certificate in education (Dec- 2012) University of Nottingham and Bachelor degree in Chemical Engineering (March-2009) University of Bahrain, Professional development program for private schools (May-2012) Bahrain teacher collage @ university of Bahrain.

13:30-14:00



Hitoshi Sakano

University of Fukui, Japan

Title: Olfactory Perception during the Respiratory Cycle in Mice

Biography: Hitoshi Sakano, who had been long engaged in research and education at the former Department of Biophysics and Biochemistry, School of Science and retired from The University of Tokyo in March 2012, won the Medal with Purple Ribbon for spring 2014.

14:00-14:30



Xiaowen Bai

Medical College of Wisconsin, USA

Title: Human brain organoids in a dish: investigation of the importance of lncRNAs in environmental stress-induced brain injury

Biography: Xiaowen Bai's research interests are centered on the application of stem cells on disease modeling and tissue regeneration. Dr. Bai's research has been documented in more than 80 research articles, reviews, and book chapters, and is focused on stem-cell-based tissue regeneration, disease modeling, and drug testing.

14:30-15:00



Thazhumpal Chacko Mathew

Kuwait University, Kuwait

Title: Supraependymal stem cells and neural pathways of the mammalian brain

Biography: Thazhumpal Chacko Mathew completed his PhD from the University of Alberta, Canada in 1992 and obtained FRCPath (UK) in 2003. In 1983, he had undergone a research training at the University of Lund, Sweden. After his postdoctoral studies at the University of Alberta, he worked as Assistant Scientist at NYU, USA. In 1993 he joined the Faculty of Allied Health Sciences (FAHS) of Kuwait University.

15:00-15:30



Marco Carotenuto

Università degli Studi della Campania, Italy

Title: Sleep macrostructure in adolescents with Anorexia Nervosa: A polysomnographic pilot case-control study

Biography: Marco Carotenuto was born on 16 February 1974 and he completed his Degree in Medicine and Surgery in 2000 and Specialist degree in Child Adolescent Neuropsychiatry in 2005. In 2008, he completed his Doctorate in Behavioural and Learning Disorders Sciences.

15:30-16:00

Networking and Refreshments Break @ 16:00-16:20



Basma Tolba

General Secretariat of Mental Health and Addiction Treatment (GSMHAT), Egypt

Title: Addiction and substance Abuse Disorders

Biography: Basma MoshenTolba Passionate Doctor with extensive experience in Psychiatric ,Mental Health field, Puplic Health, TOT mental health trainer in both governmental and private sectors. Bringing forth an empathetic and professional attitude, committed to providing patients with the best care possible.

16:20-16:50



Baitubayev Dyussengali

Semey State Medical University, Kazakhstan

Title: A fundamental discovery in the physiology of adaptation of the 21st century and Validation of Psychoactive Substance Dependence

Biography: Baitubaev DG Narcologist of the Ridder Public State Enterprise "Psychiatric Dispensary" of the Health Department of the East Kazakhstan regional akimat, Ridder, Kazakhstan "The psychiatric dispensary". He is an Assistant-lecturer at Semey State Medical University.

16:50-17:20

Panel Discussions | Closing Ceremony

Scientific Program

Day 2 | March 28, 2023
Virtual | GMT

09:00-09:15 Opening Ceremony

Speaker Sessions:

Session Chair: Peter Nara, Keystone Bio Inc., USA

Keynote Forum



Ken Ware

Neuro Physics Therapy Institute, Australia

Title: Lateralization of the Hemispheres and Exploiting Central Patterns Generators for Functional Recoveries Following Stroke and or Acquired Brain Injuries Through Neuro-Physics Therapy (NPT)

Biography: Ken Ware NeuroPhysics Therapy was founded upon innocent paradigm-shifting discoveries that Ken Ware made back in 1982, relating to the extreme sensitivities there are surrounding the intrinsic relationship the human nervous system has with its environment. He observed that because of this extreme sensitivity.

09:30-10:00



Peter Nara

Keystone Bio Inc., USA

Title: Porphyromonas gingivalis Outer Membrane Vesicles as the Major Causative factor of Neuro-inflammation/degeneration leading to Cognitive Decline, Dementia and Alzheimer's Disease

Biography: Nara is one of the co-founders, the Chief Scientific Officer and President Business Development for Keystone Bio Inc. in St. Louis, Mo.,

10:00-10:30

10:30-11:00



Brandon Lucke-Wold
University of Florida, USA

Title: Early Signs of Elevated Intracranial Pressure (ICP) on Computed Tomography Correlate with Measured ICP in the Intensive Care Unit and Six-Month Outcome in the Progesterone for Traumatic Brain Injury, Experimental Clinical Treatment (ProTECTIII) Trial Cohort

Biography: Brandon Lucke-Wold was born and raised in Colorado Springs, CO. He graduated magna cum laude with a BS in Neuroscience and distinction in honors from Baylor University.

11:00-11:30



Jun Hua
University School of Medicine, Baltimore, Maryland, United States

Title: High-resolution functional MRI of differential laminar activation in the human entorhinal cortex

Biography: Hua is an associate professor in the F.M. Kirby Research Center for Functional Brain Imaging at Kennedy Krieger Institute. He also holds a joint appointment as an associate professor in the Russell H. Morgan Department of Radiology at Johns Hopkins University.

11:30-12:00



Gabriele Saretzki
Newcastle University, United Kingdom

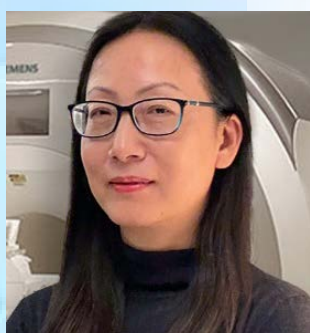
Title: Increased telomerase improves motor function and alpha-synuclein pathology in a transgenic mouse model of Parkinson's disease associated with enhanced autophagy

Biography: Gabriele has completed her PhD 1990 at Humboldt University Berlin and performed most of her postdoctoral studies at the Institute for Ageing and Health in Newcastle upon Tyne (UK) where she is a Lecturer in Ageing Research since 2002.

Networking and Refreshments Break: 12:00-12:10

Speaker Sessions:

12:10-12:30



Wen Li
Florida State University, USA

Title: Identifying hidden brain states responsive to transcranial stimulation

Biography: Li received a PhD in Psychology at Northwestern University (IL, USA), followed by a postdoctoral fellowship in cognitive affective neuroscience at the Feinberg Medical School of Northwestern University.

12:30-12:50



Raquel L. Pereira
University of Porto, Portugal

Title: Electrochemical miRNA-34a-based biosensor for the diagnosis of Alzheimer's Disease

Biography: Raquel L. Pereira is a research fellow at BioMark, Sensor Research at ISEP, Porto, and has an MSc in Molecular Bioengineering from the University of Porto. Raquel started working with biosensors in her Master Thesis.

12:50-13:10



Priyanka Chandolia

National Institute of Medical Sciences University of Jaipur, India

Title: Herbal remedies for cerebral ischemia and other neurological issues

Biography: Priyanka Chandolia is a healthcare professional, with a diversified experience in research and academia domain, currently working as an Assistant Professor in National Institute of Medical Sciences, Jaipur Rajasthan, India.

13:10-13:30



Andrea L Small-Howard

GbS Global Biopharma, Canada

Title: Case Study: Identification of minimum essential therapeutic mixtures from Cannabis plant extracts by screening in cell and animal models

Biography: Andrea Small-Howard has 25 years of scientific research and executive experience in the biopharma industry supervising research & development, manufacturing, and quality control in global divisions. Dr. Small-Howard has taken novel biological products from ideation through commercialization.

Break: 13:30-13:40

13:40-14:00



Raffaele Pilla

St. John of God Hospital, Italy

Title: Therapeutic ketosis and the broad field of applications for the ketogenic diet: Ketone ester applications & clinical updates

Biography: Raffaele Pilla, Pharm.D., Ph.D., Doctor Europaeus, received his Master's degree in Pharmacy at G.d'Annunzio University in Chieti-Pescara, Italy in 2005, where he also served internships at the CellPhysiology Laboratory and Molecular Biology Laboratory.

14:00-14:20



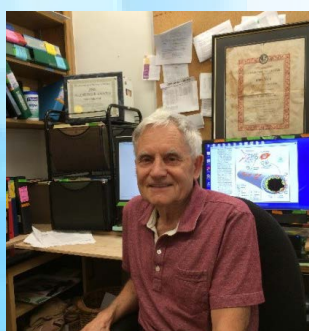
Lama Saad El-Din Mahmoud

October 6 University, Egypt

Title: Artificial intelligence and virtual reality Kinect rehabilitation in stroke patients with Unilateral spatial neglect

Biography: Lama Saad El-Din Mahmoud has been currently working as lecturer of physical Therapy for Neuromuscular disorders & its surgery, faculty of physical therapy, October 6 university, Egypt.

14:20-14:40



Milan Fiala

UCLA, Los Angeles, CA, USA

Title: PUFA repair macrophage transcriptome and glycome for amyloid- β brain clearance and dementia protection in Alzheimer's disease

Biography: Milan Fiala, M.D. (Geneva), M.Sc. (Harvard), Research Professor MCDB, UCLA Life Sciences. After M.D. graduation from the University of Geneva, he trained at Harvard and University of Washington in epidemiology and virology.

14:40-15:00



Ana Marques

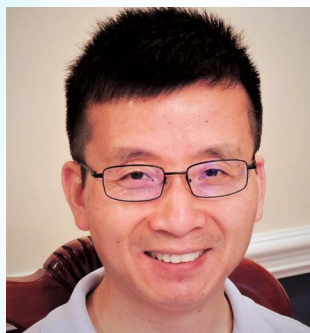
Clermont-Ferrand University Hospital, France

Title: Two-Year Longitudinal Follow-Up of Visual Illusions and Hallucinations In Parkinson's Disease

Biography: Marques works in Clermont, FL and specializes in Geriatric Medicine. Ms. Marques is affiliated with South Lake Hospital.

Plenary Speaker

15:00-15:30



Qingzhong Kong

Case Western Reserve University, United States

Title: Development of Effective Gene Therapy for CJD

Biography: Kong graduated with BS and MS degrees in Biochemistry at Nanjing University in 1987 and 1990, respectively, and he obtained his PhD degree in Molecular Virology at the University of Massachusetts. He received his postdoctoral training in Molecular Immunology at Yale University from 1996 to 2000, and joined the Department of Pathology at Case Western Reserve University as an assistant professor in 2000. He is currently a tenured Associate Professor of Pathology and Neurology and associate director of the National Prion Disease Pathology Surveillance Center at the School of Medicine, Case Western Reserve University.

E-Poster

15:30-15:50



Laura Natalia Milla Sanabria

National Univeristy of Rio Cuarto, Argentina

Title: Resistance of glioblastoma cells to photodynamic therapy

Biography: Laura N. Milla Sanabria develops her research work looking for mechanisms of tumor resistance to photodynamic therapy (PDT). She has developed studies on bio-distribution, biocompatibility and phototherapeutic efficacy in mice using synthetic photosensitizers.

Closing Ceremony

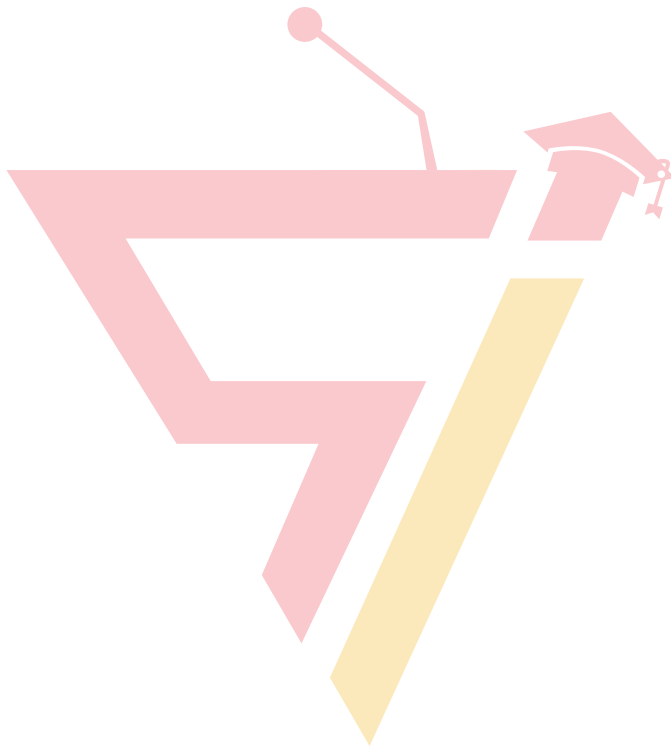
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**KEYNOTE
SPEAKERS
Day 1**





Jesus Prayers Applied in Separation of Craniopagus Twins

András Csókay

Hungarian Defence Forces Medical Center, Hungary

Purpose: It is a frequent experience that creative scientific ideas do not necessarily realize, or come to life during professional considerations and forced thinking. The solution or key to a long awaited innovative step can find us, surgeons, as a strong revelation in deep contemplation or meditations just as artists or thinkers do experience it. At times like this the thinking man arrives quicker to the truth, be it also professional insights. During the 2 year period while preceding the final separation of three-year-old craniopagus twins, we consciously practiced contemplation, 5 neurosurgical innovations were born.

Methods: The twins shared a common superior and inferior sagittal and a circumferential sinus. The separation of sinuses surgically seemed to be a very difficult life threatening procedure. The one of the most important innovation came to realization, was the multi staged endovascular venous separation. Four further novel neurosurgical consideration were applied.

Results: One of the little girls advanced to the GOS 4-5 score three months after the surgery. The other little girl despite of non-surgical septic complications continued to progress well, but on the thirty third post-operative day, she suffered a severe cerebral hemorrhage, as a non-surgical complication, because of which at present she is still in GOS 3.

Conclusion: The neurosurgical separation, initially thought to be impossible, was carried out successfully with the help of the new innovations conceived in the Jesus prayer. We hope that our innovations can be applied in the future.

Biography

András Csókay born on 16 February 1956 and he is a Hungarian neurosurgeon with international recognition in the field of neurosurgery for his development of a technique to enhance microsurgical precision in the vascular tunnel and for the separation of a pair of Bangladeshi (Islam) Craniopagus Twins. András Csókay graduated from Apáczai Csere János Gymnasium of the Eötvös Loránd University (ELTE) in 1974. From 1975 to 1980 he studied at the Faculty of Civil Engineering of the Budapest University of Technology and Economics.

From 1989 Csókay became a specialist at the National Institute of Neuroscience (OKITI) in Budapest and from 1993 he worked at the National Clinic and Trauma Institute, Department of Neurosurgery. Between 2003 and 2007 he lived in Szombathely and headed the neurosurgery department of Markusovszky Hospital. In 2007 he moved back to Budapest and directed the Neurosurgery Department of Szent János's Hospital. He became a university lecturer at his alma mater, Semmelweis University. From 2010 he became head of neurosurgery at the Borsod-Abaúj-Zemplén County Central Hospital in Miskolc.



Biochaga and Biodihydroquercetin, two Siberian supplements, very good in Brain disorders Cardiovascular Rehabilitation and prevention, than in Oncology and like Nutrition supplement

Dimitrijevic G

Institute for Blood transfusion of Vojvodina, Novi Sad, Serbia

Aim: We speak about Biochaga and Biodihydroquercetin, two Siberian supplements that are very good for prevention of brain disorders, as well as, for treatment and rehabilitation. It is very common in Serbia, and especially in my region brain insults and some other disorders among elderly people. In many other countries it is common as well. Method: the methodology of using those two extremely natural supplements (powder consistency) is easy and there are no side effects of using them, how we recommend it.

Methodology and Results: Biodihydroquercetin is capillary protective and protects blood vessels walls against corrosive compounds damage, normalize permeability of the blood vessel wall, reduces blood viscosity, improves microcirculation. It promotes establishment of microcirculation, improves metabolism of brain cells, and regulates the metabolism process of **neurotransmitters and peroxidation re-**

action in the cerebral cortex, visual nerve and retinal neurons. In neurology it is used for neurasthenia, neuralgia, neuritis, radiculitis, Parkinson's disease, Alzheimer's disease, headaches, migraine." If you increase the breathing capacity, the flow of oxygen to the brain and other organs, if you open the way to tens of thousands of closed capillaries, then you will not encounter any disease that cannot be cured."

(A.Zalmanov)

Biochaga (Inonotus Obliquas) is phytogetic parasitic fungus growing on white birch trees and is known for its medicinal properties. In USA it is classified as a dietary supplement and in Europe and Russia as a medicinal mushroom used for medicinal properties. Beta glucans is known to establish better intercellular communication. In neurology it is used for relieves stress and anxiety, establishes transport of substances in the brain tissue after injuries and stroke, increases work capacity, life force, improves memory, fight insomnia.

What is important is that together they are very useful and effective. Nobel prize winner Linus Pauling said : "Regular use of Dihydroquercetin can extend human life by 25 years

Biography

Dr Gradimir Dimitrijevic has 30 years' experience in transfusion medicine, most of the time as expert in clinical transfusion but with very good experience in therapeutic apheresis and donor apheresis, as well as, blood component therapy. From few years ago introduced irradiation of blood components in Serbia, in Novi Sad, and most of the blood components that are irradiated are for oncology, hematology, in adults and children. He is more than 15 years dealing with Siberian natural products, some Chinese, one African and one South American. All are extremely effective and helpful. This is his experience in all this together.



Fostering Creativity using AI Robotics in Curriculum

Um Albaneen Yusuf Jamali

Deena Institute of Technology, Bahrain

The chapter reports on a longitudinal study, which investigated the impacts of AI robotics programs on fostering creativity among primary school students. A mixed methods of pre-post CAP test, observations and semi structured interviews was used for the purpose of this study, which was carried out over two years. A sample of 60, 10-12 year-old female students from middle socio-economic status participated in

the study. They were randomly assigned into two treatment and control groups. An AI robotics program using Arduino was administered to the students in the treatment group while the students in the control group did not receive any robotics intervention. The results from pre-post tests indicated that AI robotics programs had significant impact upon developing all creativity thinking skills of fluency, flexibility, originality and elaboration. The chapter suggests integration of AI robotics in curriculum while calls for policymakers and school leaders to provide teachers with training opportunities regarding AI robotics.

Biography

Specialist in the Education of Gifted and Talented students for 17 years. The Kingdom of Bahrain's delegate at the World Council for Gifted and Talented students WCGTC. Board member of The Arabian Council for Gifted and Talented. Authors and researchers in the areas of robotics, AI and Creativity in Education. Presenters in 5 international conferences in 2022. International certified trainer at the Kingdom of Bahrain's Ministry of Education. Awarded by Hamadan bin Rashed Al Maktoum foundation for the distinguished GCC teacher. Other awards included Scientific research and innovation awards.

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SPEAKERS
Day 1





Primary Cerebral Venous Thrombosis in a Patient with Immune Thrombocytopenic Purpura

Christina Mari

University of Aleppo

Immune thrombocytopenic purpura is an autoimmune hematological disorder characterized by low platelet level

Due to its destruction through autoimmune antibodies. Cerebral venous thrombosis is a serious condition defined by a thrombosis in the cerebral venous sinuses that occurs mostly in the presence of a hypercoagulable state. Hemorrhage and thrombosis are processes with a paradoxical etiology; thus, the association between these two conditions seems to be extremely rare.

Case Presentation. We herein report a case of a 19-year-old female with a chief complaint of generalized tonic-clonic episode, severe headache, and blurred vision. Physical examination was significant for a bilateral Babinski's sign and severe bilateral papilledema.

Laboratory workup, computed tomography, and magnetic resonance imaging were normal except for severe thrombocytopenia.

Magnetic resonance venography was diagnostic for cerebral venous thrombosis. Her past medical history was significant for immune thrombocytopenic purpura that was treated with prednisolone 40 mg per day which posed a therapeutic challenge. Highdose

prednisolone and platelet transfusion were initiated; enoxaparin was administered and switched to warfarin after stabilization of platelet count. The patient was neurologically intact after 14 days of appropriate treatment and was on follow-up.

Many hypotheses were suggested to explain the unexpected thrombotic events in a patient with immune thrombocytopenic purpura which were related to the disease etiology or treatment, taking into account common risk factors (such as age, obesity, smoking, hypertension, diabetes mellitus, dyslipidemia, splenectomy, and oral contraceptive agents).

Conclusion: the association between immune thrombocytopenic purpura (which is a major risk factor for bleeding) and cerebral venous thrombosis (which is caused by a thromboembolic event) has carried a major challenge to the management plan. We believe that immune thrombocytopenic purpura and its treatment methods should be taken into consideration as risk factors for thromboembolic phenomenon.

Keywords: Cerebral venous thrombosis; Immune Thrombocytopenic Purpura; case report; Corticosteroids Anticoagulant agents; Risk Factor.

Biography

Christina Masri, 27 year old, graduated from Aleppo University, faculty of medicine 2014-2019, former resident Doctor in Aleppo university Hospital, department of Internal medicine-2021.

Participated as a speaker and as a mentor in CME (Continuous Medical Education) Conference in Aleppo University, participated in publishing two case reports, attended several courses in Research and EBM (Evidence-Based Medicine), then participated as a Co-director in EBM workshops.

In 2022 moved to Germany, studied and passed required exams to practice medicine in Germany, and now working as a resident doctor in the department of Anesthesia and Intensive care, in Sankt Vincentius Hospital in Speyer, Germany.

Moreover, obtained a diploma in Nutrition and had the experience to work with bariatric patients as a consultant in Life Pulse Medical Center, Aleppo, Syria.



Educational Neuroscience and Dyslexia

Fatima Jamali

Deena Institute of Technology, Bahrain

Many disciplines have come together to create a new science of learning that have the potential to transform educational practices. Educational neuroscience does that through highlighting two main streams: (i) brain structures in control for different educational processes such as attention, reading, memory, etc. and (ii) how educational processes affect brain function and structure. A proliferation of research in the field of educational neuroscience has investigated the impact of processes in learning, especially in regard to education and literacy. About 10% of children endure learning difficulties associated with developmental disorders including dyslexia, dyspraxia, dyscalculia, autism syndrome, etc. The current paper highlights a number of case studies encountering challenges in dyslexic children and examine them according to

the neuronal recycling hypothesis. In this perspective, dyslexia occur due to functional or structural impairment in brain's reading network. The developmental disorder of dyslexia has been stated to be around 15-17% of student population worldwide. Neurocognitive theories of dyslexia argue that all dyslexic children suffer from similar type of brain impairment regardless of the orthographic system. On the other hand, as indicated in this paper, the neural circuits associated with reading should vary considerably across languages, on the basis of variances in how a given orthographic system associates between written and spoken language. Furthermore, even within an orthographic community, various forms of dyslexia can be indicated. Other challenges with dyslexic children were seen in terms of exposing to more than one language and Cognitive impairment among those from socioeconomically underprivileged backgrounds. The paper recommends that in order to successful implementation special educational program, teachers, pedagogists, child psychologists and cognitive neuroscientists should collaborate together.

Biography

Fatima Jamali is a Science teacher since (2008) International school of Choeifat.

She Completed Postgraduate certificate in education (Dec- 2012) University of Nottingham and

Bachelor degree in Chemical Engineering (March-2009) University of Bahrain, Professional development program for private schools (May-2012) Bahrain teacher collage @ university of Bahrain.



Olfactory Perception during the Respiratory Cycle in Mice

Hitoshi Sakano

University of Fukui, Japan

In the mouse olfactory system, odor signals detected in the olfactory epithelium are converted to a topographic map of activated glomeruli in the olfactory bulb (1). The map information is then conveyed by projection neurons, mitral cells (MCs) and tufted cells (TCs), to distinct areas in the olfactory cortex. An odor map is transmitted to the anterior olfactory nucleus by (TCs) for odor identification and recollection of associated memory for learned decisions (2). For instinct decisions, odor information is directly transmitted to the valence regions in the amygdala by specific subsets of MCs. Transmission of orthonasal odor signals through these two distinct pathways, innate and learned, are closely related with exhalation and inhalation, respectively. Furthermore, the retro-nasal and orthonasal signals are differentially processed during the respiratory cycle, suggesting that these signals are processed in separate areas of the

olfactory bulb and olfactory cortex (3,4). I will summarize the recent progress in the study of the olfactory circuitry and odor perception during respiration.

Biography

Hitoshi Sakano, who had been long engaged in research and education at the former Department of Biophysics and Biochemistry, School of Science and retired from The University of Tokyo in March 2012, won the Medal with Purple Ribbon for spring 2014. He was honored for his neuroscience study to elucidate mammalian olfactory systems, which was initiated in 1994 when he transferred to the department. To clarify how mammals detect and recognize countless smells in nature, he first elucidated a mechanism in which each olfactory cell expresses only one olfactory receptor, and then a mechanism in which nerve fibers of the olfactory cells that express each olfactory receptor create accurate odor maps in a proper region of the brain. Different mechanisms are used for respective two-dimensional axes (the dorsal-ventral axis and the anterior-posterior axis), and the projection locations are determined by the combination of the mechanisms. He also clarified that a strong fear response due to the odor of natural enemies is regulated by a certain region of the brain. These findings were published in prestigious journals, including Science, Cell, and Nature. In 2013, after retiring from The University of Tokyo, he published his culmination of a series of research achievements in Cell, in which he resolved all questions, i.e., that each olfactory receptor has an individual basal activity in an odorless state, which regulates how olfactory sensory neurons determine the projection locations on a two-dimensional map on the brain. His excellent results were achieved by his strenuous efforts and his constant persistence



Human brain organoids in a dish: investigation of the importance of lncRNAs in environmental stress-induced brain injury

Xiaowen Bai

Medical College of Wisconsin, USA

Up to 15% of children were reported with neurodevelopmental disorders and some of these disorders were resulted from various environmental stressors such as drugs (e.g., anesthetics) and alcohol. Alcohol consumption by pregnant women can adversely affect the developing fetus, resulting in a spectrum of deficiencies known as Fetal Alcohol Spectrum Disorders (FASD), with a prevalence of 1.98% in European region and 1-5% in the USA. One significant consequence of FASD is alcohol-induced developmental neurotoxicity (AIDN) manifesting as cognitive impairment and behavioral problems throughout life, possibly related to neuronal injury and loss, with the mechanisms largely unknown and no effective neuroprotective approach available. So far, most direct evidence for AIDN stems from animal studies due to lack of human models that can adequately emulate developing brain. Emerging evidence from us and others have showed

that human induced pluripotent stem cell-derived 3D cerebral organoids can mimic many key features of human fetal brain development at molecular, cellular, structural, and functional levels. The brain organoid model has shown promise in decoding human brain development and physiology, uncovering pathogenesis of various neurological disorders, and serving as a platform for therapeutic development in the dish. Leveraging brain organoids for studying various environmental stress-induced developmental brain injury has great potential as well. Our studies include 1) characterization of brain organoids, application of brain organoids in modeling developmental brain disorders, and 3) investigation of roles and signaling of lncRNAs in AIDN. The findings of neuroprotective roles of long non-coding RNA (lncRNAs) not only provide novel insights into lncRNA-related mechanisms of cognitive and behavioral impairment observed in FASD patients as well as neuroprotective perspective, but also corroborate the versatility of brain organoids as models for developmental brain injury.

Biography

Dr. Xiaowen Bai's research interests are centered on the application of stem cells on disease modeling and tissue regeneration. Dr. Bai's research has been documented in more than 80 research articles, reviews, and book chapters, and is focused on stem cell-based tissue regeneration, disease modeling, and drug testing. Her current major focus of the laboratory is to examine the molecular mechanisms underlying the roles of non-coding RNAs, mitochondria, and genetic factors in neurodegeneration and heart injury in mice, and translate the findings to humans using human induced pluripotent stem cell-derived 3D brain organoids and heart tissue.



Supraependymal stem cells and neural pathways of the mammalian brain.

Thazhumpal Chacko Mathew

Kuwait University, Kuwait

The surface of the cerebral ventricles in rats shows the presence of a number of supraependymal cells and an immense network of nerve fibers. This study focuses on the characterization of these nerve fibers and the neurogenic potential of the supraependymal cells in adult rats.

Characterization of intraventricular cell clusters and nerve fibers in adult rats were carried out using electron microscopy, immunohistochemistry and by the administration of specific neurotoxins into the cerebral ventricles. Further studies were also carried out to understand the neurogenic potential of the supraependymal cells.

Electron microscopic studies have shown that these fibers are catecholaminergic, cholinergic or peptidergic in nature. Immunohistochemical studies revealed the presence of tyrosine hydroxylase positive fibers on the ependymal surface. Studies using selective neurotoxins have confirmed the serotonergic, adre-

nergic and/or dopaminergic nature of the fibers.

Retrograde labeling studies have suggested that some of these fibers may have originated from the superior cervical ganglia. Profound axonal regeneration of the fibers and neurogenesis of the supraependymal cells were observed following unilateral cervical sympathectomy in adult rat.

The data presented in this study shows the existence of clusters of supraependymal cells and an extensive, novel, intraventricular neural pathway in the vertebrate brain. These fibers are of varied nature and origin. In addition, preliminary studies have shown that the supraependymal cells may contribute to an adult neurogenic niche in mammalian brain.

Biography

Thazhumpal Chacko Mathew completed his PhD from the University of Alberta, Canada in 1992 and obtained FRCPATH (UK) in 2003. In 1983, he had undergone a research training at the University of Lund, Sweden. After his postdoctoral studies at the University of Alberta, he worked as Assistant Scientist at NYU, USA. In 1993 he joined the Faculty of Allied Health Sciences (FAHS) of Kuwait University. Also, he had a joint appointment in the Department of Anatomy of the Faculty of Medicine (FOM), Kuwait University. Currently he is Professor and Chairman of the MLS Department. He was also Vice Dean for Research at the FAHS and the Director of the Electron Microscope Unit in the FOM. His research is in molecular neurobiology. He is one of the members of the international advisory board of the Netter's Atlas of Human Anatomy. Prof. Mathew received several awards and published more than 75 papers and attended over 100 conferences.



Sleep macrostructure in adolescents with Anorexia Nervosa: A polysomnographic pilot case-control study

Marco Carotenuto

University of Campania "Luigi Vanvitelli", Italy

Sub-topics: Pediatric Neurology

Background and aims: Anorexia nervosa (AN) is an eating disorders affecting in Italy between 0.2-0.8% of adolescent subjects. AN represents a severe mental disorder considering the high suicidal risk across the lifespan. Sleep troubles are frequently reported in AN.

Aim of study is assessing sleep macrostructural findings in AN adolescents.

Methods: 22 AN subjects (20 females and 2 males; aged 10.3-18.12 ys; mean 14.09 ± 1.74) assessed nocturnal PSG and the following parameters were recorded: Time in Bed (TIB), Sleep Partial Time (SPT), Total Sleep Time (TST), Sleep Onset Latency (SOL), First REM Latency (FRL), Stage Shifting/h (SS/h), Awakenings/h (AWN/h), Sleep Efficiency% (SE %), Wake Af-

ter Sleep Onset (WASO)%, Sleep Stage (N1, N2, N3, REM)%, duration in minutes and sleep stage total duration. PSG data were compared with matched control group. T-test and Cohen's d analysis were calculated. p values ≤ 0.05 were considered as statistically significant.

Results: The two groups (AN vs. C) were similar for age (t-test(42) = -0.32; $p=0.74$) and sex (Chi-square(0) = 0.275; $p=0.59$). t-test showed significant reduction in: sleep duration parameters (TIB, $p<0.001$; SPT, $p<0.001$; TST, $p<0.001$; SOL, $p=0.035$; N2, $p<0.001$; N3, $p<0.014$; N2%, $p=0.008$), while AWN-h were higher in AN ($p<0.001$). Effect size analysis showed very large effect for TIB, SPT, TST, AWN-h, N2-min and large effect for WASO%, N2%.

Conclusions: AN can affect significantly sleep macrostructure and PSG analysis may considered as mandatory for the clinical management of Eating disorders, particularly in developmental age.

Biography

Marco Carotenuto was born on 16 February 1974 and he completed his Degree in Medicine and Surgery in 2000 and Specialist degree in Child Adolescent Neuropsychiatry in 2005. In 2008, he completed his Doctorate in Behavioural and Learning Disorders Sciences. From 2008 to 2017, he was Researcher and in December 2017 he became Associate Professor of Child and Adolescent Neuropsychiatry at Università degli Studi della Campania Luigi Vanvitelli.

Since January 2018 he is the Chief of the Clinic of Child and Adolescent Neuropsychiatry. The main research areas have been focused on child neurology, pediatric sleep disorders, polysomnography, pediatric primary headaches, and pediatric rehabilitation.



A fundamental discovery in the physiology of adaptation of the 21st century and Validation of Psychoactive Substance Dependence

Baitubaev D.G

psychiatrist-narcologist of the Department of Psychiatric and drug addiction in the Psychiatric Dispensary

Summary. The article shows that the current level of physiology does not disclose the biological mechanisms of the organism transition from one range to adapt to a higher with an increase in the regular forces of the stimulus above sub-extreme. A new trend in the physiology of adaptation - progredient adaptation, explains the mechanism of increasing the tolerance of the organism, with dependence on psychoactive substances (PAS). It is scientifically proved, that dependences of the organism on PAS not the disease, and the states like progredient (progressive) adaptation.

Keywords: Hypertrophy of the endocrine system; A state of regular, unfinished stresses; A progredient (progressive) adaptation.

Urgency of the issue: It is known, that at the pick of dependence on any psychoactive substance (PAS), a person, for example, an opium (heroin) addict uses doses, which are multiple times, almost 10 times, higher than the lethal dose for an ordinary person [3, p.23].

The fact, that the drug user does not die, is explained by the increase in the body's tolerance in response to the increase in the dose of PAS [3, p.25].

Urgent issues of medicine are not only identification of mechanisms for increasing tolerance, but also validation of the physiological process occurring on exposure to increasing doses of a psychoactive substance and the response increase in tolerance of a PAS-dependent organism.

Purpose and objectives of the study: Lack of adaptive reactions of the organism already known in modern physiology to explain the adaptation mechanisms in response to a further increase in the regular stimulus strength above the sub-extreme level in PAS dependent patients.

The pronounced reactions by the vegetative nervous system (VNS) in PAS dependent patients indicate the vegetotrophy of most of these substances. The amount of their influence is closest to the sub-extreme level. With regular exposure to some kind of irritant. Under the influence of sub-extreme stimuli, an activation reaction with the stages of primary and persistent activation occurs, indicating a higher activity of protective systems. The stage of persistent activation is true, active resistance, stable and long enough - up to six months - in contrast to the training reaction and in the absence of constant exposure [4, p.79]

But in PAS dependence, the process does not result in the reaction of persistent activation; the dose to which the adaptation has occurred is habitual and results in no euphorizing effect.

To achieve neurophysiological shift sufficient for euphoria, a larger dose is required.

But increase in the dose of PAS after the activation reaction is stressful for the organism. Stress in its development has three stages.

The first stage is the “anxiety reaction”, the second one is the stage of tolerance, when hypertrophy of the adrenal cortex with a steady increase in the formation and secretion of corticosteroids develops. The tolerance of the organism to the stimulus increases. Prolonged exposure to the stimulus results in the stage of exhaustion, and death may occur. Doses of PAS above the stress level are lethal [1].

L.Kh.Garkavi and co-authors showed that: “the reactivity of the organism is represented by a number of floors (ranges), which does not exceed ten. In each floor: a weak stimulus causes the training reaction, an average sub-extreme stimulus - the activation reaction, a strong stimulus – the stress. The ranges are separated by the zone of non-reactivity, when increasing the stimulus level above the stress one or decreasing below the training one causes no reaction.

But L.Kh.Garkavi and co-authors could not explain the mechanisms providing the human organism’s transition (bypassing exhaustion and death stages) from one floor (range) of adaptation to a higher one, under the conditions of further increase in the force of impact above stress level.

Indeed, according to pathophysiology, without such adaptation mechanisms increasing the tolerance, the body must die from “exhaustion”, from failure of adaptation mechanisms, when the organism transits from the first adaptation range to the second. This indicates failure of the current level of physiology to explain the mechanisms providing the body transition from one adaptation range (reactivity) to a higher one.

In the history of narcology, attempts were made to explain the increase in tolerance organism by different causes. They are accelerated disintegration of PAS in the addict’s, development of chronic stress, activation of other states inactive in normal conditions, or activation of systems that fulfil other functions, but with an increase in a PAS dose are forcedly involved in detoxification, etc. But all those assumptions have not been scientifically confirmed.

No matter how full modern scientific research explain qualitative changes at the cellular and molecular level that lead to an increase in tolerance in PAS dependent patients, it is clear that these changes can only be of adaptive, not pathological and damaging nature, otherwise they would lead not to an increase in tolerance, but rather to a decrease in it, and the body would already die when transiting from the first floor of adaptation to the second. Also, according to the dialectical principle of the mutual transition of qualitative changes to quantitative ones, accumulation of these changes should lead to qualitative and quantitative changes in the neuroendocrine system which is responsible for the adaptation of the whole body. Consequently, we can speak about change in the body’s response to a drug.

Object and methods of investigation: Features of the response of the neuroendocrine system to any external stimulus. Capacity of the endocrine system for positive trophic changes. Hypertrophy and hyperfunction of the endocrine system - histological and biochemical evidence.

The increase in tolerance of the PAS dependent organism can be explained by the functional tension of the neuroendocrine system and by the reaction of persistent activation only within one adaptation range. It is good health, physical activity, increased protective capacities of the body to various hazards - hypothermia, etc., which are clinically observed in the prodroma and possibly in the initial stage of alcohol dependence.

But tension in the neuroendocrine system and the reaction of persistent activation fail to explain the transition from a lower to a higher adaptation range following PAS exposure above sub-extreme level and its further increase! After all, in such a situation, the body must experience stress with exhaustion and death! This can only be explained by the transcendental functioning of the neuroendocrine system, which can be possible only due to its physiological adaptive hypertrophy, in response to the regular exposure to the external factor. But is it possible? Even in the ear-

ly 1800s, J. Lamarck suggested that “the work builds up the organs”. P. Lesgaft’s merit was the explanation of a specific morphological alteration of the organism during the exercise process. V.Ru showed that due to “trophic stimulation” in the working organ, the assimilation process begins to dominate over the dissimilation process, and morphological changes occur at the physiological level. The increase in energy reserves results in an increase in working efficiency. It can be argued that the regular use of PAS - addressing the high response range - leads the entire body to the state of the activation reaction - hypermetabolic state, which does not contribute to the accumulation of reserves and the occurrence of positive trophic changes in the body. But one should remember that the hypermetabolic state develops in the “metabolic boiler” - at the level of tissue adaptation mechanisms [2, p.500]. Perhaps, in the higher adaptation mechanisms - the neuroendocrine system - despite their tension, there are no hypermetabolization processes, which contributes to the accumulation of reserves leading to morphological changes in the neuroendocrine system in the form of hypertrophy, are there? The observations of L.Kh. Garkavi and co-authors indirectly proves possible accumulation of reserves in the neuroendocrine system during the activation reaction; “Although the metabolism is highly active during the activation reaction, it is characterized by an equilibrium” [4, p.79], since to ensure “equilibrium” of constantly growing metabolic processes, a “powerful” neuroendocrine system is necessary. But in PAS dependence, after the completion of the activation reaction and in further enhancement of the stimulus above the sub-extreme level and transition to the subsequent adaptation floor, the “equilibrium” of the metabolic processes takes place, too. But this is possible only when the functional adequacy of the neuroendocrine systems grows in direct proportion to the strength of the external factor, which is possible only with hypertrophic neuroendocrine system and, as a consequence, its hyperproductivity. The neuroendocrine system consists of the vegetative nervous system (VNS) and the endocrine part - the endocrine glands. In the functioning of the vegetative nervous system, a special mechanism is evolutionary provided that contributes to the accumulation of reserves - “advanced excitation” described

in the 1930s by P.K. Anokhin. Vegetative nervous system (VNS) responds to any stimulus with a somewhat excessive neurotransmitter ejection, as if in anticipation of possible future high consumption. VNS through neurotransmitters activates auxiliary and tissue adaptation mechanisms, and due to excesses of neurotransmitter ejection “takes a break” for its own recovery trophic processes. Although VNS regulates all the processes in the body, it has been established that there are biologically active substances produced by different cells of the body that have a trophic effect on VNS itself. One of such substances is the nerve growth factor (NGF) - an insulin-like substance that stimulates the growth of sympathetic ganglia. But, despite the restorative and trophic processes, the vegetative nervous system cannot hypertrophy (the adrenal medulla is a modified sympathetic ganglion).

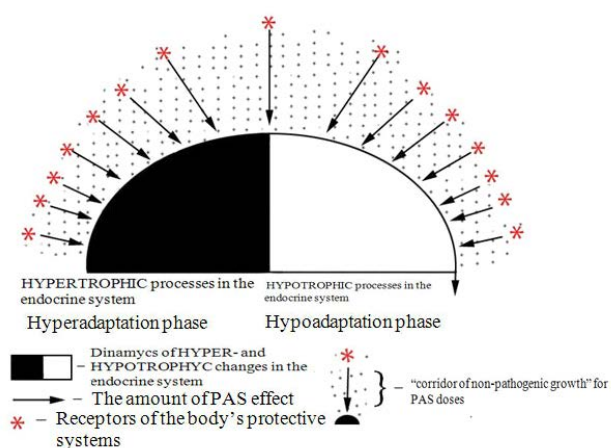
Adaptive, positive, trophic changes, during pauses, allow the sympathetic VNS just not to be exhausted, to maintain high activity for a long time - a kind of hyperfunctionality.

But there is no doubt that the mechanism of “advanced excitation” also inherents in the endocrine part of the neuroendocrine system, when the endocrine glands, releasing excessive hormones, also “take a pause” for their own trophic recovery processes, but unlike the VNS, these processes lead them to hypertrophy and hyper productivity. After all, hypertrophy resides in structures. Histological evidence of the endocrine system physiological hypertrophy with regular exposure to a medium-strength stimulus is Selye’s stress research: “adrenal glands bloom”

Speaking of adrenal hypertrophy, one should mean the adrenal cortex. As early as in 1930s, it was found that chronic morphinization causes hypertrophy of the cortical layer of the adrenal glands in rats, which produces the “adaptation hormones” - glucocorticoids (hydrocortisone, cortisone and corticosterone), increasing the tolerance of the organism to intensive stimuli [3, p.260]. There is no doubt that physiological hypertrophy of the adrenal cortex begins already during the activation reaction, since the process of

adrenal hypertrophy is not an abrupt process. There is no doubt that due to the mechanism of “advanced excitation” other endocrine glands also “take a pause” for trophic recovery processes, which leads to their physiological hypertrophy and hyperfunctionality. Evidences of adaptive hypertrophy of the endocrine system are L. Kh. Garkavi and co-authors’ observations under conditions of training and activation reactions – enlargement of the thymus gland and adrenal cortex, a prolonged increase in the thyroid and reproductive gland functions [4, p.78].

Results of the study and their discussion: Thus, under the regular exposure to PAS as a sub-extreme stimulus, while hypermetabolic processes occur in the “metabolic boiler,” accumulation of reserves takes place in the endocrine system, as a result of “advanced excitation”. This accumulation of reserves leads to adaptive physiological hypertrophy and hyperfunction of the endocrine system, which results in an increase in the tolerance of the body. That is why, a subsequent, increasing, potentially extreme dose of PAS has a sub-extreme non-pathogenic effect on the body. The condition persists for the further adaptation (see the figure below).



Thus, in PAS dependence, in each range and in the transition to a higher adaptation range, one should speak not of the reaction dyad: activation and persistent activation, but of the reaction tetrad: activation, persistent activation, then stress with “anxiety

reaction”, and the stage of resistance. Stress is considered to be a non-specific morbid basis, only if the stage of exhaustion sets in, which always reduces the body’s resistance to damaging factors. And the hypertrophy of the endocrine system that has developed to this moment, does not allow development of the final stage of stress - exhaustion. At this moment, the zone of non-reactivity separating the ranges, is observed, when the intensification of the stimulus above the stress level (in the range where adaptation has already occurred), or the weakening below the training one (the next range) does not cause any reaction. With an increase in the dose of PAS and transition to another range, everything comes around. It is more correct to call such a process not a state of chronic stress, but a state of regular, unfinished stresses. Stress without the exhaustion stage, no matter how regular it is, cannot be considered as a disease. That allows the body to transit to a higher range of adaptation without death.

This process is called (authors of this work) progressive (progressive) adaptation. Beliefs about the unity of form and function, the stereotyped thinking that “if changes in the body are acquired and irreversible, therefore, they are pathological,” have led to the erroneous judgment that the body’s dependencies on PAS should be considered as diseases. There is the expression “any disease is an adaptation.” But the opposite statement that “any adaptation is a disease” in relation to PAS dependencies is inadmissible. Thus, increase in adaptive capacity is directly proportional to the increase in a dose; the role of receptors of the body’s protective systems (* - in the figure) indicating possible PAS overdose, experience of narcotization are also important.

In PAS dependence, the increase in the exposure dose occurs through the “non-pathogenic corridor” - between the signals of the body’s protective systems - receptors indicating a possible overdose, and the hypertrophying endocrine system (see Fig.). That is why the acquired biological changes in PAS dependence are only of adaptive nature. And thereby, one should talk about the adaptive attraction, adaptively changed

behaviour, adaptively changed reactivity to PAS or, conversely, about the readaptation - deprivation syndrome, and so on.

In the final stage of the dependence, depletion of the adaptive capabilities of the organism, due to the hypertrophy of the endocrine system, the receptors of the body's protective systems indicate possible PAS overdose. This leads to a parallel decrease in the dose of PAS that a person is able to adapt, the effect of PAS turns out to be sub-extreme again, and pathology is not observed either (see Fig.).

Pathology in PAS dependence is an accompanying phenomenon.

Under alcohol exposure, when abuse with adaptive, qualitative or quantitative changes in the mechanisms responsible for the euphoria is required to achieve euphoria and acquire dependence, the accompanying increase in tolerance can be explained by the endocrine system hypertrophy.

The VNS activity and productivity of the hypertrophying endocrine system in the first stage of alcohol dependence explain maintaining the body tone during the week intervals of sobriety, in the absence of alcohol stimulation.

Compensatory stress of VNS and sufficient production of neurotransmitters or residual neurotransmitter excess, explain adrenergic tension and expressed vegetative disorders in the alcohol withdrawal syndrome - during readaptation.

The activity of the sympathetic part of VNS against the background of the gradual exhaustion of the parasympathetic department (the adrenergic system is more stable in ontogenesis, too) also explains the qualitative change (according to narcotism age) of

the sedative PAS (hypnotics, alcohol, opiates) effect on the body, transformation of their initial sedative action into a stimulating one.

The hypertrophy of the endocrine system due to prior narcotization (and hence an increase in overall resistance) explains the rapid development of alcohol dependence in former opium addicts in alcoholization: rapid increase in alcohol tolerance, the rapid formation of alcohol abstinence syndrome, the development of binge drinking (to develop alcoholism in former drug addicts, it is sufficient to develop only a specific tissue adaptation to alcohol).

As the PAS dependence develops, due to the mechanism of "advanced excitation", contributing to adaptive activity-hyperfunctionality of the sympathetic VNS, the physiological hypertrophy and hyperproductivity of the endocrine system lead to the fact that the role of the entire neuroendocrine system as a functional mechanism of protection and adaptation increases and becomes the leading one.

Conclusions:

1. Under regular sub-extreme exposure of the organism to psychoactive substance, the mechanism of "advanced excitation" allows to maintain the activity of the sympathetic VNS, leads to physiological hypertrophy of the adrenal cortex.
2. Under regular sub-extreme exposure to psychoactive substance, adaptive maintenance of sympathetic VNS activity and leads to physiological hypertrophy of the adrenal cortex. adaptive hypertrophic changes in the endocrine system lead to an increase in the tolerance of the body.
3. In psychoactive substances dependence, due to the adaptive activity of the sympathetic VNS, physio-

logical adaptive hypertrophy and hyperproductivity of the endocrine system, potentially extreme doses have a nonpathogenic sub-extreme effect on the human organism.

4. Dependence of the body on psychoactive substances due to the increased tolerance of the organism and the transformation of the effect of potentially extreme doses into the sub-extreme effect is the adaptation process.

Recommendations: It is necessary to validate the de-

pendence of the body on psychoactive substances not as a disease, but as a state of progredient (progressive)adaptation.

Biography

Baitubaev DG Narcologist of the Ridder Public State Enterprise "Psychiatric Dispensary" of the Health Department of the East Kazakhstan regional akimat, Ridder, Kazakhstan "The psychiatric dispensary"

He is Assistant-lecturer of the Semey State Medical University.



Addiction and substance Abuse Disorders

Basma Moshen Tolba

General Secretariat of Mental Health and Addiction Treatment (GSMHAT), Egypt

In my presentation I will focus on addiction and substance use disorders, taking in consideration the important definitions, which is needed to be known. The difference between substance use, abuse and dependence. The neurobiology of addiction, and epidemiology of substance use disorders (USD) as well

as symptoms and signs of USD, highlighting withdrawal symptoms, and detoxifications symptoms. How to deal with a person of drug overdose. Explain in a broad way, why addiction is a chronic disease, speaking about relapse as a part of recovery process and what are the steps that should be done during relapse by both the patient and caregivers. Represent prevention types and programs in details, world wide, in African region and in the Middle East countries respectively.

Biography

Basma Moshen Tolba Passionate Doctor with extensive experience in Psychiatric ,Mental Health field, Puplic Health, TOT mental health trainer in both governmental and private sectors. Bringing forth an empathetic and professional attitude, committed to providing patients with the best care possible. Experienced in counseling patients.I am eager to learn and improve myself as well as helping my Colleague to learn more.I hope I could help as many people as I can to see the beauty that lies in their soul and have a better life.

Scholars World Congress on
NEUROSCIENCE AND BRAIN DISORDERS FORUM

27-28 Mar 2023 | London, UK

A large red circle with a white border, containing the text 'KEYNOTE SPEAKERS Day 2'. A thin red line connects the top of the circle to a thick red horizontal bar above it.

**KEYNOTE
SPEAKERS
Day 2**





Lateralization of the Hemispheres and Exploiting Central Patterns Generators for Functional Recoveries Following Stroke and or Acquired Brain Injuries Through NeuroPhysics Therapy (NPT).

Ken Ware

NeuroPhysics Therapy Institute, Queensland, Australia

Assisting stroke survivors and patients with acquired brain injuries to begin to restore motor functions in their affected limb/s and their extremities, is best achieved when the NPT practitioner assists these patients to move both limbs, being arms and or legs simultaneously, as they initiate a mild stimulus to their psychophysical system in a prescribed manner while using select pieces of resistance exercise machines, thereby assisting them to regain awareness of a centered, bilaterally equal experience, as their limbs move in and away from their bodies in a synchronised manner and through the same positions in space time opposite each other. They can then acquire the sensation that both limbs are working together to complete the task and build upon this to amplify this experience. It usually requires the detraining of common over exertion of unaffected limbs that have been overcompensating for the affected limbs. This

then enables the affected limbs to begin to produce associated bilateral synchronized responses through up-organization of communication within relative assemblies of synapse within the affected hemispheres, circumventing and bypassing lesioned regions. Essentially the unaffected hemispheres are entraining the affected hemispheres to synchronise and mirror behaviour. From a systems perspective the two hemispheres of the brain desire to synchronise with each other under certain conditions. Central pattern generators that govern synchronised bipedal limb movements become stimulated in a manner that begins to produce bipedal activity once a certain level of structure and functionality has been achieved. This presentation would include video recordings of such patients and their outcomes that have been taken place over a very small timeframe with NeuroPhysics Therapy.

Biography

Ken Ware NeuroPhysics Therapy was founded upon innocent paradigm-shifting discoveries that Ken Ware made back in 1982, relating to the extreme sensitivities there are surrounding the intrinsic relationship the human nervous system has with its environment. He observed that because of this extreme sensitivity, very tiny influences could cause a major up or down-shift in the psychophysical stability of the system. Ken has globally famed Ken Ware NeuroPhysics Therapy through his unprecedented accomplishments with his patients who travel to see him from all over the world. These accomplishments have attracted credible media exposure which has accelerated the global knowledge and respect of Ken Ware NeuroPhysics Therapy and consequently the global demand for therapy. Ken's dream is to have a large number of Ken Ware NeuroPhysics Therapy practitioners trained and educated and practicing all over the globe to enable many more people in the world to access this unique results-producing therapy.



Porphyromonas gingivalis Outer Membrane Vesicles as the Major Causative factor of Neuro-inflammation/degeneration leading to Cognitive Decline, Dementia and Alzheimer's Disease

Peter L. Nara

Keystone Bio Inc., USA

Addressing novel mechanisms and effective therapeutic treatments for cognitive decline, Dementia and Alzheimer's Disease is a major public health need. Keystone Bio, have identified that specific virulent strains of *Porphyromonas gingivalis* (Pg) and the release of specific virulence factors/toxins in the oral cavity as the primary driver/causation of systemic/neuro-vascular inflammation/degenerative diseases i.e. cognitive decline/dementias/Alzheimer's disease (Nara et. al 2021). A recent landmark finding was reported in a sub-cohort analysis from a Phase 2/3 GAIN trial (n=238) demonstrated that lowering the load of Pg in the mouth leads to a significant improvement of cognitive slowing at both 24 and 48 weeks in participants with mild to moderate AD. Another study showed lowering the load of Pg in the mouth had a favorable effect on AD-related brain atrophy (<https://doi.org/10.1002/alz.12378>). Pg OMVs and systemic system diseases has many well defined examples such as: cardiometabolic diseases- Pg OMVs atten-

uate insulin induced Akt/GSK-3_β signaling in hepatic HepG2 cells, thereby causing changes in glucose metabolism in the liver and promoting the development of diabetes and increase vascular permeability by cleaving endothelial cell connexins such as PECAM-1, thereby promoting cardiovascular diseases.

Keystone Bio has further developed both a companion diagnostic (CDx) and a clinical, proof-of-concept tested, first generation, safe, efficacious, precision, bio-therapeutic murine monoclonal antibody (KB-001) for the diagnosis, treatment and monitoring against the oral bacteria and major virulent factor/toxin of Pg. The antibody engagement is with the later stages of the complex virulent factor/toxin secretion containing outer membrane vesicles from the bacteria thereby interfering/stopping all necessary metabolic, host defense, energy-producing sources, adherence and biofilm formation and integrity (Nara et. al 2021). The talk will review what now seems like a solid case for causation in the role of virulent/toxin secreting strains of in neuro-inflammation leading to cognitive decline, dementia, Sporadic Alzheimer's disease and possibly Parkinson's.

Biography

Dr. Nara is one of the co-founders, the Chief Scientific Officer and President Business Development for Keystone Bio Inc. in St. Louis, Mo., a Systemic-Oral Health Biotech with bio-therapeutics and CDx or the elimination of a specific oral virulent bacterial associated with systemic inflammation. He holds a M.Sc. in Immunopharmacology, a combined Doctor of Veterinary Medicine and Ph.D. (retro-virology/oncogenesis) from The Ohio State University, 4 year combined residency in Comparative Pathology and NIH post-doctoral Fellowship at the Armed Forces Institute of Pathology and a NIH. He is also elected Fellow of the American Association for the Advancement of Science in 2011 and distinguished Alumni of The Ohio State University College of Veterinary Medicine 2014.



Early Signs of Elevated Intracranial Pressure (ICP) on Computed Tomography Correlate with Measured ICP in the Intensive Care Unit and Six-Month Outcome in the Progesterone for Traumatic Brain Injury, Experimental Clinical Treatment (ProTECTIII) Trial Cohort

Brandon Lucke Wold

University of Florida, USA

Background: Traumatic brain injury (TBI) is a leading cause of death and disability in the United States. Early triage and treatment after TBI have been shown to improve outcome. However, identifying patients at risk for increased intracranial pressure (ICP) via baseline computed tomography (CT) has not previously been validated in a prospective dataset. The predictive values of acute CT findings of elevated ICP and direct ICP measurement are correlated with 6-month patient outcomes after TBI.

Methods: Data were obtained from the Progesterone for Traumatic Brain Injury, Experimental Clinical Treatment (ProTECTIII) multicenter clinical trial. Baseline CT scans for 881 participants were individually reviewed by a blinded central neuroradiologist. Five signs of elevated ICP were measured (sulcal obliteration, lateral ventricle compression, 3rd ventricle compression, midline shift, and herniation). Associations between signs of increased ICP and outcomes (6-month functional outcome and mortality) were assessed. Sec-

ondary analyses explored the relationships between bleed phenotype/anatomic location, sustained ICP ≥ 20 mmHg, and surgical intervention(s). Univariate and multivariate logistic / linear regressions were performed; $p < 0.05$ is defined as statistically significant. SASS JUMPIN SPSS R ? □

Results: Imaging characteristics associated with ICP include sulcal obliteration ($p=0.029$) and third ventricular compression ($p=0.039$). Univariate regression analyses indicated that increasing combinations of the five signs of elevated ICP were associated with mortality, poor functional outcome, and time to death. There was also an increased likelihood of mortality if patients required craniotomy (OR=4.318, 95% Confidence Interval [1.330–16.030]) or hemicraniectomy (OR=2.993 [1.109–8.482]). On multivariate regression analyses, hemorrhage phenotype was associated with mortality (posterior fossa, OR=3.208 [1.120–9.188] and basal ganglia, OR=3.079 [1.178–8.077]). Volume of hemorrhage > 30 cc was associated with increased mortality, OR=3.702 [1.575–8.956]). The proportion of patient hours with sustained ICP ≥ 20 mmHg, and maximum ICP ≥ 20 mmHg, were also directly correlated with increased mortality (OR=64.99 [7.731–635.51]; and OR=1.025 [1.004–1.047]), but not with functional outcome. Poor functional outcome was predicted by concurrent presence of all five radiographic signs of elevated ICP (OR=4.44 [1.514–14.183]) and /or presence of frontal lobe (OR=2.951 [1.265–7.067]), subarachnoid (OR=2.231 [1.067–4.717]), or intraventricular (OR=2.249 [1.159–4.508]) hemorrhage. Time to death was predicted by total patient days of elevated ICP ≥ 20 mmHg (OR=4.597 [2.182, 6.993]) in the first two weeks of hospitalization.

Conclusions: Sulcal obliteration and third ventricular compression are radiographic signs of elevated ICP associated with measured ICP ≥ 20 mmHg. These radiographic biomarkers are associated with patient outcome. There is potential utility of ICP-related imaging variables in triage and prognostication for patients following moderate-severe TBI.

Biography

Brandon Lucke-Wold was born and raised in Colorado Springs, CO. He graduated magna cum laude with a BS in Neuroscience and distinction in honors from Baylor University. He completed his MD/PhD, Master's in Clinical and Translational Research, and the Global Health Track at West Virginia University School of Medicine. His research focus was on traumatic brain injury, neurosurgical simulation, and stroke. At West Virginia University, he also served as a health coach for the Diabetes Prevention and Management program in Morgantown and Charleston, WV, which significantly improved health outcomes for participants. In addition to his research and public health projects, he is a co-founder of the biotechnology company Wright-Wold Scientific, the pharmaceutical company CTE cure, and was a science advocate on Capitol Hill through the Washington Fellow's program.

He has also served as president of the WVU chapters for the American Association of Pharmaceutical Scientists, Neurosurgery Interest group, and Erlenmeyer Initiative Entrepreneur group. In addition, he has served as vice president for the graduate student neuroscience interest group, Nu Rho Psi Honor Society, and medical students for global health. He was an active member of the Gold Humanism Honor Society and Alpha Omega Alpha Honor Society. He is currently a member of the Young Neurosurgeons' Committee. He is married to Noelle Lucke-Wold, and has a toddler daughter named Esme. As a family, they enjoy running with their dogs, rock climbing, and traveling the world. In his spare time, Brandon frequently runs half marathons and 10ks together with his wife. Brandon also enjoys reading and discussing philosophy and playing chess. He is excited to join the neurosurgery residency program at University of Florida.



High-resolution functional MRI of differential laminar activation in the human entorhinal cortex

Jun Hua

Johns Hopkins University School of Medicine, Baltimore, Maryland, United States

We provide new evidence for differential neuronal activation in the superficial versus deep layers of the entorhinal cortex associated with encoding and retrieval memory processes respectively in cognitively normal adults. A novel functional MRI method was employed allowing us to measure robust functional MRI signals in both the medial and lateral entorhinal cortex that was not possible in previous studies. The methodology established here in healthy human subjects lays a solid foundation for subsequent studies investigating layer-specific and region-specific changes in the entorhinal cortex associated with memory impairment in various conditions such as Alzheimer's disease.

Biography

Dr. Hua is an associate professor in the F.M. Kirby Research Center for Functional Brain Imaging at Kennedy Krieger Institute. He also holds a joint appointment as an associate professor in the Russell H. Morgan

Department of Radiology at Johns Hopkins University. Dr. Hua received his master's (2005) and doctoral (2009) degrees in biomedical engineering and electrical engineering at the Johns Hopkins University. His doctoral training centered on the development of novel MRI technologies for in vivo physiological imaging in the brain, such as protein content and cerebral blood volume. After completing a post-doctoral fellowship in the Department of Radiology at the Johns Hopkins University from 2009 to 2010, Dr. Hua became a faculty member in the Department of Radiology at Johns Hopkins University School of Medicine and Kennedy Krieger Institute. Dr. Hua's research has centered on the development of novel MRI technologies for in vivo functional and physiological imaging in the brain, and the application of such methods for studies in healthy and diseased brains. These include the development of human and animal MRI methods to measure functional brain activities, cerebral perfusion and oxygen metabolism at high (3 Tesla) and ultra-high (7 Tesla and above) magnetic fields. He is particularly interested in novel MRI approaches to image small blood and lymphatic vessels in the brain. Collaborating with clinical investigators, these techniques have been applied 1) to detect functional, vascular and metabolic abnormalities in the brain in neurodegenerative diseases such as Huntington's disease (HD), Parkinson's disease (PD), Alzheimer's disease (AD) and mental disorders such as schizophrenia; and 2) to map brain functions and cerebrovascular reactivity for presurgical planning in patients with vascular malformations, brain tumors and epilepsy.



Increased telomerase improves motor function and alpha-synuclein pathology in a transgenic mouse model of Parkinson's disease associated with enhanced autophagy

G. Saretzki

Biosciences Institute, Newcastle University

Protective effects of the telomerase protein TERT have been shown in neurons and brain. We previously demonstrated that TERT protein can accumulate in mitochondria of Alzheimer's disease (AD) brains and protect from pathological tau in primary mouse neurons. This prompted us to employ telomerase activators in order to boost telomerase expression in a mouse model of Parkinson's disease (PD) overexpressing human wild type α -synuclein. Our aim was to test whether increased Tert expression levels were able to ameliorate PD symptoms and to activate protein degradation.

We found increased Tert expression in brain for both

activators which correlated with a substantial improvement of motor functions such as gait and motor coordination while telomere length in the analysed region was not changed. Interestingly, only one activator (TA- 65) resulted in a decrease of reactive oxygen species from brain mitochondria. Importantly, we demonstrate that total, phosphorylated and aggregated α -synuclein were significantly decreased in the hippocampus and neocortex of activator-treated mice corresponding to enhanced markers of autophagy suggesting an improved degradation of toxic α -synuclein. We conclude that increased Tert expression caused by telomerase activators is associated with decreased α -synuclein protein levels either by activating autophagy or by preventing or delaying degradation mechanisms which are impaired during disease progression. This encouraging preclinical data could be translated into novel therapeutic options for neurodegenerative disorders such as PD.

Biography

Gabriele has completed her PhD 1990 at Humboldt University Berlin and performed most of her postdoctoral studies at the Institute for Ageing and Health in Newcastle upon Tyne (UK) where she is a Lecturer in Ageing Research since 2002. Her main interests are telomeres, telomerase, senescence, ageing, oxidative stress, mitochondria stem cells and brain. She has pioneered work on non-canonical functions of the telomerase protein TERT shifting her focus recently to brain ageing and neurodegenerative diseases. She has published more than 87 papers in peer-reviewed journals and is an editorial board member of BMC Biology, PloS One and Oxidative Medicine and longevity.

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A large red circle with a white border, containing the text 'SPEAKERS Day 2'. A thin red line connects the top of the circle to a thick red horizontal bar above it.

SPEAKERS
Day 2





Identifying hidden brain states responsive to transcranial stimulation

Wen Li

Florida state University, USA

Transcranial alternating current stimulation has been increasingly recognized in research and clinical intervention. However, the efficacy of tACS (and other non-invasive brain stimulation technologies) remains modest. A major and yet underappreciated reason is that the brain undergoes spontaneous fluctuations in its activity (aka, "hidden states"), only some of which would respond to and benefit from brain stimulation. To date, little is known about such dynamics in the brain's responsiveness. Here, we approached this problem by acquiring functional magnetic resonance imaging (fMRI) during alpha-frequency (10 Hz) transcranial alternating current simulation (tACS) while participants performed a standard sustained attention task. Behaviourally, we demonstrated significant improvement in sustained attention under tACS (vs. sham stimulation). Applying machine learning and Hidden Markov modelling of fMRI timeseries, we identified eight brain states, of which five were functionally meaningful. We further observed that two of

these five states were responsive to alpha-tACS, both of which were task-negative states (characterized by the deactivation of the executive control network and salience network and/or activation of the default mode network). These two states were rendered less stable (i.e., shorter lifetime) by tACS (vs. sham stimulation). These results thus confirm the brain-state dependency of tACS, highlighting the need to track real-time brain states for optimal stimulation. Importantly, our study identified useful biomarkers that could be integrated into closed-loop brain stimulation in general. Finally, future directions will be discussed with respect to applying such biomarkers for transcranial modulation of threat learning and related pathophysiology in fear-related disorders.

Biography

Dr. Li received a PhD in Psychology at Northwestern University (IL, USA), followed by a postdoctoral fellowship in cognitive affective neuroscience at the Feinberg Medical School of Northwestern University. She then took on an assistant professor position at the University of Wisconsin-Madison and was recruited to Florida State University through the campus-wide Brain Initiative to lead research in human neuroimaging. Currently, she is an Associate Professor in psychology and neuroscience and directs the Cognitive-Affective Neuroscience Laboratory at Florida State University. Dr. Li has consistently published high-quality work, appearing in *Science*, *Neuron*, *Brain*, and *PNAS*, and has been awarded over \$3M research funding from major agencies such as the National Institute of Health and Department of Defense. Dr. Li has received multiple investigator awards from prestigious scientific societies. She has been elected as an NIH study section Regular Member and served many European government funding agencies as an expert reviewer.



Electrochemical miRNA-34a-based biosensor for the diagnosis of Alzheimer's Disease

Raquel L. Pereira

University of Porto, Portugal

Alzheimer's Disease (AD) is the most common form of dementia and a major cause of death and disability in the elderly. The diagnostic tools currently available are expensive and invasive, so there is an urgent need to develop new, less-costly, and less-invasive tools for this disease. The work presented here reports the development of an electrochemical miRNA-based biosensor for the diagnosis of AD, based on the modification of carbon screen-printed electrodes (C-SPEs) with gold nanostructures and a complementary anti-miR-34a oligonucleotide probe. The designed biosensor showed good target affinity and allowed the detection of miR-34a within a linearity range of 100

pM to 1 μ M, both in buffer and in foetal bovine serum. Moreover, the biosensor's response remained unaffected in the presence of two potentially interfering serum compounds (miR-107 and creatinine), indicating that it is selective for the target miRNA. As a proof of concept, the biosensor detected the presence of miR-34a in the cell culture media of the SH-SY5Y neuronal cell line, a common AD cellular model. Furthermore, the biosensor was able to detect an increase in extracellular miR-34a when this cell line was exposed to a neurotoxicant stimulus, 6-hydroxidopamine (6-OHDA), which is known to boost the expression of miR-34a. Overall, this new biosensor represents a breakthrough for the introduction of a low-cost, minimally invasive sensor for the diagnosis of AD, even at the earliest stages.

Biography

Raquel L. Pereira is a research fellow at BioMark, Sensor Research at ISEP, Porto, and has an MSc in Molecular Bioengineering from the University of Porto. Raquel started working with biosensors in her Master Thesis, during which she developed an electrochemical miRNA-based biosensor for the diagnosis of Alzheimer's Disease. This work received great appraisal by the judging committee and is expected to be published soon. Since then, Raquel has branched-out within the field of biosensors and is now working on a project which aims to develop self-indicated biosensors integrated into flexible membranes of natural origin for application in chronic wounds.



Herbal remedies for cerebral ischemia and other neurological issues

Priyanka Chandolia

Nims Institute of Pharmacy, National Institute of Medical Sciences University, Jaipur, Rajasthan, India

Cerebral ischemia is a disease with major mechanism of acute brain damage caused by a decrease in blood supply to the brain and damages other parts. Cerebral ischemia is a medical emergency that, if left untreated, can lead to cerebral infarctions or worldwide hypoxic-ischemic encephalopathy, both of which can end in death or lifelong impairment. Herbal medications have potent therapeutically value that may treat cerebral ischemia and other brain disorders. The intriguing function of herbal medicine, a natural bioactive chemical present in vegetables, fruits, and traditional medicines. Curcumin, lycopene, ginsenoside, vitexin, and baicalin, have demonstrated remarkable neuroprotective benefits against ischemic-induced harm. In addition to anticancer, antioxidant, and immunomodulatory qualities, these reported herbal medications possess neuroprotective benefits by increasing neuronal survival, tissue perfusion, and ce-

rebral blood flow, and decreasing ischemic-related apoptosis. Furthermore, these herbal preparations has an anti-amyloidogenic impact and slows the death of dopaminergic neurons in the brain. These findings show that herbal medications might be used as a possible therapeutic agent in cerebral ischemia and brain disorders.

Biography

I am a healthcare professional, with a diversified experience in research and academia domain, currently working as an Assistant Professor in National Institute of Medical Sciences, Jaipur Rajasthan, India. My background interest area is based on neuroscience field and neurodegenerative disorders such as Huntington's Disease, Alzheimer's Disease and many more. Additionally I have participated in many neuroscience conferences such as International Brain Research Organization, and Alzheimer's Association International Conferences. I have also awarded with the Travel Fellowship for the Alzheimer's Association International Conference® 2021 (AAIC®) which was hosted in Denver, Colorado, United States. Furthermore I have participated in various webinars, seminars, poster and oral presentations and awarded with the certificate of appreciation and participation. I have also worked on research papers, review papers and book chapter publications and still working on publications. I am compassionate and expert in delivering the lectures and actively participate in all aspects of education. Looking to contribute my knowledge, skills and to explore more in research, teaching and pharmacovigilance field that offers a genuine opportunity for career progression. I have remarkable capabilities to guide, develop and motivate the students at higher levels.



Case Study: Identification of minimum essential therapeutic mixtures from Cannabis plant extracts by screening in cell and animal models

Andrea L. Small-Howard

GbS Global Biopharma, Canada

Medicinal Cannabis has shown promise for the symptomatic treatment of a variety of human disorders, but patient exposure to whole plant extracts may be undesirable due to concerns around safety, consistency, legality, psychoactivity, and standard routes of delivery (i.e., smoking and vaping). We hypothesized that within Cannabis plant extracts there would be a minimal essential compound set that could safely and consistently reproduce the positive therapeutic effects of Cannabis without the need to use whole plant extracts. Using sequential *in silico*, *in vitro*, and *in vivo* screens, unique and patentable subsets of Cannabis components with therapeutic potential have been identified and validated in cell and animal models. Cell-based screening has revealed promising complex therapeutic mixtures for the treatment of Parkinson's disease, chronic pain, and inflammation. Using animal-based screening, we have validated the therapeutic potential of simplified disease-specific, minimum essential mixtures (MEM), each containing 3 to 5 cannabinoids and terpenes. The case study presented herein highlights the potential for the development of disease-specific, cannabinoid-based therapeutics for the prescription drug market to treat Parkinson's disease, among others. Our disease-specific MEM are produced for clinical evaluation using synthetic homologs of cannabis-based ingredients

incorporated into Oral Dissolving Tablets (ODT) to increase the stability, bioavailability, and ease-of-use of the ingredients relative to Cannabis plant extracts. Minimum Essential Mixtures are designed to retain increased therapeutic effectiveness from molecular synergies within the original plant extracts, but with the manufacturing efficiencies, quality assurances, and regulatory advantages of single ingredient drugs.

Biography

Dr. Andrea Small-Howard has 25 years of scientific research and executive experience in the biopharma industry supervising research & development, manufacturing, and quality control in global divisions. Dr. Small-Howard has taken novel biological products from ideation through commercialization. She has been named an inventor on seventy+ patent applications, taken the lead in obtaining regulatory approvals from the U.S. Food and Drug Administration ("US FDA"), and orchestrated commercial licensing deals.

Currently, Dr. Small-Howard leverages her broad biopharmaceutical industry knowledge as the President, Chief Science Officer, and member of the Board of Directors at both GB Sciences, Inc. (OTCQB:GBLX), and their wholly-owned Canadian subsidiary, GBS Global Biopharma, Inc. Dr. Small-Howard brings her passion for advancing research on phytochemical compounds to her current roles. She envisages bringing more phytomedicines to market through an innovative AI-based drug discovery engine and biopharmaceutical drug development program for disease-specific indications.

Dr. Small-Howard has researched cannabinoids for over 20 years, leading a project group dedicated to the study of cannabinoids in the immune system as an NIH-funded post-doctoral fellow. In this work she published one of the earliest studies of cannabinoid impacts on pro-inflammatory immunocytes. More recently she has contributed to published studies on consumer protection issues surrounding 'medicinal' Cannabis chemovars in Nevada, co-authored scholarly reviews on cannabinoids in heart disease and Parkinson's Disease, co-authored mechanistic studies on cannabinoid and terpene regulation of ion channels,

and co-authored an innovative study demonstrating the utility of nanoparticles as delivery vehicles for Cannabis-derived therapeutic compounds.

Dr. Small-Howard is the architect of a strategic vision at Gb Sciences/GbS Global Biopharma to make safe, effective, standardized cannabinoid medicines avail-

able to patients where its use can be supported with rigorous evidence. To achieve standardization in their cannabinoid-containing, optimized therapeutic mixtures, the Company is using synthetic cannabinoids produced under current Good Manufacturing Practices (cGMP), which are identical in both structure and function to the homologous plant cannabinoids.



Therapeutic ketosis and the broad field of applications for the ketogenic diet: Ketone ester applications & clinical updates

Raffaele Pilla

St. John of God Hospital – Fatebenefratelli, Benevento, Italy

It has been recently shown that nutritional ketosis is effective against seizure disorders and various acute/chronic neurological disorders. Physiologically, glucose is the primary metabolic fuel for cells. However, many neurodegenerative disorders have been associated with impaired glucose transport/metabolism and with mitochondrial dysfunction, such as Alzheimer's/Parkinson's disease, general seizure disorders, and traumatic brain injury. Ketone bodies and tricarboxylic acid cycle intermediates represent alternative fuels for the brain and can bypass the rate-limiting steps associated with impaired neuronal glucose metabolism. Therefore, therapeutic ketosis can be considered as a metabolic therapy by providing alternative energy substrates. It has been estimated that the brain derives over 60% of its total energy from ketones when glucose availability is limited. In fact, after prolonged periods of fasting or ketogenic diet (KD), the body utilizes energy obtained from free fatty acids (FFAs) released from adipose tissue. Because the brain is unable to derive significant energy from FFAs, hepatic ketogenesis converts FFAs into ketone bodies-hydroxybutyrate (BHB) and acetoacetate (AcAc)-while a percentage of AcAc spontaneously decarboxylates to acetone. Large quantities of ketone bodies accumu-

late in the blood through this mechanism. This represents a state of normal physiological ketosis and can be therapeutic. Ketone bodies are transported across the blood-brain barrier by monocarboxylic acid transporters to fuel brain function. Starvation or nutritional ketosis is an essential survival mechanism that ensures metabolic flexibility during prolonged fasting or lack of carbohydrate ingestion. Therapeutic ketosis leads to metabolic adaptations that may improve brain metabolism, restore mitochondrial ATP production, decrease reactive oxygen species production, reduce inflammation, and increase neurotrophic factors' function. It has been shown that KD mimics the effects of fasting and the lack of glucose/insulin signaling, promoting a metabolic shift towards fatty acid utilization. In this work, the author reports a number of successful case reports treated through metabolic ketosis.

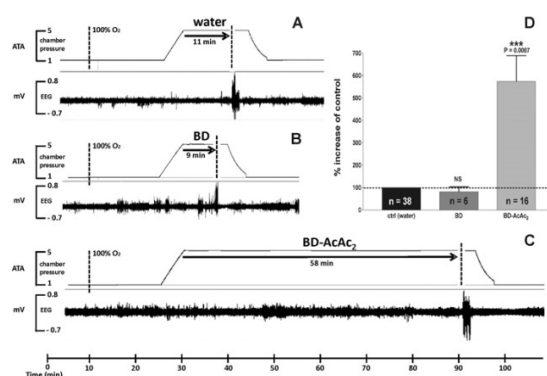


Figure 1: Ketone Ester significantly increased resistance against Central Nervous System Oxygen Toxicity seizures (D'Agostino D.P. et al., 2013 Am J Physiol Regul Integr Comp Physiol. 304(10):R829- 36).

Biography

Raffaele Pilla, Pharm.D., Ph.D., Doctor Europaeus, received his Master's degree in Pharmacy at G. d'Annunzio University in Chieti-Pescara, Italy in 2005, where he also served internships at the Cell Physiology Laboratory and Molecular Biology Laboratory. Prior, he was an Erasmus Student at Faculté de Pharmacie de Reims in Reims, France. He received his Doctor Europaeus in 2010 from Pitié-Salpêtrière Institute in Paris,

France. Also in 2010, he received his Ph.D. in Biochemistry,

Physiology, and Pathology of Muscle at G. d'Annunzio University in Chieti-Pescara, Italy. He was hired as a Postdoctoral Scholar in the Department of Pharmacology and Physiology at the University of South

Florida in Tampa, on two research grants funded by the Office of Naval Research (US Navy) and Divers' Alert Network. He has written and lectured widely worldwide. He has been involved in ongoing research at the University of South Florida with the use of ketone esters.



Artificial intelligence and virtual reality Kinect rehabilitation in stroke patients with Unilateral spatial neglect

Lama Saad El-Din Mahmoud

October 6 University, Egypt

Background: People with neglect suffer from various spatial deficits in several modalities, which in many cases impair everyday functioning. Virtual reality (VR) is a form of interaction between humans and computers in which a real or imaginary environment is simulated. Users interact with that world and manipulate it. Artificial intelligence (AI) can increase the efficacy of promoting and strengthening human activities

Purpose: to investigate the extent to which the use of VR as an effective AI treatment technique for patients experiencing unilateral spatial neglect after stroke.

Subjects: Thirty patients experiencing unilateral spatial neglect after stroke.

Methods: patients were randomly assigned to two groups; a study group and a control group. The study group received VR Kinect rehabilitation and conventional treatment for eight weeks and the control group received conventional treatment using behavioral rehabilitation methods of physical therapy. The disorder was diagnosed with paper and pencil tests of extrapersonal neglect, Catherine Bergego Scale (CBS) and recently, promising new methods based on number of repetitions of tasks on VR.

Results: There was a highly significant difference between study and control groups as the p-value was (0.0001) which indicated that the study group shows improvement more than the control group, and there was correlation between the line cancellation task, the CBS, and the VR repetitions.

Conclusion: This study revealed that eight weeks of VR as an effective AI rehabilitation for every patient was a beneficial therapeutic technique on unilateral spatial neglect in stroke patients.

Biography

Lama Saad El-Din Mahmoud has been currently working as lecturer of physical Therapy for Neuromuscular disorders & its surgery, faculty of physical therapy, October 6 university, Egypt and working as Neurology and Neurosurgery Consultant for Neuro-Rehabilitation . Ph.D. degree, Department of Physical Therapy for Neuromuscular Disorders and its Surgery, faculty of physical therapy, Cairo university



PUFA repair macrophage transcriptome and glycome for amyloid- β brain clearance and dementia protection in Alzheimer's disease. Milan Fiala, M.D. UCLA, Los Angeles, CA 90024

Milan Fiala

UCLA, USA

BACKGROUND: Macrophages of healthy subjects have a pro-resolution phenotype, upload amyloid- β ($A\beta$) into endosomes, and degrade $A\beta$, whereas macrophages of patients with Alzheimer's disease (AD) generally have a pro-inflammatory phenotype and lack energy for brain clearance. **OBJECTIVE:** To clarify the pathogenesis of sporadic AD and therapeutic effects of polyunsaturated fatty acids (PUFA) with vitamins B and D and antioxidants on monocyte/macrophage (MM) migration in the AD brain, MM transcripts in energy and $A\beta$ degradation, MM glycome, and macrophage clearance of $A\beta$. **METHODS:** We followed for mean 31.3 months 10 PUFA-supplemented neurodegenerative patients (3 with subjective cognitive impairment (SCI), 2 with mild cognitive impairment (MCI), 3 MCI/vascular cognitive impairment, 2 with dementia with Lewy bodies) and 7 non-supplemented caregivers. We examined monocyte migration in

the brain and a blood-brain barrier model by immunohistochemistry and electron microscopy; macrophage transcriptome by RNAseq; macrophage glycome by N-glycan profiling and LTQ-Orbitrap mass spectrometry; macrophage phenotype and phagocytosis by immunofluorescence microscopy; and energetic effects in XF96 Seahorse Flux Analyzer. **RESULTS:** MM invade $A\beta$ plaques, upload but do not degrade $A\beta$, and release $A\beta$ into vessels, which develop cerebrovascular amyloid angiopathy (CAA); PUFA upregulate $A\beta$ degradation enzyme transcripts and energy in macrophages; PUFA enhance sialylated N-glycans in macrophages; PUFA reduce oxidative stress and increase pro-resolution MM phenotype, mitochondrial membrane potential, and $A\beta$ phagocytosis ($p < 0.001$). **CONCLUSION:** Macrophages of SCI, MCI, and AD patients have interrelated defects in the transcriptome, glycome, $A\beta$ phagocytosis, and $A\beta$ degradation. PUFA mend macrophage transcriptome, enrich glycome, enhance $A\beta$ clearance, and benefit the cognition of early-stage AD patients.

Biography

Milan Fiala, M.D. (Geneva), M.Sc. (Harvard), Research Professor MCDB, UCLA Life Sciences. After M.D. graduation from the University of Geneva, he trained at Harvard and University of Washington in epidemiology and virology. He is Board Certified in Internal Medicine, Infectious Diseases, and Clinical Microbiology. He investigated cytomegalovirus (CMV) opportunistic infections in organ transplantation and HIV-1/CMV in AIDS encephalopathy. His laboratory is studying the immune and central nervous systems of HIV-1, Alzheimer's disease and amyotrophic lateral sclerosis patients by RNA-seq and functional testing with the goal to develop immune therapies: in AD to increase energy by the immune system for brain clearance, and in ALS to inhibit autoimmune inflammation in the brain and spinal cord.



TWO-YEAR LONGITUDINAL FOLLOW-UP OF VISUAL ILLUSIONS AND HALLUCINATIONS IN PARKINSON'S DISEASE

Ana MARQUES

Clermont-Ferrand University Hospital, France

Background: Previous longitudinal studies assessing visual hallucinations in Parkinson's disease (PD) have not specifically considered the respective evolution of visual illusions (VI) and visual hallucinations (VH), neither did they assess the role of ocular pathology on the evolution of those manifestations.

Objective: We aimed to determine whether VI evolve towards VH along the time in PD, and whether ophthalmological treatment may have a positive effect on the prognosis of those visuo- perceptive manifestations.

Methods: PD patients from a previous cohort (PD with VI (n=26), PD with VH (n=28), and PD without VI or VH (n=28)) were contacted by phone two years later and questioned regarding the current presence of VI or VH, any current visual complaints, and the occurrence of any ophthalmological or antipsychotic treatment during the two-year period, as well as any dopathery adjustment.

Results: Among PD-VI patients, 43% normalized, 48% remained PD-VI, 9% evolved towards coexisting VI and VH, and none converted to pure VH. Among PD-VH patients, 42% normalized, 32% remained PD-VH, 21% evolved towards coexisting VI and VH, and only 5% converted to pure VI. At follow-up, visual complaints remained greater among PD-VI and PD-VH compared to controls (p=0.005). Among PD-VI and PD-VH who became control at up, 35% received ophthalmologic treatment, 29% antipsychotic treatment, and 23% a dopathery reduction.

Conclusion: PD Patients with VI do not necessarily evolve towards VH over time, and ophthalmological treatment may have a positive effect on the prognosis of those visuo- perceptive manifestations in PD similar to antipsychotic treatment and dopathery adjustment.

Biography

Ms. Marques works in Clermont, FL and specializes in Geriatric Medicine. Ms. Marques is affiliated with SouthLakeHospital.



Development of Effective Gene Therapy for CJD

Qingzhong Kong

Case Western Reserve University, United States

Creutzfeldt-Jakob disease (CJD) is the most common prion disease in humans, which

progresses rapidly, is always fatal, and has no treatments. Effective and long-lasting therapeutics against CJD and other human prions is urgently needed.

The cellular prion protein (PrP) is essential for both prion replication and prion pathogenesis but not required for life or cell survival, making it an attractive target for prion therapeutics development. Knocking out or knocking down the PrP gene expression with siRNA/shRNA or antisense oligonucleotides (ASOs) targeting the PrP gene has been shown to be safe and effective against rodent prions in mouse models. But the ASO and shRNA/siRNA approaches have not been

tested against human prions, and there has been no report of rAAV-based shRNA/siRNA gene therapy for any prion disease.

We show that 4 shRNAs each knocked down human PrP by ~90% in a human neuroblastoma cell line, and one rAAV-shRNA administered retro-orbitally at near clinical onset knocked down human PrP by ~26% in the brain and led to a significant extension of survival in CJD-inoculated transgenic mice overexpressing human PrP-129M, a well-established mouse model for human CJD diseases. Our data indicate that rAAV-based gene therapy via systematic shRNA/siRNA delivery is a promising and realistic approach for the development of effective CJD treatments. Moreover, this gene therapy approach also has great potential in the treatment of Alzheimer's disease, Parkinson's disease and several other common neurodegenerative diseases where the cellular PrP plays a critical role in pathogenesis.

Biography

Kong graduated with BS and MS degrees in Biochemistry at Nanjing University in 1987 and 1990, respectively, and he obtained his PhD degree in Molecular Virology at the University of Massachusetts. He received his postdoctoral training in Molecular Immunology at Yale University from 1996 to 2000, and joined the Department of Pathology at Case Western Reserve University as an assistant professor in 2000. He is currently a tenured Associate Professor of Pathology and Neurology and associate director of the National Prion Disease Pathology Surveillance Center at the School of Medicine, Case Western Reserve University.



Resistance of glioblastoma cells to photodynamic therapy

Laura N. Milla Sanabria

National Univeristy of Rio Cuarto, Argentina

Glioblastoma (GBM) is the most common and most severe form of primary brain cancer. Despite multi-modal therapy combining surgery, radiotherapy and chemotherapy, prognosis of patients is dismal. Photodynamic therapy (PDT) is based on the activation of a photosensitizer by light in a determined wavelength, which generates reactive oxygen species in the target tissues, leading to cell death. It has been observed that the surgical resection guided by photosensitizer fluorescence have improved the results of treatment against this disease, prolonging the survival of patients by a few months. Also, clinical trials have reported potential improvements in the therapeutic re-

sponse after PDT. Among some of the difficulties that treatments against GBM still have to overcome are the infiltrative capacity of GBM cells, the blood-brain barrier that makes it difficult for chemotherapeutic drugs to reach the tumor, the cellular heterogeneity, the resistance mechanisms of the neoplastic cells and the presence of tumor stem cells. In our laboratory we are characterizing cell populations of human GBM lines with the aim of describing mechanisms of cell resistance to PDT. There is still much to investigate with regard to the response of the GBM population to this treatment. Studies of GBM resistance would help to better understand the causes of tumor recurrence after PDT and to develop new therapeutic proposals in this field of oncology.

Biography

Dr. Laura N. Milla Sanabria develops her research work looking for mechanisms of tumor resistance to photodynamic therapy (PDT). She has developed studies on biodistribution, biocompatibility and phototherapeutic efficacy in mice using synthetic photosensitizers. L. Milla has completed her doctorate at National University of Río Cuarto (under the supervision of Dr. Viviana A. Rivarola) and at Autonomous University of Madrid (under the supervision of Dr. Ángeles Juarranz). She has isolated and characterized PDT-resistant glioblastoma cells with the aim of studying possible therapeutic targets and will expand her studies on this topic to contribute to the treatment of this severe type of cancer.



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