

Global Summit on **BRAIN DISORDERS AND THERAPEUTICS**

June 07, 2021 | Webinar

Application of human induced pluripotent stem cell-derived threedimensional cerebral organoids in modeling developmental brain disorders**Xiaowen Bai, Thiago Arzua, Yasheng Yan***Department of Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, U.S.A*

Maternal alcohol exposure during pregnancy can substantially impact the development of the fetus, causing cognitive dysfunction and psychiatric disorders, with the mechanisms largely unknown. Recently developed 3D human cerebral organoids from induced pluripotent stem cells are similar to fetal brains in the aspects of development and structure. These models allow more relevant in vitro systems for studying FASDs than animal models. We found that 50 mM alcohol exposure for 6 hours induced acute apoptosis on organoids. The apoptotic effects of alcohol depended on alcohol concentration and varied between cell types. Specifically, neurons were more vulnerable to alcohol-induced apoptosis than astrocytes. The alcohol-treated organoids also exhibit disrupted mitochondria cristae and decreased intensity of mitochondrial matrix. Additionally, alcohol resulted in metabolic stress in the organoids as evidenced by 1) decreased mitochondrial oxygen consumption rates being linked to basal respiration, ATP production, proton leak, maximal respiration and spare respiratory capacity, and 2) increase of non-mitochondrial respiration in alcohol-treated organoids compared with control groups. Furthermore, we found that alcohol treatment affected the expression of 199 genes out of 17,195 genes analyzed. Bioinformatic analyses showed the association of these dysregulated genes with 37 pathways related to clinically relevant pathologies. Collectively, this human organoid model allows in-depth analyses of alcohol neurotoxicity at cellular, subcellular, bioenergetic metabolism, and molecular levels. Our findings provide novel insights into alcohol-induced pathologic phenotypes in developing human brains and potential neuroprotective strategy by targeting affected mitochondrial metabolisms and molecular networks.

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Salutogenesis, stress responsivity, and Neurobiological mechanisms associated with vertebral subluxation. Review and commentary**Christopher Kent***Sherman College of Chiropractic. USA*

The term salutogenesis was coined by sociologist Aaron Antonovsky in 1979. It is derived from the Latin *salus*, meaning health, and *genesis*, meaning to give birth. The salutogenic model addresses the causes of global well-being rather than the origins of specific disease processes. It focuses on strategies and lifestyle choices that empower individuals to experience the full spectrum of the human experience. Salutogenic theory goes to the very essence of neurobiology. It has been noted that neurological processes (as well as anatomical structures) are remodeled by sensory input. These processes, collectively termed neuroplasticity, are operative at all levels of the nervous system. Furthermore, whether a challenge is perceived as a threat (dis-stress) or an opportunity for growth (eu-stress) determines the nature of the response by the nervous system. The ability of the nervous system to mount qualitatively and quantitatively appropriate responses to changes in the internal and external environments. Vertebral subluxations occur when misalignment of a vertebra results in abnormal nerve function. Putative neurobiological mechanisms include spinal cord compression and adverse cord tension, nerve root compression, local irritation, vertebral artery compromise, autonomic dysfunction, ephaptic transmissions and coherence and oscillatory patterns. As human beings, we have the ability to control the modulating factors in salutogenesis. We can choose to experience social support, spirituality, happiness, humor and love through a nervous system free of distortion and interference. We can exercise control, commitment, and challenge through biomechanisms that are not compromised.

Biography

Christopher Kent, D.C., J.D. is a Professor and Director for Scholarly Activity at Sherman College of Chiropractic. He is president of the Foundation for Vertebral Subluxation. Dr. Kent was named a Fellow of the College of Chiropractic Imaging, and completed visiting fellowship programs in magnetic resonance imaging. He is an active member of the State Bar of California and is admitted as an attorney of the U.S. District Court, Southern District of California. His research interests include diagnostic imaging and neurological assessments associated with vertebral subluxation.

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The clinical significance of small sharp spikes: a Retrospective study of 909 patients in Epilepsy monitoring unit**James X. Tao, Ziyi Chen***Department of Neurology, The University of Chicago, USA*

Statement of the Problem: Small sharp spikes (SSS) have been generally considered benign EEG variants. Because SSS can occur as frequently in patients without epileptic seizures as in those with epileptic seizures. Recent study demonstrated that a subset of SSS on scalp EEG are time-locked to hippocampal epileptiform discharges in patients with mesial temporal lobe epilepsy (MTLE), which strongly suggested that SSS might be an EEG marker of hippocampal epileptogenesis. The purpose of this study is to determine the incidence and clinical significance of small sharp spikes (SSS) in the patient population of the adult Epilepsy Monitoring Unit (EMU). Methodology: This is a retrospective study of EEG data and medical records from consecutive patients who underwent video-EEG recording in the adult EMU from March 2013 to February 2019. SSS, interictal epileptiform discharges (IEDs), and ictal patterns were identified. Findings: Of the 909 patients reviewed, SSS were observed in 110 (12.1%) patients. Epilepsy was present in 101 of the 110 (91.8%) patients with SSS and in 441 of the 799 (55.2%) patients without SSS. The incidence of epilepsy was significantly higher in patients with SSS than in those without SSS (OR=9.1, 95% CI: 4.5-18.3, P<0.01). The sensitivity of SSS for epilepsy was 18.6% and the specificity was 97.5%. The incidence of SSS was strongly correlated with the frequency of IEDs (OR 1.89; 95%CI: 1.60-2.24, P<0.01). When both present, SSS and IEDs were co-lateralized in the same hemisphere. Conclusion and Significance: There is a statistically significant association between SSS and focal epilepsy. SSS have similar clinical implications to IEDs in the lateralization and localization of temporal lobe seizures. SSS can be an epileptiform EEG pattern for temporal lobe.

Biography

James Tao, MD, PhD is the director of adult epilepsy center and the clinical neurophysiology Laboratory at the University of Chicago. Dr. Tao is specialized in the use of surgery and neurostimulation devices for treating patients with medically resistant epilepsy, with a particular interest in the minimally invasive surgery such as laser ablation. His clinical research focuses on the use of electrophysiology and different types of neuroimaging to localize the seizure focus and guide epilepsy surgery. Dr. Tao is also interested in the mechanism and prevention of sudden unexpected death in epilepsy (SUDEP), which is the leading cause of mortality in patients with chronic uncontrolled epilepsy.

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Glomerular filtrate dynamics in patients with acute ischemic stroke**Kononets Oksana***Shupyk National Healthcare University of Ukraine*

Objective: to specify the clinical and paraclinical characteristics of the concomitant lesions of the nervous system and the kidneys in patients with acute stroke. **Material & Methods.** This paper presents the case report of 240 patients, aged 72 ± 6.64 , who suffered from ischemic stroke. The comprehensive examination, including a detailed clinical and neurological check-up (evaluating the patients' condition severity with the NIHSS) on the 1st and 21st day of the disease), laboratory analysis and instrumental examination. **Results.** In all the patients, we followed up renal function, more specifically, we monitored both urea and creatinine levels in the serum, and the glomerular filtration rate (GFR). It's worth paying attention to an important fact: in the 1st day of the disease, only 5.6 % of patients with right and left hemispheric carotid strokes and 6.92 % of patients with ischemic stroke in the vertebrobasilar system were observed to have normal GFR. No patient with hemispheric carotid stroke had a normal GFR. The vast majority of patients was found to have moderate impairment in the renal filtration-concentration function. The patients with acute brain-stem and cerebellar ischemia were found to have no very severe and end-stage renal dysfunction. The neurological deficit severity was detected to correlate to the GFR in the patients with right hemispheric ischemic stroke, as confirmed by hemispheric asymmetry role in renal filtration functioning. Moreover, our findings showed that the more severe was neurological deficit in patients with right hemispheric ischemic stroke, the better was the renal concentration-filtration capacity (the higher GFR).

Conclusion:

1. It was found a significant relationship between the renal concentration and the filtration function in patients with ischemic stroke.
2. It was discovered that the right brain was more important for the renal function regulation in patients with acute cerebral ischemia.

Biography

Kononets Oksana, Associate Professor, MD, PhD, Department of Neurology No. 2, Shupyk National Healthcare University of Ukraine, 9 Dorohozhytska Str., Kyiv, 04112 Ukraine. At the Department of Neurology No. 2 the investigations concerning the nervous system state under somatic pathology, in particular the kidneys, are under way. The investigations concerning the nervous system state in renal pathology in patients with different neurological diseases, in particular, have been carried out by PhD in Medicine, Associate Professor Oksana Kononets.

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Association of Parkinson's disease progression and Gastrointestinal Dysfunction in the Hawai'i population**Kylee-Ann Tawara, Pauly Kwak, Enjolie Vadella, Jason Viereck, Kore Kai Liow, Beverly Rice***Clinical Research Center, Hawaii Pacific Neuroscience, Honolulu, HI, University of Hawaii at Manoa, Honolulu, HI, University of Washington, Seattle, WA, Bowdoin College, Brunswick, ME, University of Miami, Coral Gables, FL*

Parkinson's Disease (PD) is a progressive disorder of dopaminergic neurons in the brain, resulting in symptoms such as tremor, muscle rigidity, bradykinesia, and cognitive impairment. Clinical indicators of PD progression include changes in motor function (using the Unified Parkinson's Disease Rating Scale, UPDRS), drug dosage (Levodopa Equivalent Daily Dose, LEDD) and impairment of daily living activities (dementia, falling). This study evaluated the relationship between PD and GI dysfunction in the Hawai'i population. A retrospective medical chart review of 193 patients diagnosed with Parkinson's Disease at Hawaii Pacific Neuroscience between June 2010 and July 2020 was conducted. Results show a positive correlation between PD progression and GI symptoms for all 193 patients ($r = 0.21$, $p = 0.01$). Women appeared to have a stronger positive correlation ($r = 0.30$, $p = 0.01$). Positive correlation between speech/ facial expression and diarrhea, hand movement and diarrhea, and leg movement and diarrhea ($p = 0.05$, 0.0001 , 0.0004) were also observed. Of patients with worsening motor symptoms, there appeared to be additional positive correlations between tremor and diarrhea, gait/balance and diarrhea, and gait/balance and swallowing ($p = 0.056$, 0.007 , 0.012). Results show that as PD symptoms progress, GI-related issues tend to be more frequent and/or severe. These findings on the Hawai'i population support current literature correlating progression of gastrointestinal symptom severity and PD severity in the continental US. Correlations between diarrhea and individual motor symptoms appeared to be particularly strong and should be considered in future studies.

Biography

The team is composed of undergraduate students, graduate students, and physicians at their respective clinics and universities listed above. The presenting author is majoring in Public Health. Dr. Liow is the PI at the Clinical Research Center. Dr. Viereck is the academic director and each has more than 30 papers published in clinical and scientific journals.

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Breaking the spell: narrative medicine applications for Psychogenic Nonepileptic Seizures (pnes)**Robert B. Slocum***University of Kentucky HealthCare, Lexington, Kentucky, USA*

Statement of the Problem: Psychogenic Non-Epileptic Seizures (PNES) can be understood as a communication disorder in which distress is expressed somatically in a pathological way instead of an adaptive and verbal manner. Patients with PNES are frequently misdiagnosed, and accurate diagnosis may be delayed for many years. PNES may cause severe disruption of the patient's quality of life in terms of employment or schooling as well as relationships and activities of daily living. Methodology & Theoretical Orientation: This is a narrative review with an illustrative case report indicating Narrative Medicine (NM) applications to help a patient with PNES to communicate about a traumatic past that has been avoided and address psychogenic symptoms. Conclusion & Significance: NM sessions draw out the patient's narrative of illness or injury and treatment in the context of the patient's whole life story. The focus is to discover topics and areas in the patient's narrative that the patient needs to explore. NM sessions can help patients communicate more effectively concerning their traumas and overwhelming experiences. They can discover how to speak about the unspeakable in their lives, and experience improvement as they face their dilemmas and causes of distress. Patients can begin a process of communication and self-reflection about traumatic subjects that continues beyond the NM sessions. Patients may overcome family or personal barriers and taboos about communication on those difficult topics. NM sessions encourage patients to become more open to help and less inclined to hold their pain inside. Patients can discover new perspectives and insights to reframe their understanding of traumatic events. They can renegotiate self-identity with new hope, leading to improved resilience and quality of life. NM sessions encourage patients to communicate more effectively about their unspeakable traumas to reclaim their lives from the communication disorder of PNES.

Biography

Robert B. Slocum, Ph.D., is the Narrative Medicine Program Coordinator at University of KentuckyHealthCare, Lexington, Kentucky. He has taught undergraduate courses in religious studies and ethics. He is currently appointed and in good standing as an Assistant Professor within the voluntary faculty title series in the Department of Behavioral Science and Department of Internal Medicine at the University of Kentucky College of Medicine. He is a member of the Hospital Ethics Committee. He teaches an elective rotation for senior medical student on the narrative basis for patient care and resilient practice. He leads journal workshop groups for patients and staff. He is the author, editor, or co-editor of 13 books, including a journal of reflections. He is interested in the clinical application of narrative and the significance of narrative for identity formation.

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Value of therapeutic blood level monitoring when treating patients with Epilepsy**Roy G Beran***Neurology Department, Liverpool Hospital, Australia*

This presentation was invited following a publication which reported interaction between lamotrigine and female sex hormones which reduced the antiseizure medication (ASM) blood levels, placing the patient at risk of break through seizures, without warning of such potential. This was identified following routine ASM blood level measurement. At much the same time, a previously uncontrolled patient with epileptic seizures, who had been seizure free on a stable ASM monotherapy, presented with a further seizure. ASM blood levels were half what they should have been and the patient was accused of non-compliance. She subsequently reported that, when admitted to hospital, she had been given a generic alternative to her usual ASM and, upon return to her usual ASM, her level thereof doubled to its previous result. Neither she nor her treating neurologist had been advised of the generic substitution. It further reports medication toxicity when a pharmaceutical company changed manufacturers of Lamictal® which translated to selling a generic as the parent compound. The presentation highlights the benefits of using ASM blood level monitoring, especially when treating patients with epilepsy, and examines the problems arising from the use of generic alternatives, especially if the patient and his/her doctor were not informed of the change. It explores bioequivalence, brand substitution and how ASM blood level monitoring adds an extended benefit to manage patients with epilepsy who have a narrow therapeutic index. It advocates use of proprietary trade names, to identify prescribed medications, even if using generic alternatives, to obviate substituting one generic compound for another and provides the rationale behind such proposition. It demonstrates how therapeutic ASM blood levels can be used to individualise treatment and to improve patient management. It advocates the need for patient informed consent, should any change in treatment, including generic substitution, be contemplated and the reasoning behind same.

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Depressive symptoms associated with loneliness and physical activities among graduate university students in Bangladesh: findings from a cross-sectional pilot studySatyajit Kundu¹, Jhantu Bakchi², Md. Hasan Al Banna³¹Department School of Public Health, Southeast University, Nanjing, China²Department of Public Health, North South University, Dhaka, Bangladesh³Department of Food Microbiology, Patuakhali Science and Technology University, Patuakhali, Bangladesh

Introduction: In low-resource settings like Bangladesh, there is a dearth of research on the mental health of university students. This pilot study aimed to identify the prevalence of depressive symptoms, loneliness, and physical activities as well as the associated factors of depressive symptoms among graduate students in a public university of Bangladesh.

Methods: This cross-sectional study was carried out among 323 graduate students between February 2019 and May 2019. By the convenience sampling technique, data were collected by a pretested, structured questionnaire. Depressive symptoms were assessed by the validated Patient Health Questionnaire-9 (PHQ-9) tool with a cut-off score of ≥ 10 vs. less; University of California, Los Angeles (UCLA) loneliness scale was applied to assess loneliness, International Physical Activity Questionnaire (IPAQ) scale was used to measure physical activity level.

Results: The overall prevalence of depressive symptoms was 52% and about 43% of participants felt most lonely. About 32.8% of students were involved in low physical activity. Being female, from lower income families, having poor academic performance, experiencing shorter sleep time, lower physical activity, and being lonely were potential risk factors for depressive symptoms among graduate university students. A positive correlation was found between loneliness and depressive symptoms of students ($r=0.367$, $p < 0.001$).

Conclusion: The higher prevalence of depressive symptoms among Bangladeshi graduate university students suggests the need for situation analysis, confirmatory clinical diagnosis, in-depth qualitative explorations, and large-scale surveys to explore the burden of such disorders and design appropriate low-intensity interventions like implementing student counselling service, offering mental assistance or other mental health support program in the country.

Biography

Mr. Satyajit Kundu studied Bachelor of Science in Nutrition and Food Science at Patuakhali Science and Technology University, Bangladesh, and also completed his MS in Biochemistry and Food Analysis in 2019 from the same university. He then joined the research group of Lina Wang at the School of Public Health, Southeast University, China. Currently, he is doing Master of Public health (MPH) in China. He has published more than 10 research articles in SCI(E) journals and also several articles in SCOPUS indexed journals.

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Optic neuropathy: retrospective observational study and diagnosis change during patients follow-up**Sofia Bezerra, José Miguel Alves, Mafalda Seabra,, Luís Braza, Joana Guimarães***Faculty of Medicine of the University of Porto, Portugal**Department of Neurology, Centro Hospitalar Universitário de São João, Porto, Portugal*

Introduction: Optic neuropathies (ON) have several aetiologies and sometimes the diagnosis established ab initio is redefined after further investigations and/or new neurological events. The aim of this study was to identify possible predictive factors that may dictate that diagnostic change during follow-up. A second arm of this study is still ongoing, and aims to search new biomarkers for ON, with special interest in optic neuritis. Important attention will be given to the eye's posterior pole findings using Spectral-Domain Optical Coherence Tomography and OCT Angiography. We intend to study these parameters as potential structural biomarkers that could improve the sensitivity and specificity predicting the treatment response and to determine its prognostic value at the acute phase of optic neuritis.

Methods: We retrospectively reviewed the medical records of 156 patients with ON admitted to the ward of our Neurology Department, between January 2004 and August 2019. Clinical, laboratory and imaging data, as well as treatment protocols and follow-up were analyzed. The second arm will feature a descriptive analysis of every patient diagnosed with optic neuritis from January 2004 and August 2020 and followed in our center until date. A single ophthalmologic evaluation of those patients will include all visual function tests and optic imaging structural evaluation.

Biography

Sofia Bezerra is Medical Doctor, graduated at School of Medicine of Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre/Brazil. She has multicultural background, and values highly a good medical practice and integrative research. Her career reflects the multidisciplinary curriculum that has characterized her academic and experimental profile, having studied in Germany and UK. In 2016, she has applied for the Equivalence of Academic Degree at School of Medicine of University of Lisbon, Portugal, which has been successfully completed. Currently, she is at International Doctoral Program in Neuroscience, in Faculty of Medicine, University of Porto, as research collaborator and under supervision of Professor Doctor Joana Guimarães, with main interest in Optic Neuropathies. Her project aims to provide objective biomarkers that could be used to predict the treatment and its response.

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To sleep or not to sleep during deep brain stimulation surgery for Parkinson disease**Tipu Z Aziz, F.Med.Sci***Nuffield Department of Surgical Sciences
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Over the last two decades or more Functional Neurosurgery from being dormant had become one of the fastest growing subspecialties. Two schools of practice emerged with time. To avoid causing neurological deficits prior to lesioning, patients were done awake, with one school confirming target by stimulation to elicit the desired response and a second school of utilising micro-electrode recordings. This was necessary as targeting was based on ventriculography in relation to the mid-commissural point as landmark. Such targeting had errors of up to 5mm. The advent of CT stereotaxy eliminated the need for ventriculography but target localisation still required awake surgery for physiological confirmation be it stimulation or MER. Modern MRI imaging has transformed functional neurosurgery. Certain targets have become directly visible to plan surgery pre-operatively such as the STN and GPi though thalamic targets are still acquired proportionately to land marks such as the MCP. Even so with modern imaging processing, even thalamic implants are done with direct targeting. Given this what is the role of surgery with patients awake? Well established targets such as the STN and GPi are clearly visible on modern imaging and with decades of experience, the best site to implant are known. There is also patient choice in that some people would not be willing to undergo awake surgery. Therefore awake surgery may not be possible. Development of telemetric pacemakers now also make it possible to research disease states in the long term and possibly improve surgical outcomes. There are few studies from a single centre comparing awake vs asleep surgery and those that are available do not show advantages to the former and may have more complications. In conclusion, we believe that except in certain indications awake surgery and MER are no longer necessary in DBS Functional Neurosurgery for PD.

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