

Report on the IUPS-BRICS Symposium on Stress held on September 23, 2019

The IUPS-BRICS Symposium on Stress was organized and hosted by Professor Ludmila Filaretova, Director of the Pavlov Institute of Physiology of the Russian Academy of Sciences at Saint Petersburg, Russia and Council Member, Commission III - Endocrine, Reproduction & Development of the IUPS. The IUPS-BRICS Symposium on Stress was held at the Pavlov Institute of Physiology of the Russian Academy of Sciences (RAS) at Saint-Petersburg, Russia on September 23, 2019.

The BRICS Symposium was attended by the President of International Union of Physiological Sciences (IUPS), Professor Julie Chan, Kaohsiung Chang Gung Memorial Hospital Kaohsiung, Taiwan, Professor Jayasree Sengupta, Chairperson of the Board of the General Assembly (BGA) of IUPS and Former Professor and Head, Department of Physiology, All India Institute of Medical Sciences, New Delhi, India, Professor Vagner Roberto Antunes, IUPS Regional Representative-North/South America, Institute of Biomedical Sciences – ICB, University of São Paulo – USP, São Paulo, Brazil, Professor M. Faadiel Essop, Member of the BGA, Department of Physiological Sciences, Stellenbosch University, Stellenbosch, South Africa, Professor Samuel Chan, Director, Institute for Translational Research in Biomedicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan and Professor Debabrata Ghosh, Head, Molecular Physiology Laboratory, Department of Physiology, All India Institute of Medical Sciences, New Delhi, India.

The BRICS Symposium was also attended by Professor Georgy Baffy, VA Boston Healthcare System and Brigham Women's Hospital, Harvard Medical School, Boston, USA, Professor Dora Zelena, Institute of Experimental Medicine, Budapest, Hungary, Ms. Elizaveta Savochkina, Professor Elena Rybnikova, Professor Yuri Shelepin, and Professor Yuri Gerasimenko from the Pavlov Institute of Physiology, RAS, St. Petersburg, Russia.

The symposium began with a warm welcome note extended by Professor Ludmila Filaretova to all participants to the Pavlov Institute and to the IUPS-BRICS Symposium on Stress. Professor Julie Chan began her welcome address by sharing with all participants that the primary purpose and basic foundation of the symposium was to realize one of the seven commitments the IUPS had made to the global community of physiologists, in *Physiology-Current Trends and Future Challenges* (2017) that “*Networks and working groups should be created, domestically and internationally, by IUPS and member societies to facilitate the exchange of knowledge and best practice in teaching and research.*” J. Chan remarked that it was a historic moment for the IUPS since for the first time scientists from Brazil, Russia, India, China and South Africa (BRICS) had gathered at the Pavlov Institute in Russia to forge together a research network towards understanding the integrative physiology of stress.

The morning session had speakers that included J. Chan, F. Essop, S. Chan and V.R. Antunes, D. Ghosh, D. Zelena and G. Baffy. The post-lunch session speakers included, L. Filaretova, E. Savochkina, E. Rybnikova, Y. Shelepin and Y. Gerasimenko.

J. Chan discussed the role of maternal nutritional stress on the programming of hypertension and metabolic syndrome in young offspring and the role of pharmacological treatments that targeted at nutrient sensing signals, oxidative stress and gut microbiota for reprogramming of disease in offspring in an animal model.

F. Essop presented his observations on the evaluation of stress-mediated cardiovascular pathology using a preclinical experimental system. The unpredictable chronic mild stress model (UCMS) model employed on rats subjected to *ex vivo* ischemia reperfusion in Langendorff perfusion apparatus to study endothelial function, markers of oxidative stress and inflammation.

S. Chan discussed the interplay between brain-derived neurotrophic factor (BDNF) and oxidative stress in animal models of diseases. BDNF was shown to function as an endogenous antioxidant at the rostral ventrolateral medulla (RVLM) in neurogenic hypertension and temporal lobe status epilepticus (TLSE).

V. Antunes deliberated upon the hypothalamic-brainstem circuitry as a coordinator of autonomic functions and blood pressure control during osmotic stress. He projected upon the sympathetic activation caused by high salt intake correlated with the osmosensing system in the subfornical organ, in glial cell sodium signalling that led to activation of hypothalamic neurons within the parvocellular neurons of the paraventricular nucleus projecting to brainstem - rostral ventrolateral medulla and spinal cord, as the main sympathetic outflow to control blood pressure.

D. Ghosh deliberated on the issue that chronic cell stress links several human diseases that include cancer, atherosclerosis, diabetes and neurodegenerative disorders and that recent evidence points to epigenetic anomalies as contributions to stress-induced pathologies. Chronic stress elicit changes in the chromatin landscape that 'lock' cells in dysregulated states. He then presented his hypothesis that stress may influence the phenotypes of emigrated cells into pelvis and other ectopic sites, immune and endocrine responsiveness by influencing the epigenetic landscape untowardly leading to cellular heterostasis that results in endometriosis and infertility. He also presented his experimental study design to examine in an integrative approach using cellular and molecular biology tools the epigenetic landscape in endometriosis and its links to stress.

D. Zelena discussed post-traumatic stress disorder (PTSD) a severe mental disorder that develops in some but not all individuals after exposure to extreme traumatic event that has high comorbidity with metabolic disorders. Employing electric footshock induced PTSD-like symptoms in a rat model the metabolic changes were examined. The pre-or post-trauma glycome as studied from N-glycan measurements in blood and brain samples were not of much useful predictive value but the trauma led to metabolic changes by increasing energy expenditure.

G. Baffy explained the current scenario that prevails in scholarly communications and scientific publications. Scientific publications now include many stakeholders: Not-for-profit, for-profit publishers, government and private research funders, academic institutions, university libraries and the investigators and research scholars who contribute and read the scientific literature. Digital communication has further led to overgrowth of this sector together with the introduction of predatory journals and oligopolization that result in large for-profit publishers. The open access publishing which comes with a large financial cost to research investigators however provides readers with free access to scientific literature.

L. Filaretova deliberated on the Hypothalamic-Pituitary-Adrenal axis (HPA) system as a key component of the brain-gut-axis in stress. Bi-directional communication between the brain

and gut play critical role in health and disease. The first demonstration of such a communication was made by Ivan Pavlov in the cephalic phase of gastric and pancreatic secretions. The research data presented by L. Filaretova amplified the gastroprotective role played by glucocorticoids in co-operation with prostaglandins, nitric oxide, capsaicin-sensitive neurons in maintaining homeostasis through blood glucose levels and blood pressure. The activation of the HPA system in stress response and the protective influence of preconditioning mild stress on the gastric mucosa further confirmed that in contrast to the several decades old notion that glucocorticoids are ulcerogenic, and HPA functioning leads to gastric ulcer disease, data now substantiates that activation of the HPA system is a gastroprotective component of the brain-gut axis.

E. Savochkina elaborated on the basic type of digestion first discovered by the Russian scientist A.M. Ugolev in the last century. The Laboratory of Physiology of Nutrition at the Pavlov Institute continues with research in this area to understand the effects of immobilization stress on increases in glucose absorption in small intestine with changes in enzyme activities related to membrane digestion. Elevation of blood corticosterone through its administration to simulate chronic stress increased the rate of glucose absorption via its transport system with no change in enzyme activities and were dependent on ambient temperature.

E. Rybinkova discussed the convergences and differences in hypoxic and psychoemotional stress. Hypoxia as an acute stressor and mild hypoxia at a chronic level both activate the HPA system but the profiles differ from that which occurs during psychoemotional stress considered. In both stress types the HPA is activated with elevation in glucocorticoid levels followed by negative feedback inhibition, but in psychoemotional stress there is long-term maintenance of elevated glucocorticoid levels in circulation. In hypoxia stress besides activation of the HPA axis, specific cellular and molecular mechanisms are induced that include inactivation of prolyl hydroxylases, stabilization of HIF-1 and activation of hypoxia-responsive genes.

Y. Shelepin identified the conscious and unconscious visual stress factors in his deliberation. The perceived images of the environment through spatial-frequency analysis of digital images of natural landscapes and of human faces were described. Awareness of the presence of stress factors and the unconsciousness -semantic stress factors examined by analysing facial expressions to evaluate former stress and experienced emotions.

Y. Gerasimenko elaborated on the regulation of somatic-visceral interactions and emotional stress during spinal cord stimulation. Spinal cord stimulation and neuromodulation of lower urinary tract function via frequency-dependent stimulation patterns was associated with acute epidural spinal cord stimulation and locomotion in rats. Sensorimotor networks controlling bladder and locomotion are highly integrated neuro-physiologically and behaviourally.

At the conclusion of the IUPS-BRICS symposium all participants were invited to visit the Pavlov Museum located in the apartment close to the Pavlov Institute, in which Ivan Pavlov and his family had lived. It was a memorable visit as the apartment has been kept as in the time of residence of Ivan Pavlov and his family with family photographs, books, art, and butterfly and beetle collections. During the tea-time, all members had the opportunity to discuss the science and logistics of creating the proposed collaborative research networks.

The meeting then ended with sincere thanks expressed to Professor Ludmila Filaterova and to her team members for the successful conclusion of the IUPS-BRICS Symposium.