

THE INTERNATIONAL STRESS AND BEHAVIOR SOCIETY (ISBS)

Program and Proceedings

**13th International Neuroscience and BioPsychiatry
ISBS Regional (S. America) Conference**

“Neuroscience of Stress”



*Rio de Janeiro, Brazil
December 1-3, 2017*

Day 1. Friday, December 1, 2017

Windsor Excelsior Hotel, Av. Atlântica, 1800, Copacabana, Rio de Janeiro, Brazil

08.30-17.00 REGISTRATION

Morning session

**09.00-09.15 ISBS OPENING CEREMONY AND WELCOMING ADDRESSES
CELEBRATING 20 YEARS TO ISBS CONFERENCES**

**09.15-09.45 LECTURE 1. IRVING I GOTTESMAN LECTURE: STRESS ENHANCED
MOTIVATION FOR HIGH CALORIC FOOD REWARDS IN SATIATED RATS:
DEPENDENCE ON EXTRAHYPOTHALAMIC CRF NEUROTRANSMISSION, BUT
NOT HPA AXIS ACTIVATION.** X Liu, ISBS Fellow, L Armstrong, A Decoteau and
A Covacevich, University of Mississippi Medical Center, Jackson, MS, USA

**09.45-10.15 LECTURE 2: MULTIPARAMETRIC NEUROIMAGING MODALITIES IN
DETECTION OF SUBTLE BRAIN DAMAGE IN PATIENTS WITH MILD
COGNITIVE IMPAIRMENT.** D Kozic, ISBS Fellow, University of Novi Sad Faculty
of Medicine, Novi Sad, Serbia

**10.15-12.30 SYMPOSIUM 1. ZUKOWSKA SYMPOSIUM ON BIOLOGICAL PSYCHIATRY
CHAIRS: X LIU (USA), AV KALUEFF (USA)**

**10.15-10.40 AN ASSOCIATION OF *PLA2G4A* AND *PLA2G6* GENE POLYMORPHISMS WITH
SMOKING RISK AND ILLNESS SEVERITY IN SCHIZOPHRENIA PATIENTS.** S
Nadalín, J Rebić, K Ružić, M Kapović and A Buretić-Tomljanović, Department of
Biology and Medical Genetics, School of Medicine, University of Rijeka, Psychiatry
Clinic, Clinical Hospital Center Rijeka, Croatia

**10.40-11.00 DAILY STRESS IN MIDLIFE AND EARLY AGING: COMPLEX PSYCHO-
PHYSIOLOGICAL APPROACH.** O Strizhitskaya and L Golovey, St. Petersburg
State University, St. Petersburg, Russia

11.00-11.25 COFFEE BREAK

**11.25-11.40 THE EFFECTS OF STRESS AND BELIEF IN JUST WORD ON COLLEGE
STUDENTS' AGGRESSIVE BEHAVIOR.** W Wang, M Chen, Y Lin, T Liu and C
Wan, Research Center on Quality of Life and Applied Psychology, School of
Humanities and Management, Guangdong Medical University, Dongguan, China

**11.40-12.00 AN ASSOCIATION ANALYSIS ON CLINICAL OBJECTIVE INDICATORS AND
PATIENT-REPORTED OUTCOMES IN PATIENTS WITH STROKE BASED ON
THE SF-36 SCALE.** CH Wan, QA Xu, WN Wang, LH Chang, FQ Sun and CZ Xu,
Research Center on Quality of Life and Applied Psychology, School of Humanities
and Management, Guangdong Medical University, Dongguan, The First Affiliated
Hospital of Kunming Medical University, Kunming, China

12.00-12.30 NEUROPHYSIOLOGICAL AND NEUROMORPHOLOGICAL ALTERATIONS OF COCHLEA INDUCED BY STRESSOR INFLUENCE OF NOISE AND VIBRATION. NN Petrova, NS Saponov and EV Petrova, North-Western State Medical University I.I. Mechnikov, Institute of Experimental Medicine, St. Petersburg, Russia

12.30-13.30 LUNCH BREAK (FREE TIME)

Afternoon session

13.30-16.20 SYMPOSIUM 2. LAPIN SYMPOSIUM ON TRANSLATIONAL NEUROSCIENCE CHAIRS: PD SHABANOV (RUSSIA), DB ROSEMBERG (BRAZIL)

13.30-13.40 INTRODUCTION

13.40-14.00 EARLY MATERNAL SEPARATION INDUCES OXIDATIVE STRESS IN DIFFERENT RAT BRAIN REGIONS AND LEADS TO ANXIETY-LIKE BEHAVIOR. J Novotny, G Pallag, M Vodicka, R Moravcova, Z Bendova and L Hejnova, Department of Physiology, Faculty of Science, Charles University, Prague, Czech Republic

14.00-14.20 DAILY STRESSORS, PERCEIVED STRESS AND SATISFACTION WITH PROFESSIONAL ACTIVITY AMONG ADULTS WITH DIFFERENT RESISTANCE OF NERVOUS REACTION. M Petrash and V Grebennikov, St. Petersburg State University, The City Ambulance Station, St. Petersburg, Russia

14.20-14.40 DAILY HASSLES, STRESS AND COPING IN WOMEN: DOES MARITAL STATUS MATTER? S Savenysheva, St. Petersburg State University, St. Petersburg, Russia

14.40-15.00 COFFEE BREAK

15.00-15.30 OXR1 OREXIN BRAIN RECEPTORS ARE INVOLVED IN EFFECTS OF CHRONIC ALCOHOLIZATION AND AMPHETAMINE-ACTIVATED SELF-STIMULATION VIA SIMILAR MECHANISMS INVOLVING DA2/OXR1 DIMER COMPLEX FORMATION. PD Shabanov, ISBS Fellow, ER Bychkov, PP Khokhlov and AA Lebedev, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

15.30-15.45 INTERACTIVE POSTER: THE ROLE OF OREXIN A IN STRESS-INDUCED BEHAVIORAL PATTERNS OF OBSESSIVE-COMPULSIVE BEHAVIOR IN A RAT MARBLE TEST. AA Lebedev, ND Yakushina, IYu Tissen, AG Pshenichnaya, ER Bychkov and PD Shabanov, ISBS Fellow, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

15.45-16.20 LECTURE 3: ISBS PRESIDENTIAL LECTURE: MODELING SOCIAL STRESS IN RODENTS. AV Kalueff, ISBS Fellow, DA Meshalkina and KA Demin, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; Southwest University, Chongqing, China

16.20-17.00 ROUND TABLE: ETHICS IN BIOMEDICINE – CURRENT CHALLENGES

Day 2. Saturday, December 2, 2017

Windsor Excelsior Hotel, Av. Atlântica, 1800, Copacabana, Rio de Janeiro, Brazil

09.10-12.00 REGISTRATION

Morning session

09.40-14.00 SYMPOSIUM 3. ALTERNATIVE MODELS IN STRESS BIOMEDICINE. Sponsored by the International Zebrafish Neuroscience Research Consortium (ZNRC). CHAIRS: LJG BARCELLOS (BRAZIL), DB ROSEMBERG (BRAZIL), AV KALUEFF (USA)

09.40-09.50 INTRODUCTION

09.50-10.10 ZEBRAFISH LISTENING TO VIVALDI ARE CALMER AND LESS ANXIOUS! H Barcellos, G Koakoski, F Chaulet, K Schreiner Kirsten, LC Kreutz, AV Kalueff, ISBS Fellow, and LJG Barcellos, University of Passo Fundo, Passo Fundo, Brazil, St. Petersburg State University, Institute of Experimental Medicine of Almazov Center, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; Southwest University, Chongqing, China

10.10-10.45 ZNRC LECTURE 4: THE STRESS RESEARCH IN UPF: SOCIAL STRESSORS AND WELFARE. LJG Barcellos, University of Passo Fundo (UPF), Passo Fundo, Brazil

10.45-11.15 ZNRC LECTURE 5: ZEBRAFISH AS A MODEL ORGANISM FOR ASSESSING ANXIETY- AND FEAR-LIKE BEHAVIORAL ENDOPHENOTYPES. DB Rosenberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

11.15-11.35 MODELING ANTIDEPRESSANT DISCONTINUATION SYNDROME (ADS)-STUDIES OF BEHAVIORAL EFFECTS OF CHRONIC AMITRIPTYLINE AND SERTRALINE IN ADULT ZEBRAFISH. TO Kolesnikova, SL Khatsko and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

11.35-11.50 TAURINE ATTENUATES SEIZURES AND PREVENTS OXIDATIVE STRESS INDUCED BY PENTYLENETETRAZOLE IN ZEBRAFISH. BD Fontana, PR Ziani, J Canzian, NJ Mezzomo, TE Muller, MM Santos, VL Loro, NBL Barbosa, CF Mello and DB Rosenberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

11.50-12.05 DIFFERENT EFFECTS OF CONSPECIFIC ALARM PHEROMONE ON ECTONUCLEOTIDASE AND ACETYLCHOLINESTERASE ACTIVITY IN BRAIN TISSUE OF TWO ZEBRAFISH POPULATIONS. J Canzian, BD Fontana, VA Quadros and DB Rosenberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

12.05-12.30 COFFEE BREAK

12.30-12.45 ETHANOL-INDUCED AGGRESSIVE BEHAVIOR IN ZEBRAFISH: PUTATIVE INVOLVEMENT OF SEROTONERGIC PATHWAY. TE Muller, PR Ziani, BD Fontana, J Canzian, FV Stefanello, ARS Santos and DB Rosenberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

- 12.45-13.00 FEAR CONDITIONING RESPONSES TO THE CONSPECIFIC ALARM SUBSTANCE IN ZEBRAFISH.** FV Stefanello, BD Fontana, NJ Mezzomo, DL Meinerz, C Maximino, MG Lima and DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil
- 13.00-13.15 NICOTINE MODULATES CONTEXTUAL FEAR CONDITIONING INDUCED BY ALARM SUBSTANCE IN ZEBRAFISH.** T Duarte, PR Ziani, TE Muller, FV Stefanello, BD Fontana, J Canzian and DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil
- 13.15-13.45 ZNRC LECTURE 6: ZEBRAFISH MODELS OF CHRONIC STRESS.** AV Kalueff, ISBS Fellow, ZENEREI Research Center, Slidell, LA, USA; Southwest University, Chongqing, China; St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia
- 13.45-14.00 EFFECTS OF U-49900, A μ -OPIOID RECEPTOR AGONIST, ON ADULT MICE AND ZEBRAFISH.** TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia
- 14.00-14.15 SCHIZOPHRENIA: IMPACT ON FAMILY DYNAMICS.** A Caqueo-Úrizar, M Rus-Calafell, TKJ Craig, M Irarrazaval, A Urzúa, L Boyer and DR Williams, Universidad de Tarapacá, Escuela de Psicología y Filosofía, Arica, Chile; Department of Health Service and Population Research, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; Departamento de Psiquiatria, Facultad de Medicina, Hospital Clínico Universidad de Chile, Instituto Milenio para la Investigación en Depresión y Personalidad, Santiago, Universidad Católica del Norte, Antofagasta, Chile, Aix-Marseille University – Public Health, Chronic Diseases and Quality of Life Research Unit, Marseille, France, Department of Social and Behavioral Sciences, Harvard School of Public Health, Department of African and African American Studies, Harvard University, Cambridge, MA, USA
- 14.15-14.25 INTERACTIVE POSTER: EFFECT OF TOLUENE CHRONIC EXPOSURE ON EXPLORATORY BEHAVIOR AND RECOGNITION MEMORY IN ADOLESCENT AND ADULT RATS.** NO Pochkhidze, MG Zhvania, NJ Japaridze and MD Dashniani, Institute of Chemical Biology Ilia State University, I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia
- 14.25-14.40 ART MEETS NEUROSCIENCE: AN ARTIST'S PERSPECTIVE.** D Raytchev, London, UK
- 14.40-15.00 CONCLUDING REMARKS AND CLOSING
ANNOUNCING FORTHCOMING 2018 ISBS CONFERENCES**

Day 3. Sunday, December 3, 2017

Optional Educational Tours (admissions)

CELEBRATING 20 YEARS OF ISBS “STRESS AND BEHAVIOR” CONFERENCES

Dear Colleagues,

On behalf of the Stress and Anxiety Research Society (STAR), I am pleased to congratulate the International Stress and Behavior (ISBS) conferences for their twenty years of history. Our two scientific societies pursue common goals and have maintained synergistic relationships over time, and which may be enhanced in the future.

Modern societies are becoming increasingly prevalent in stress and anxiety and require immediate and effective responses. Therefore, any research and applied effort that contributes to the reduction of its prevalence should be welcomed. And in this, both ISBS and STAR must become a global reference in the fight against such threats to the mental health of people. As President of STAR, I would like to convey to ISBS members my deep satisfaction with their scientific achievements, and wish them a bright future.

Sincerely,

Prof. Albert Sesé, PhD
Department of Psychology, Faculty of Psychology, Balearic Islands University, Palma (SPAIN)
President of the Stress and Anxiety Research Society (STAR)

Dear ISBS friends,

It is with great pleasure that I am writing to congratulate you on the 20th anniversary of “Stress and Behavior” meetings. The International Stress and Behavior Society has made a remarkable progress in promoting research in biology of stress and biological psychiatry in all corners of the globe. Your annual meetings in beautiful Saint Petersburg and regional conferences always attract prominent researchers and young scientists from different fields of biological psychiatry.

Few probably remember how much effort was required for organizing and developing this society into a major scientific organization. It was all started back when the economical hardship was palpable and seemingly insurmountable - not for you. Your dedication and passion made it happen, and remain absolutely critical for the continuing success of the society and its meetings held for 20 (!) years.

As current President of the International Behavioral Neuroscience Society (IBNS), I would like to warmly congratulate you on this anniversary and express my confidence that your meetings will continue to make important contributions to science of stress and cultural enrichment of investigators throughout the world.

With best wishes,

Mikhail V. Pletnikov, MD, PhD
Professor of Psychiatry, Neuroscience and Molecular and Comparative Pathobiology
Johns Hopkins University School of Medicine, Baltimore, MD
President, The International Behavioral Neuroscience Society, IBNS

Dear ISBS Colleagues,

Greetings from Taiwan. On behalf of the Mind-Body Interface Laboratory (MBI-Lab) and the Taiwanese Society for Nutritional Psychiatry Research (TSNPR), I would like to express my heartfelt congratulations on the 20th anniversary of the annual conference of International Society of Stress and Behavior (ISBS). This

ISBS Conference “Neuroscience of Stress”, December 1-3, 2017, Rio de Janeiro, Brazil

society, indeed, has a significant impact in these past 20 years - becoming one of the most influential scientific societies in its field, and making great contribution to the development of translational neuroscience, neurobehavioral sciences, biopsychology and bio-psychiatry for the past two decades.

ISBS conference series, with no doubt, provides an excellent platform for researchers alike from worldwide to meet, to share and to collaborate, as well as to keep tackling the complexity of stress and behaviors together. Here, I would like to invite everyone to participate in this great event to recognize this outstanding society, and I wish their nearest and future conferences a big success!

Sincerely,

Kuan-Pin Su, MD, PhD
Chairman & Professor of Graduate Institute of Neural and Cognitive Sciences
Director of Mind-Body Interface Laboratory (MBI-Lab), China Medical University & Hospital TAIWAN
President of Taiwan Society for Nutritional Psychiatry Research (TSNPR)

Dear ISBS:

We are writing to congratulate you as the Stress and Behavior conferences mark 20th anniversary of these meetings. Chris and I were both speakers at the meeting held in Zhanjiang, China last fall and entitled, "Neurobiology of Mind and Body, Behavior, Stress, Brain Diseases, Immunity, Drugs and Nutrition." That meeting was a very successful international event that was attended by leading scholars from around the world.

We were particularly impressed that four international symposia were co-organized by leading scientific groups that were represented by the International Stress and Behavior Society (ISBS), the Psycho-neuroimmunology Research Society (PNIRS, USA), the Mind-Body Interface Laboratory (MBI-Lab, Taiwan) and Research Institute for Marine Drugs and Nutrition (RIMND, China). Success of the meeting in Zhanjiang was in part responsible for prompting the PNIRS to recently expand its very successful PNIRChina committee to the PNIRAsia-Pacific committee.

Best wishes for another successful IBNS meeting as you celebrate your platinum anniversary year.

Sincerely,

Keith W. Kelley, Ph.D., University of Illinois at Urbana-Champaign
Christopher Coe, Ph.D., University of Wisconsin at Madison
Co-Chairs, PNIRAsia-Pacific committee, the Psycho-neuroimmunology Research Society

Dear ISBS Colleagues,

The International Society for Serotonin Research (formerly known as the Serotonin Club) would like to offer it's congratulations to you on the celebration of your conferences' 20th Anniversary. Our two societies have overlapping interests and several joint members. Small specialised societies such as ours provide a unique scientific forum for international experts in the field to interact and above all to foster the development of young scientists to enhance their career. We particularly congratulate you on that ambition. Like you, our Society is celebrating its anniversary; the 30th. We would warmly welcome any of you to attend our ISSR meetings, to continue our joint scientific adventure.

Sincerely,

Professor Kevin C F Fone FBPhS
Professor of Neuroscience, School of Life Sciences
Queen's Medical Centre, The University of Nottingham, UK
President, International Society for Serotonin Research

ABSTRACTS

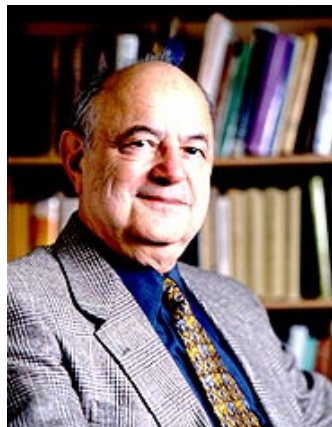
Day 1. Friday, December 1, 2017

Windsor Excelsior Hotel, Av. Atlântica, 1800, Copacabana, Rio de Janeiro, Brazil

Morning session

ISBS OPENING CEREMONY AND WELCOMING ADDRESSES CELEBRATING 20 YEARS TO ISBS CONFERENCES

LECTURE 1. IRVING I GOTTESMAN LECTURE



PROFESSOR IRVING (IRV) I GOTTESMAN (1930-2016) was born in Cleveland, OH to Hungarian-Romanian Jewish parents. Irv was a science enthusiast from an early age and began a physics degree while serving as an officer in the US Navy, later switching to psychology. He completed his PhD at the University of Minnesota on the genetics of personality, but initially had great difficulty in getting his findings published because of the prevailing orthodoxy in US academia in the late 1950s that behavior was entirely due to nurture, and nothing to do with nature. After his postdoctoral fellowship in London, Irv returned in 1966 to the biology-friendly department of Psychology in Minneapolis, and set up one of the first behavior genetics training programs in the US. He thereafter held chairs in Washington University in St Louis (1980-85), and at the University of Virginia (1986-2001), where he set up a clinical psychology doctorate, before returning to Minnesota, where he remained for the rest of his career. Irv won many plaudits and prizes worldwide but retained particular affection for and gratitude to the UK, where

his recent awards included honorary fellowship of the Royal College of Psychiatrists and King's College London. His far-reaching conceptual innovation was their idea of "endophenotypes", proposed (with J. Shields) in their 1972 book, *Schizophrenia and Genetics*. Specifically, they posited that the genetic basis of psychiatric disorders could be better understood, and specific genes more readily identified, by the discovery of biological characteristics that lie a step closer to DNA/genes than the clinically observable symptoms and signs ('exophenotypes'), by which disorders are defined. Irv continued to elaborate the endophenotype concept over ensuing years and it provoked thousands of papers by others (P. McGuffin, 2016). Today, Gottesman's endophenotype concept remains one of the most influential thoughts in biological psychiatry. Irving was also a good friend of ISBS, advising our members and enthusiastically contributing to many ISBS publications. Recognizing his critical impact on the field, this Special Lecture, as part of the Gottesman Lecture Series established by ISBS in 2016, continues to advance stress neurobiology, and highlights the emerging promising new areas of research in this direction.

STRESS ENHANCED MOTIVATION FOR HIGH CALORIC FOOD REWARDS IN SATIATED RATS: DEPENDENCE ON EXTRAHYPOTHALAMIC CRF NEUROTRANSMISSION, BUT NOT HPA AXIS ACTIVATION. X Liu, ISBS Fellow, L Armstrong, A Decoteau and A Covacevich, University of Mississippi Medical Center, Jackson, MS, USA

INTRODUCTION: Overeating beyond individuals' energy homeostatic need leads to obesity. Exposure to stressful life events is proposed to be an environmental and psychological factor that may promote overeating behavior. However, the neurobehavioral mechanisms of excessive food intake under stress are not fully understood. The present study using a rat model of overeating examined whether a pharmacological stress challenge enhances the motivation for procuring high-fat food reward in satiated rats and determined whether the stress-enhanced motivation requires hypothalamic-pituitary-adrenal (HPA) axis activity or/and extrahypothalamic corticotropin-releasing factor (CRF) neurotransmission. **METHODS:** Male Sprague-Dawley rats with ad libitum access to standard rodent chow in their home cages were trained to press a lever for deliveries of high caloric food pellets containing 35% fat contents. To measure the motivation of rats for the

reward, a progressive-ratio schedule of reinforcement was used. Ten min prior to test sessions, rats were challenged with an intraperitoneal administration of a pharmacological stressor yohimbine. Fifty min prior to yohimbine challenge, rats received an administration of a CRF1 receptor antagonist NBI or a glucocorticoid receptor antagonist mifepristone or a glucocorticoid synthesis inhibitor metyrapone. **RESULTS:** The satiated rats emitted lever responses, indicating their motivation for procuring the calorie-condensed food pellets. Yohimbine stress challenge significantly increased lever responses, indicating the enhanced motivation. Pretreatment with NBI prior to stress challenge effectively blocked the behavior motivational effect of yohimbine. However, neither mifepristone nor metyrapone altered the enhancing effect of yohimbine on rat lever responses. **CONCLUSIONS:** These data demonstrated that pharmacological stress challenge significantly enhanced the motivation for obtaining high-fat food reward beyond rat energy homeostatic need. Moreover, the results also revealed that the enhancing effect of yohimbine stress on motivation for high-fat food reward required activation of the CRF1 receptors but not activity of HPA axis, suggesting a role of the extrahypothalamic CRF neurotransmission in overeating behavior under stressful situations. These findings would shed a light on our understanding of the neurobehavioral mechanisms of overeating/obesity. **RESEARCH SUPPORT:** NIH grants R01DA017288 and R01DA037277.

LECTURE 2: MULTIPARAMETRIC NEUROIMAGING MODALITIES IN DETECTION OF SUBTLE BRAIN DAMAGE IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT. D Kozic, ISBS Fellow, University of Novi Sad Faculty of Medicine, Novi Sad, Serbia

INTRODUCTION: Mild cognitive impairment (MCI) is most frequently considered as an intermediate state between cognitive changes of ageing and early dementia. It is characterized by cognitive deficits that are noticeable to the patients or their families, that represent a decline from the past, yet do not interfere significantly with the patients' ability to function at work or in usual daily activities. Patients with MCI are at a higher risk of developing dementia than the general population. However, not all patients with MCI develop dementia. It is important to recall that MCI is a syndrome that could be caused by many etiologies. **METHODS:** Magnetic resonance volumetry is a diagnostic modality that detects the atrophy of specific brain areas. Quantification can be performed via segmentation of the brain parenchyma, in BrainMagix's SurferMagix module (Hermoye et al., 2014). Multivoxel magnetic resonance spectroscopy is able to detect subtle neurometabolic changes, while MR perfusion may detect brain regions of decreased blood supply. Diffusion tensor imaging is able to reveal disturbance of neuronal connectivity network. Amyloid imaging represents a major advance in neuroscience, enabling the detection and quantification of pathologic protein aggregations in the brain, focusing on PET with (11)carbon-labelled Pittsburgh Compound-B ((11)C-PIB), the most extensively studied and best validated tracer. **RESULTS AND DISCUSSION:** Reduced N-acetyl aspartate on magnetic resonance spectroscopy in different brain regions can be detected in patients with MCI. The global brain volume loss is evident in Alzheimer disease, predominantly affecting the gray matter. The hippocampus is typically the most prominently prone to changes, and may serve as the most useful paramete. Bilateral hippocampal volume decrease was significant in Alzheimer disease compared to controls, and in MCI compared to controls, as well as in AD compared to MCI. **RESEARCH SUPPORT:** Provincial Secretariat for Science and Technological Development of the Autonomous Province of Vojvodina, project number 114-451-2730/2016-01.

SYMPOSIUM 1. ZUKOWSKA SYMPOSIUM ON BIOLOGICAL PSYCHIATRY
CHAIRS: X LIU (USA), AV KALUEFF (USA)

INTRODUCTION: PROFESSOR ZOFIA M ZUKOWSKA



Prof. ZOFIA M. ZUKOWSKA (1949-2012) received her M.D. and Ph.D., trained in cardiovascular medicine at the Warsaw Medical Academy (Poland). She pursued post-doctoral training at the NIH, working with such renowned scientists as Irwin I. Kopin, Scientific Director of NINDS, and Julie Axelrod, a Nobel Laureate. During this research period, her interest in stress and neuropeptides became galvanized. For the 25 years, she was a professor (and, later Chair) of the Department of Physiology and Biophysics at Georgetown University, before moving to the University of Minnesota as the Director of Stress Physiology Center. Her research examined how stress affects cardiovascular and metabolic health and diseases, and the role of peptides, in particular neuropeptide Y (NPY), a sympathetic neurotransmitter and stress mediator. She was the first to determine that NPY mediates stress-induced prolonged vasoconstriction and vascular mitogenic and pro-atherosclerotic effects (via Y1 receptors) and potent angiogenic actions (via Y2 receptors), establishing the role of NPY in ischemia, retinopathy, tumors and obesity. Professor Zukowska (or Zosia, as she

was known and admired by many) was a good friend and a strong supporter of the ISBS, serving as a regular plenary speaker at our conferences. Her scientific vision, extraordinary creativity, kindness to colleagues, and the talent to be daring, continue to inspire all her ISBS colleagues and their research. This regular ISBS symposium continues Zofia's scientific legacy in the field of biological psychiatry of stress.

AN ASSOCIATION OF *PLA2G4A* AND *PLA2G6* GENE POLYMORPHISMS WITH SMOKING RISK AND ILLNESS SEVERITY IN SCHIZOPHRENIA PATIENTS. S Nadalin, J Rebić, K Ružić, M Kapović and A Buretić-Tomljanović, Department of Biology and Medical Genetics, School of Medicine, University of Rijeka, Psychiatry Clinic, Clinical Hospital Center Rijeka, Croatia

INTRODUCTION: Hypodopaminergy in the prefrontal cortex may explain negative symptoms, cognitive deficits, as well as high smoking rate in schizophrenia patients. Evidence indicates that increased phospholipase A2 (PLA2) activity, repeatedly observed in brain and various peripheral tissues among schizophrenia individuals, could accelerate the breakdown of membrane phospholipids and contribute to a prefrontal hypodopaminergy. Data regarding the relevance of PLA2 genes in the clinical expression of schizophrenia are sparse and no studies have elucidated the associations between the PLA2 genes and nicotine dependence. We investigated the plausible relationship between the rs10798059 (BanI) and rs4375 polymorphisms in (PLA2)G4A and PLA2G6 genes and the risk for nicotine dependence among Croatian schizophrenia patients. We also examined whether these polymorphic variants alone, or in interactions with smoking status, might contribute to schizophrenia onset and scores for the Positive and Negative Syndrome Scale (PANSS) during an acute state of the illness requiring hospitalization.

METHODS: Genotyping was performed by polymerase chain reaction for 263 patients (males/females: 139/124) who met DSM-IV criteria for schizophrenia. **RESULTS AND**

DISCUSSION: We demonstrated three significant, yet weak effects, manifesting in a gender-specific fashion. An overrepresentation of PLA2G6-CC homozygous and CT heterozygous genotypes was detected in male nonsmokers compared to smokers ($\chi^2=3.03$, $P<0.05$); PLA2G6-CC homozygous and CT heterozygous males had about a 2.5-fold lower smoking risk than TT homozygous. Furthermore, females carrying the G allele in their PLA2G4A genotype (PLA2G4A-GG homozygous and AG heterozygous) manifested a significantly lower negative and total PANSS scores compared to AA homozygous ($P<0.05$ and $P<0.01$). Finally, we detected an intriguing PLA2G6 genotype-smoking interaction that predicted the time of illness onset among

males ($P < 0.05$); an earlier onset was observed for smokers PLA2G6-TT homozygous in comparison to nonsmoking TT homozygous ($F = 4.07$, $P < 0.05$). **RESEARCH SUPPORT:** University of Rijeka, Croatia Grants 13.06.1.3.39 and 16.06.2.1.03.

DAILY STRESS IN MIDLIFE AND EARLY AGING: COMPLEX PSYCHO-PHYSIOLOGICAL APPROACH. O Strizhitskaya and L Golovey, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: Modern reality with its fast growing speed of life, increase in ambiguity of developmental situation, including family, professional and social spheres, demands a lot of coping resources. Research on daily stress in aging suggests controversial data: on one hand, researchers show that with aging there is a decrease in daily stressors and better adaptation to them, on the other hand, older adults meet different challenges and lose some of their resources, including health-related and social resources. In the present study we tried to address the problem of interaction between psychological and physiological parameters of stress in midlife and early aging in Russian sample. **METHODS:** Participants of the study, presented in this paper, were 100 adults aged 45-65 (Males – 37, females - 63). To approach daily stress, we used: Scale of Perceived Stress (Russian version by Ababkov, 2017); List of daily stressors (82 items; Petrash et al., 2016); self-report diary for systematic observation of daily stress and self-report daily lifestyle; semi-structured phone interview (adapted from DISE, Almeida, Wethington, Kessler, 2002). To estimate physiological responses to daily stress we used Express diagnostics of functional status and efficiency by Moroz; oxygen saturation, variability measures of ECG. Our model included psychological predictors such as self-esteem and locus of control and psychological outcomes – such as self-report mood and activity. **RESULTS AND DISCUSSION:** Our results show that daily stress is differentially perceived in midlife and aging with a light tendency to decrease with age. We also found that women were prone to perceive more daily stresses. Next step in the analysis was to compose integrative objective (physiological) and subjective (psychological and self-report) measures of stress. We identified that these two measures can form four “stress-type” groups. We found that our participants who experience higher levels of physiological stress compared to perceived psychological stress had higher scores for self-esteem and mostly had internal locus of control, their everyday lifestyle was less affected by stress. We suppose that these psychological resources can make a person more vulnerable since their compensatory resources “hide” the symptoms of exhaustion and stress. We suggest that these results open a perspective for study of daily stress, but to get a more precise data we need to combine systematic and longitudinal approach to see a long-term perspective of the daily stress effects both objective and subjective. **RESEARCH SUPPORT:** Russian Science Foundation project 16-18-10088 “Complex study of the daily stressors and resources for coping with them in different periods of adulthood”.

THE EFFECTS OF STRESS AND BELIEF IN JUST WORD ON COLLEGE STUDENTS' AGGRESSIVE BEHAVIOR. W Wang, M Chen, Y Lin, T Liu and C Wan, Research Center on Quality of Life and Applied Psychology, School of Humanities and Management, Guangdong Medical University, Dongguan, China

Many factors influence the presentation of aggressive behaviors. The present research examined the influence of school students' stress, belief in a just world (BJW) and aggressive behavior in both questionnaire and experiment study. In Experiment 1, a survey enclosed in Perceived Stress Scale (PSS), belief in a just world scale (BJW) and Buss-Perry Aggression Questionnaire (BPAQ) were measured for 549 Chinese college students. Regression analyses revealed that (1) the higher stress students perceiving the more aggressive behavior they reported; (2) however, the more strongly students believed in a personal just world and the less aggressive behavior they

reported. (3) Moreover, the mediating role of stress was also examined. It showed that stress mediated the relation between BJW and aggressive behavior. In Experiment 2, the hot sauce allocation task was applied in both before and after threatened BJW time slot for the same students from Experiment 1; the changes of aggressive behavior were effectively indexed by the changing allocated amount of hot sauce between the two measure time slots. A 2 by 2 experiment were manipulated with the factors of Stress (high/low level) and BJW (strong/weak level) for participants. According to the scores which were tested in Experiment 1, the participants were divided into HS (high stress-strong BJW), HW (high stress-weak BJW), LS (low stress-strong BJW) and LW (low stress-weak BJW) groups. The ANOVA result showed there was no evidence of an interaction between stress and BJW, but both two main effects were significant. When the BJW was threatened, (1) participants with high stress represented much more aggressive than that for the low one; (2) participants with weak BJW would behave much more aggressive while the strong BJW one would behave less aggressive. **RESEARCH SUPPORT:** Guangdong Natural Science Foundation (2015A030310517).

AN ASSOCIATION ANALYSIS ON CLINICAL OBJECTIVE INDICATORS AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH STROKE BASED ON THE SF-36 SCALE. CH Wan, QA Xu, WN Wang, LH Chang, FQ Sun and CZ Xu, Research Center on Quality of Life and Applied Psychology, School of Humanities and Management, Guangdong Medical University, Dongguan, The First Affiliated Hospital of Kunming Medical University, Kunming, China

INTRODUCTION: The patient-reported outcomes (PRO) for patients with stroke is now concerned worldwide, but the relationships between PRO and clinical objective indicators is seldom. Here, we aimed to explore this association. **METHODS:** Using the SF-36 questionnaire, one hundred cases of patients with stroke were investigated and the data was used to explore the associations between patient-reported outcomes and clinical objective indicators by the simple correlation and the canonical correlation. **RESULTS:** The Pearson correlation analysis among domains scores of the scale and clinical objective indicators showed that there were significant associations between the following two parts: physical function with blood urea, blood potassium, platelet count and education level; physical role with albumin; body pain with globulin and education level; general health status with fasting glucose; vitality with globulin, activated partial thromboplastin time and education level; role emotional with education level. The Canonical correlation analysis showed that two canonical variables were statistically significant ($P < 0.05$) with the canonical correlation coefficient being 0.5360 and 0.3256 respectively, and the cumulative contribution rate being 0.6143. The indices of globulin, fasting glucose, blood potassium, and platelet count were related to patient-reported outcomes. **DISCUSSION:** There is relevance between clinical objective indicators and patient-reported outcomes, giving attention to indicators and taking corresponding measures may have a certain value to improve the patient-reported outcomes in patients with stroke. However, the sample size of the study is not very large, and the subjects in this study were selected from the inpatient population at hospitals. **RESEARCH SUPPORT:** The National Natural Science Foundation of China (71373058, 81460519).

NEUROPHYSIOLOGICAL AND NEUROMORPHOLOGICAL ALTERATIONS OF COCHLEA INDUCED BY STRESSOR INFLUENCE OF NOISE AND VIBRATION. NN Petrova, NS Saprionov and EV Petrova, North-Western State Medical University II Mechnikov, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Today, when considering occupational health problems, much attention is paid to the psychosocial factors of the working environment, which include such physical stressors as noise and vibration. The aim of the study was to evaluate the neurophysiological and neuromorphological changes developing in the cochlea under the influence of noise and vibration.

METHODS: The experiments were carried out on 20 guinea pigs weighing 250-300 g, subjected to general vibration and noise for 4 weeks for 3 hours daily. The technique of recording acoustic evoked potentials was used to study the neurophysiological changes in the cochlea. Neuromorphological studies of the surface of the spiral organ were examined in a scanning electron microscope JSM-T-300. **RESULTS AND DISCUSSION:** The results showed that the amplitudes of the action potential peaks N1 and N2 decrease under the influence of noise and vibration, as well as a sharp suppression of the microphone potential over the entire frequency range. Guinea pigs which were exposed to noise and vibration, got significant pathological changes in the reticular plate of the apical section of the cochlea. Due to the adhesion of microvilli and the reduction in their total number, a kind of "smoothing" of the apical surface of the supporting cells was observed everywhere. Numerous "hernial" protrusions were detected on the apical surface of the inner hair cells, which were detected much more rarely by the outer hair cells. Both types of receptor cells are characterized by the destruction of bonds between individual stereocilia in the bundle and, as a result, disruption of the ordering of the beams. **CONCLUSIONS:** The impact of the noise-vibration factor causes significant neurophysiological and neuromorphological alterations in the cochlea, manifested by changes in the amplitudes of the microphone potential, the action potential of the auditory nerve, and changes in the reticular plastic of the apical section, which characterizes the development of metabolic stress in sensitive cochlea cells.

Afternoon session

SYMPOSIUM 2. LAPIN SYMPOSIUM ON TRANSLATIONAL NEUROSCIENCE CHAIRS: PD SHABANOV (RUSSIA), DB ROSEMBERG (BRAZIL)

INTRODUCTION: PROFESSOR IZYASLAV P LAPIN



This regular ISBS symposium is dedicated to Professor Izyaslav 'Slava' P. Lapin (1930-2012), a true pioneer of experimental neuro-psychopharmacology and biological psychiatry. Slava Lapin graduated from Pavlov Medical School in St. Petersburg, and shortly after receiving PhD, was invited in 1960 to establish the first psychopharmacology laboratory at the Bekhterev Psychoneurological Institute. The most important scientific contribution of Prof. Lapin was establishing the link between serotonin levels and mood-elevating (thymoleptic) action of antidepressants. He suggested that enhanced central serotonergic tone is essential for the mood-elevating effects of antidepressants. Lapin's serotonin hypothesis of antidepressant action, published (together with G Oxenkrug) in Lancet in 1969, became one of the most cited papers published in this journal in the last 50 years. Lapin's studies have contributed greatly to the development of newest serotonergic antidepressants, such as SSRIs, currently representing the most prescribed group of psychotropic drugs in the world. Prof. Lapin was also the first to report the neuroactive effects of kynurenine and its derivatives – a discovery that opened another rapidly expanding area of glutamatergic psychopharmacology. A talented professional musician, prolific writer, painter, and an enthusiastic athlete, Prof. Lapin was a strong supporter of ISBS, and generously shared his knowledge with colleagues and students at our "Stress and Behavior" conferences and ISBS summer schools. His enthusiasm, friendship, generous support of junior colleagues, and the deep knowledge as both a clinical and experimental neuropharmacologist ('humanists' and 'animalists', as he called them), made a long-lasting impact on his colleagues and students. This ISBS symposium will continue Lapin's scientific legacy in the field of biological psychiatry and translational neuroscience.

EARLY MATERNAL SEPARATION INDUCES OXIDATIVE STRESS IN DIFFERENT RAT BRAIN REGIONS AND LEADS TO ANXIETY-LIKE BEHAVIOR. J Novotny, G Pallag, M Vodicka, R Moravcova, Z Bendova and L Hejnova, Department of Physiology, Faculty of Science, Charles University, Prague, Czech Republic

INTRODUCTION: Mother-infant contact has apparently an important role in the shaping of newborns' physiological system along with the development and maturation of the brain and behavior. There are some indications that stressful experiences in the early neonatal period may adversely affect the development of brain neurotransmitter systems and contribute to the development of certain mental illnesses. Here we investigated the impact of early maternal separation on several markers of oxidative stress in selected brain regions and, in parallel, we monitored behavior of rat pups in a light-dark box. **METHODS:** A total of 2 male and 6 female Long-Evans rats were used in this study. Rat pups were separated from their mothers on postnatal days 2 to 21 for 3 h per day or normally reared. On day 22, some animals were subjected to the light-dark box test and the others were used for the isolation of brain tissue (cortex, hippocampus and cerebellum). The level of reduced glutathione (GSH), lipid peroxidation (TBARS) and protein carbonyl formation were determined in tissue homogenates as markers of oxidative stress. **RESULTS AND DISCUSSION:** In the light-dark box test, the stressed rats did not cross from one compartment to the other and spent practically the whole period of their time in the dark compartment. On the other hand, control animals moved repeatedly between the dark and light compartment and spent about 25 % of time in the light area. Maternal separation resulted in distinct changes in the individual markers of oxidative stress. Whereas there was only mild increase in the amount TBARS in the cerebellum, a significant increase (> 10 %) of TBARS was found in the cortex and hippocampus. We also observed elevated levels (by about 15 %) of protein carbonylation in the hippocampus, but not in the other brain regions. The levels of GSH were only slightly decreased (by about 7 %) in the cortex and hippocampus, but not in the cerebellum. Collectively, our findings showed that early adverse life events may enhance oxidative stress in some brain regions. Animals subjected to maternal separation exhibited a strong anxiety-like behavior. These data indicate that increased brain oxidative stress induced by stressful experiences can be associated with the development of some mental disorders. **RESEARCH SUPPORT:** Grant 16-13399 from the Czech Science Foundation and grant SVV-260434/2017 from Charles University in Prague.

DAILY STRESSORS, PERCEIVED STRESS AND SATISFACTION WITH PROFESSIONAL ACTIVITY AMONG ADULTS WITH DIFFERENT RESISTANCE OF NERVOUS REACTION. M Petrash and V Grebennikov, St. Petersburg State University, The City Ambulance Station, St. Petersburg, Russia

INTRODUCTION: The lives of people in modern society can be called stressful. People daily affected by many stressors, which inevitably affect different aspects of life and professional activity. Professional life is very important in one's life and occupies a large part of his/her time. We assumed that adults with different resistance of nervous reaction will differ on the parameters of professional development. We suggested that the expressiveness of daily stressor and level of the perceived stress will differ in the allocated groups. And the relationship of daily stressors and satisfaction in professional activities in groups will be different. We also believe that various parameters of professional factors will be resources of perceived stress. **METHODS:** Questionnaire "The professional development factors" (by Petrash); Scale of Perceived Stress (Russian version by Ababkov, 2017); List of daily stressors (82 items; Petrash et al., 2016); To estimate physiological responses to daily stress we used Express diagnostics of functional status and efficiency by Moroz; and the stress index by Angioscan. Participants: 313 adults aged 21 to 65 years were divided into three groups: the normal nervous reaction; slightly reduced nervous reaction; reduced nervous reaction. **RESULTS AND DISCUSSION:** Our study revealed

differences in the situation of professional development, satisfaction with professional activity, daily stressors, perceived stress in the groups: higher scores of "satisfaction with professional activity" in the first and second groups; higher expressiveness of daily stressors, higher levels of "overstrain", "scale of perceived stress" and the stress index within third group. Study revealed that in groups with different resistance of nervous reaction the parameters of satisfaction with professional activity and the perceived stress are provided by different daily stressors. Using regression analysis, we have shown that the factor of professional development "emotional stability" reduces the level of perceived stress in the first and second groups; and in the third group such factor is a factor «satisfaction with professional activity". Our results suggest that the professional factors and daily stressors are differently associated with the perceived stress within groups with different resistance of nervous reaction and create an additional mechanism to reduce perceived stress. **RESEARCH SUPPORT:** Russian Science Foundation project 16-18-10088 "Complex study of the daily stressors and resources for coping with them in different periods of adulthood".

DAILY HASSLES, STRESS AND COPING IN WOMEN: DOES MARITAL STATUS MATTER? S Savenysheva, St. Petersburg State University, St. Petersburg, Russia

Investigation of daily hassles influence showed that the accumulation of daily hassles has a stronger negative impact than the life events on the physical health and well-being. The gender analysis indicated a higher level of both general stress and everyday stress in women. However, differences in the types and level of stressors in women with different marital status have been poorly studied, as well as psychological and physiological resources of coping-behavior. **AIMS:** to investigate daily hassles, perceived stress, life event and their relation to coping and functional efficiency in women with different marital status. The experimental sample included 144 women aged 25-50 years (mean age 36.3 years) with different marital status lived in Russia. Methods. Questionnaire of everyday hassles, The Life events scale, Scale of perceived stress-10, Technique of studying of Functional efficiency, Ways of Coping Questionnaire. **RESULTS:** A comparative analysis of the level of stress and daily hassles in women, depending on the marital status and the presence of children, revealed no differences in the level of perceived stress and general indicators of daily hassles. The intensity of work daily stressors was higher in women who are married than for single women; the intensity of daily stressors associated with the household are higher in women with children, compared with women without children. An analysis of the relation between perceived stress in women with everyday stressors and life events has shown that perceived stress is more closely related to everyday stressors than to life events. It's interesting that the level of functional efficiency negatively correlates with the overall intensity of stressors, however, it is not related to life events and perceived stress. Perceived stress is most closely related to occupational stressors and personal experiences. The relationship between stress indicators and coping strategies has shown that the greatest intensity of everyday stressors and perceived stress is observed in the application of the accepting responsibility strategy, and the low level of the strategy of problem-solving planning. A comparative analysis of the relationship structure of perceived stress, everyday stressors and psychological and physiological resources in groups of women with different marital status, as well as in groups of women with children and without them, revealed their significant differences. **CONCLUSION:** Daily hassles play a key role in the level of perceived stress, as well as the functional efficiency of women, compared to life events. The most significant role in stress emergence is played by the coping strategy of planning problems and accepting responsibility. Differences in groups of women with different marital status are manifested more in the relationships with psychological and physiological resources than in level characteristics. **RESEARCH SUPPORT:** Grant of RNA 16-18-10088.

OXR1 OREXIN BRAIN RECEPTORS ARE INVOLVED IN EFFECTS OF CHRONIC ALCOHOLIZATION AND AMPHETAMINE-ACTIVATED SELF-STIMULATION VIA SIMILAR MECHANISMS INVOLVING DA2/OXR1 DIMER COMPLEX FORMATION. PD Shabanov, ISBS Fellow, ER Bychkov, PP Khokhlov and AA Lebedev, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

The role of neuropeptides in addictive state formation and application of neuropeptides in pharmacological treatment should be considered nowadays as very important direction in modern biomedical researches. Particular attention is drawn the possibility of use the neuropeptides signaling systems as a pharmacological target in the alcohol and drug dependence treatment. One of the most attractive regulative peptide system is orexin system that has been nearly discovered. Orexin neuropeptides take part in high range of functions, especially in food intake behavior and sleep–awake cycle. The orexin neuropeptides' family contains orexin A that consist of 33 amino-acid residues and orexin B from 28 residues. Orexin A and orexin B producing neurons are localized preferably in the lateral hypothalamus. They direct their projections to almost all brain structures. Orexin peptides link to receptors of two types: OXR1 and OXR2. Orexin B has an equal affinity to receptors of both types. Orexin A has an affinity to OXR1 receptor in 20-fold higher, than to OXR2 receptor. The OXR1 antagonists was shown to decrease the alcohol intake and ethanol-induced dopamine release in the nucleus accumbens. Moreover, OXR1 antagonists blocked conditioned place preference of alcohol. **RESEARCH AIMS:** 1) to study gene expression of orexin OXR1 antagonists in long-term alcoholization conditions and following withdrawal of ethanol; 2) to clear if SB-408124, an antagonist of the orexin A-selective receptors OXR1, injected into the central amygdala can interact with antagonist D2 receptor sulpiride on inhibition of reinforcing effects of amphetamine on self-stimulation of the lateral hypothalamus in rats. **METHODS:** 48 Wistar rats were alcoholized with 15% ethanol solution as alone liquid source and free access to dry food for 6 months. Control rats of the same age received water. The animals were decapitated immediately after alcoholization (1st group), in 24 h (2nd group) and 7 days (3rd group) after alcohol withdrawal. Gene expression of orexin receptor of 1st type was determined by the reverse transcriptase–polymerase chain reaction in real time method. The content of mRNA was determined in the frontal cortex, hippocampus and ventral tegmental area. The orexin receptor gene expression values were normalized to the level of glyceraldehyde-3-phosphate dehydrogenase gene expression in control group of animals and were presented in relative units. In the second part of investigation, 51 Wistar male rats were implanted bipolar electrodes into the lateral hypothalamus to study self-stimulation reaction in the Skinner box. Simultaneously, the microcannules were implanted into the central nucleus of amygdala (CA) to inject the drugs studied (1 µg in 1 µl in volume for each injection). Antagonist of the orexin A-selective receptors OXR1 SB-408124 was administered intrastructurally (into CA) and antagonist of D2 receptor sulpiride was injected intraperitoneally followed by pharmacological analysis. **RESULTS:** Chronic alcoholization for 6 months decreased the level of orexin receptor gene expression only in the frontal cortex. After alcohol withdrawal, the content of receptor gene expression was reduced on the 1st and 7th days. On the contrary, the orexin receptor gene expression in the hippocampus was increased on the 1st and 7th days after ethanol withdrawal compared to control group values. In the ventral tegmental area, the orexin receptor gene mRNA levels did not change after alcoholization and ethanol withdrawal in comparison with control group. Our data suggest the orexin signaling system takes part in development of dependence to alcohol. The hippocampus is known to be involved in behavioral responses to alcohol-associated contextual stimuli. As the orexin receptor gene expression is increased in the hippocampus, this mechanism may be participate in formation of pathological craving to alcohol in long-term alcoholization. SB-408124, an OXR1 receptor antagonist, injected into the extended amygdala region (CA) alone had no effect on self-stimulation of the lateral hypothalamus. Sulpiride in low dose (5 mg/kg) did not affect both the spontaneous and amphetamine-activated self-stimulation (1 mg/kg). Amphetamine as a rule increased self-stimulation measured as lowering the threshold and enhancing the frequency. Amphetamine-induced stimulatory effects on intracranial self-

stimulation were reduced by injections of SB-408124 into the CA up to the background level. Simultaneous administration of SB-408124, an antagonist of the orexin A-selective receptors OXR1, and sulpiride i.p. (5 mg/kg) inhibited amphetamine-induced self-stimulation in more degree than background level, that was sulpiride potentiated the inhibitory effect of SB-408124. These data demonstrate that OXR1 receptors play an important role in regulating the reinforcing and reward-enhancing properties of amphetamine and suggest that orexin transmission (neuromodulation) is likely essential for establishing and maintaining the amphetamine habit in human addicts. However, the observations that OXR1 antagonism reduces brain reward and blocks stress- and cue-induced reinstatement of drug-seeking suggesting that class of compounds may be useful additions to stress-reduction and other behavioral therapies in the treatment of substance abuse disorders. **CONCLUSION:** These findings suggest that the combined use of low doses of D2 antagonists (like sulpiride) and antagonists of the orexin A-selective receptors OXR1 (like SB-408124) are necessary to reorganize the central mechanisms underlying the addiction state to target correction of addictive disorders. OXR1 and D2 dopamine receptor can arrange a dimer suporeceptor structure, the functioning of which facilitates effects of subthreshold doses of dopaminergic drugs on self-stimulation phenomenon.

INTERACTIVE POSTER: THE ROLE OF OREXIN A IN STRESS-INDUCED BEHAVIORAL PATTERNS OF OBSESSIVE-COMPULSIVE BEHAVIOR IN A RAT MARBLE TEST. AA Lebedev, ND Yakushina, IYu Tissen, AG Pshenichnaya, ER Bychkov and PD Shabanov, ISBS Fellow, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Orexins A and B are hypothalamic neuropeptides involved in the regulation of circadian rhythms, energy metabolism and reward behavior. Projections of orexin neurons found in different brain structures such as the amygdala, medial prefrontal cortex, hippocampus, locus ceruleus and bed nucleus of stria terminalis. These structures are involved in the formation, consolidation and extinction of aversive memory and reinforcing properties of environmental events. Several behavioral components of obsession (obsessive and anxious ideas) and compulsions (obsessive actions) directed to anxiety reduction are modeled in a rodent marble test. Serotonin and dopamine play important roles in impulsivity and addiction (Zeeb F.D. et al., 2009). **METHODS:** Experimental animals were exposed to predator – a tiger python snake. The rats suffered from an acute stressor influence. Effect of stress influence was evaluated with behavioral tests. Orexin and OX1R antagonist SB-408124 were administrated intranasal in dose 1 mg/ml, 20 μ l, for 7 consecutive days after stress. A rodent marble test can be qualified as the most informative test of evaluation of obsessive-compulsive disorder. Rat buried glass balls (1 cm in diameter) in test cage for 30 min. Number of buried balls were evaluated. Additionally, effects of psychostimulant amphetamine on the rat behavior was studied in a marble test, anxiety-phobic model (scale), in the elevated plus maze (evaluation of anxiety), open field (evaluation of motor and emotional activity) and resident-intruder test (intraspecies behavior). **RESULTS:** Amphetamine 0.5 and 1.5 mg/kg increased a number of burying bolls and elevated anxiety level in dose dependent manner. This accompanied with reduction of explorative activity, elevation of motor activity and number of individual behavioral patterns. Number of buried balls was decreased after stress exposure (5.7 ± 3.3). For 7 days after stress exposure, the number of buried balls were 13.2 ± 3.2 . At the same time the number of buried balls were significantly decreased in group with orexin administration (7.9 ± 1.2 ; $p < 0.05$) and had no effect in OX1R antagonist SB-408124-treated group of rats. In additional experiments, the anxiogenic effect of orexin administration was shown in the elevated plus maze (control group 92.2 ± 28.1 sec, orexin group 47.0 ± 28.1 sec in the light arm, $p < 0.05$). The time in the light arm after stress was 19.0 ± 6.8 sec, in the group with orexin – 28.5 ± 14.2 sec, in SB-408124-treated group of animals – 53.2 ± 19.7 sec ($p < 0.05$). **CONCLUSION:** Therefore, dopaminergic system of the brain activated with amphetamine is involved in obsessive-compulsive behavior. Pathological gambling as a type of

addictive human pathological conditions includes motivational sphere that manifests obsessive-compulsive disorder. In particular, these actions are based on the changes in the brain activity of the dopaminergic system. Moreover, obsessive-compulsive behavior (number of buried balls) was decreased in group with orexin administration after python stress. In the elevated plus maze orexin antagonist SB408124 reduces anxiety in rats after python stress. This data is consistent with previously established experimental and clinical data showed the role of orexin A lack induced with SB334867 or narcolepsy in extinction of aversive memory. Thus, we discuss the role of anxiogenic effects of orexin and anxiolytic effects of the OX1R antagonist in stress-induced obsessive-compulsive disorder and dopamine component of pathological gambling.

LECTURE 3: ISBS PRESIDENTIAL LECTURE: MODELING SOCIAL STRESS IN RODENTS.

AV Kalueff, ISBS Fellow, DA Meshalkina and KA Demin, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; Southwest University, Chongqing, China

Despite its high prevalence and harm, the pathobiology of anxiety and depression remain poorly understood. Psychiatric disorders complexity and their polygenic nature complicate their genetic analyses, which often not only reveal disorder-specific genes, but also show significant genetic overlap and cross-disorder heritability (Murphy et al. 2003, Ivleva et al. 2010, Cross-Disorder Group of the Psychiatric Genomics et al. 2013, Ikeda et al. 2013, Schizophrenia Working Group of the Psychiatric Genomics 2014 et al. 2014). To resolve some of the complications resulting from this 'spectrum' nature of the CNS pathogenesis, the domain interplay and "interlinking" genes concepts were proposed previously by our team (Kalueff et al., 2008, 2014). We proposed that the interaction between the disordered endophenotypes (or their domains) can be based on both 1) shared molecular pathways and 2) specific 'crosstalk' mechanisms that, although not influencing the phenotypes by themselves, can modulate their interrelatedness during pathogenesis. To test this theory experimentally in a rodent model, we used chronic social defeat stress model in C57BL/6J mice, according to Kudryavtseva et al. (1994, 1996). Changes in gene expression, set enrichment and topology of differentially expressed genes and proteins connections, were examined in prefrontal cortex and hippocampus on different modeling stages of the disease progression, including well-validated anxious stage (10 days of social defeat), transitional stage (15 days of social defeat) and depressed stage (20 days). Observed changes that were conservative between brain regions can be described as follows: major disruption of neurotransmitter signaling in 'anxious' mouse group, followed by astrocyte function downregulation in 'transitional' group and ended by differential tissue-specific reactions in the 'depressed' group. These changes are mostly mediated by various patterns of signaling pathways downregulation, and were usually accompanied with changes in cell adhesion, inflammation and ion transport systems. These pilot experimental results strongly support the proposed interlinking genes that seem to play a key role in integrating anxiety and depression pathogenesis *in vivo*, and also additionally highlight the role of astrocyte pathology in major depressive disorder pathogenesis. **RESEARCH SUPPORT:** The Russian Foundation for Basic Research (RFBR) Grant 16-04-00851, and Intramural Funds from Rectorate of St. Petersburg State University.

ROUND TABLE: ETHICS IN BIOMEDICINE – CURRENT CHALLENGES

Day 2. Saturday, December 2, 2017

Windsor Excelsior Hotel, Av. Atlântica, 1800, Copacabana, Rio de Janeiro, Brazil

Morning session

SYMPOSIUM 3. ALTERNATIVE MODELS IN STRESS BIOMEDICINE

Sponsored by the International Zebrafish Neuroscience Research Consortium (ZNRC)

CHAIRS: LJG BARCELLOS (BRAZIL), DB ROSEMBERG (BRAZIL), AV KALUEFF (USA)

INTRODUCTION

ZEBRAFISH LISTENING TO VIVALDI ARE CALMER AND LESS ANXIOUS! H Barcellos, G Koakoski, F Chaulet, K Schreiner Kirsten, LC Kreutz, AV Kalueff, ISBS Fellow, and LJG Barcellos, University of Passo Fundo, Passo Fundo, Brazil, St. Petersburg State University, Institute of Experimental Medicine of Almazov Center, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; Southwest University, Chongqing, China

The environmental enrichment has been studied aiming to provide welfare and improve the performance of many animal species. Experimental, captive or livestock animals must be housed in environments with space and complexity to allow the expression of their normal behavioral repertoire. The experimental and farm facilities are usually noisy environments that are stressful to almost all species, causing behavioral and physiological changes. In this line, studies have shown that classical music decreased abnormal behaviors, stereotypic pacing, and cortisol levels in humans and nonhumans primates. Horses, cows, pigs, dogs, cats, birds and rodents were calmer when listening to classical music. The reaction of fish to music has also been studied; for example, turbot and carp submitted to classical music into the aquarium or culture ponds grew more with better-feed efficiency. In addition, it is well known that fish are capable of listening to sound and noises out of the aquatic ambient. Thus, they could be perturbed by surrounding sounds in the lab and aquarium facilities, and we hypothesized that classical music in the experimental rooms can affect fish behavior and physiology. Operationally, to test this hypothesis, we submitted the fish to 2 h of Vivaldi music (Classic Collection), twice a day for 15 days. Then, the fish was submitted to novel tank test and subsequently euthanized for trunk cortisol measurement. Here, we show that zebrafish exposed to music were less anxious. In fact, fish that listened to music preferred the top zone. At the top zone, the distance travelled and the absolute turn angle were greater, while the entries at the bottom zone were lower than controls. However, the cortisol levels after the novel tank test did not evidence statistical differences. A possible explanation is that both treatments were not challenged with an additional stress. In a practical perspective, our results point to an advantage by using music as environmental enrichment in zebrafish facilities, since we clearly demonstrated the effect of classic music auditory enrichment in this experimental fish model.

ZNRC LECTURE 4: THE STRESS RESEARCH IN UPF: SOCIAL STRESSORS AND WELFARE. LJG Barcellos, University of Passo Fundo (UPF), Passo Fundo, Brazil

Here, we summarize the scientific contribution of the Fish Physiology Lab of the University of Passo Fundo (Brazil), to the field of studying of fish stress responses. Between 1999-2017, a total of 43 papers have been published by the Lab, covering various topics of general stress response in fishes. In the initial years, the fish models studied were the Siluridae *Rhamdia quelen* and the Cichlidae *Oreochromis niloticus*. In 2007, the zebrafish (*Danio rerio*) was introduced in the Lab.

Among the Lab's 43 papers, 12 focused on social stressors and/or fish welfare. The first paper on stress, published by the Lab in 1999, showed the group potentiation of stress response in Nile tilapia, a highly social and hierarchical species. Similar results were found in zebrafish in 2015. Two sequential studies showed that the R. quelen prefers an environment with blue light and the presence of dark shelters. In line with this, a recent paper showed that environmental enrichment seems to be effective to reduce stress, with clear implications to fish welfare. In 2007, we begun a sequence of studies focusing on endocrine and behavioral changes induced in the context of prey-predator relationship and intraspecific communication about predation risk, and the effects of psychoactive substances on this communication. The different nature of the cues (visual and chemical) used in the predation risk communication was further examined in subsequent Lab's publications. Another important paper showed that zebrafish could recognize the scent of dead conspecifics, which triggers a typical anti-predatory reaction. Taken together, from the welfare perspective, we point to the fact that the absence of a typical hormonal response to stress is not a synonym of fish welfare, but the presence of the cortisol response might be used as a clear indicator of poor welfare situation. Also, we highlight the importance of environmental comfort, such as optimal light and wall colors, presence of shelters and environmental enrichment. From the social stress perspective, we show a strong relation between hormonal response to stress and the detection and response to a predation situation. The predation risk can be communicated between conspecifics by chemical and visual cues, and while this communication is not dependent on cortisol increase in the donor fish, it can be modulated by various psychoactive substances.

ZNRC LECTURE 5: ZEBRAFISH AS A MODEL ORGANISM FOR ASSESSING ANXIETY- AND FEAR-LIKE BEHAVIORAL ENDOPHENOTYPES. DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

Zebrafish is an emergent model organism in behavioral neuroscience research, especially due to their genetic tractability, evolutionarily conserved genome, and well-characterized behavioral repertoire. Despite the considerable differences between the mammalian and the teleost CNS, homologous functions in several key zebrafish brain areas have been described. For example, the lateral pallium of the zebrafish telencephalon is responsible for memory processing, whereas the habenula is associated with fear responses, similar to the hippocampus and the amygdala, respectively. These advantageous features make zebrafish an attractive model organism that help investigate the neural bases of fear and anxiety and their associated behaviors using pharmacological and/or nonpharmacological approaches. Here, I will discuss the utility of zebrafish in translational neuroscience research, considering their applicability for assessing anxiety- and fear-like behaviors. Since ethanol, caffeine, and conspecific alarm pheromone exposure trigger defensive behaviors (e.g., bottom dwelling, immobility, social interaction, freezing, and erratic movements) they serve as interesting protocols for modeling anxiety- and fear-like behaviors in zebrafish. Moreover, the association of different experimental protocols using both short-fin and leopard zebrafish represent suitable strategies for exploring the mechanisms underlying neuroprotection, defensive behaviors, and aversive responses. **RESEARCH SUPPORT:** CNPq research productivity grant (307595/2015-3).

MODELING ANTIDEPRESSANT DISCONTINUATION SYNDROME (ADS) - STUDIES OF BEHAVIORAL EFFECTS OF CHRONIC AMITRIPTYLINE AND SERTRALINE IN ADULT ZEBRAFISH. TO Kolesnikova, SL Khatsko and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: Antidepressant discontinuation syndrome (ADS) is a common problem for all classes of antidepressant drugs. Clinical ADS symptoms appear (and then quickly disappear)

within several days after withdrawal from antidepressants, and include increased anxiety, headache, dizziness, sensory deficits and nausea, with similar phenotypes also seen in rodent models of ADS. Amitriptyline and sertraline are popular antidepressants commonly used chronically to treat depression, post-traumatic stress disorder (PTSD) and anxiety. Here, we attempted to develop an ADS model based on an aquatic (zebrafish) species undergoing withdrawal from chronic amitriptyline and sertraline. **METHODS:** A total of 105 adult wild type short-fin outbred zebrafish were housed in group of 40 in 40-L tank filled with filtered water, according with the standards of zebrafish care. All fish were experimentally naïve and fed twice a day by TetraMinPro. The novel tank test was used to assess zebrafish behavior for 5 min after 7 days of chronic amitriptyline (n=15) and sertraline (n=15), as well as 1 day and 2 days after withdrawal of amitriptyline (n=15) and sertraline (n=15). We evaluated the latency (s) and number of top entries, time spent in the upper half (top), duration and frequency of freezing and the number of anxiety-like erratic movements. **RESULTS AND DISCUSSION:** Overall, chronic 7-day amitriptyline treatment significantly increased top duration compared with water-exposed control group. Conversely, chronic sertraline treatment did not change top latency and duration, but decreased the number of erratic movements. 1 day after withdrawal of amitriptyline, we did not find any differences in observed endpoints, except for fewer erratic movements, whereas a 1-day withdrawal from sertraline caused longer top duration and more erratic movements. 2 days after withdrawal of amitriptyline and sertraline, we found longer top duration in both drug groups vs. controls. Thus, the present study was first to describe behavioral effects of chronic administration of amitriptyline and sertraline in adult zebrafish. Our previous pilot study found that 2-week chronic administration of amitriptyline and sertraline did not cause overt ADS-like effects, which often occurs in antidepressant users and abusers clinically. Taken together, our results suggest that amitriptyline and sertraline are likely to have prolonged anti-stress/anxiolytic/antidepressant-like effects even with relatively short periods of administration, and that ADS-like symptoms (which are clinically known as short-time deficits) may be difficult to evoke or model in zebrafish because of this. **RESEARCH SUPPORT:** Ural Federal University.

TAURINE ATTENUATES SEIZURES AND PREVENTS OXIDATIVE STRESS INDUCED BY PENTYLENETETRAZOLE IN ZEBRAFISH. BD Fontana, PR Ziani, J Canzian, NJ Mezzomo, TE Muller, MM Santos, VL Loro, NBL Barbosa, CF Mello and DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

INTRODUCTION: Epilepsy is a common disorder characterized by seizure recurrence associated to behavioral changes and neurobiological dysfunctions. Taurine (TAU) is a sulfur amino acid that acts as an inhibitory neuromodulator via GABAA and glycine receptors. Moreover, studies have shown its antioxidant activity, which contributes for the pleiotropic role in the central nervous system (CNS). Thus, TAU may play a potential neuroprotective effect in several neurodegenerative diseases. In this study, we evaluated whether TAU pretreatment can exert a protective role in seizures, oxidative stress and neuronal viability of zebrafish challenged to PTZ. **METHODS:** Subjects were 360 adult (4-6 months old) zebrafish (Danio rerio, 50:50 male:female ratio, short fin strain). Fish were pretreated for 40 min with 42, 150, and 400 mg/L TAU and further exposed to 10 mM PTZ for 20 min. Seizure scores were evaluated every 30 seconds and seizure intensity was estimated using the area under the curve (AUC). The antioxidant defenses (SOD, CAT, and GST activities, as well as NPSH levels), oxidative damage (lipoperoxidation and carbonylated protein levels) and CNS cytotoxicity (mitochondrial viability and LDH activity) were assessed. **RESULTS AND DISCUSSION:** TAU pretreatment at 150 mg/L attenuated the seizures by decreasing seizure intensity in PTZ-exposed fish. Additionally, this concentration increased the latency to reach clonic seizures and decreased their frequency. PTZ increased lipoperoxidation and carbonylated protein levels when compared to control, whereas 150 mg/L TAU pretreatment showed a protective effect. No differences were observed for antioxidant defenses and cytotoxicity measures. Overall, we demonstrate a neuroprotective role of TAU in PTZ-exposed

zebrafish since it attenuated the seizure intensity and prevented the increased lipoperoxidation and carbonylated protein levels in the brain. **RESEARCH SUPPORT:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Amparo à Pesquisa do Rio Grande do Sul (FAPERGS), and Conselho Nacional de Pesquisa e Tecnologia (CNPq).

DIFFERENT EFFECTS OF CONSPECIFIC ALARM PHEROMONE ON ECTONUCLEOTIDASE AND ACETYLCHOLINESTERASE ACTIVITY IN BRAIN TISSUE OF TWO ZEBRAFISH POPULATIONS. J Canzian, BD Fontana, VA Quadros and DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

INTRODUCTION: The zebrafish is an emergent model organism for assessing fear and anxiety-like phenotypes. The short fin wild-type (WT), and leopard (leo) populations have several behavioral differences, in which leo displays pronounced defensive responses. Mounting evidence suggests a modulatory role of cholinergic and purinergic signaling in fear and anxiety, but the involvement of these neurotransmitter systems in the behavioral profile of zebrafish is obscure. **OBJECTIVE:** Here we tested whether acute exposure to conspecific alarm pheromone (CAP) alters acetylcholinesterase and ectonucleotidase activities in brain tissue of WT and leo. **METHODS:** CAP was extracted in 10 mL of distilled water by damaging epithelial cells with a razor blade using donor cold-anesthetized fish. Four fish were simultaneously placed in a novel tank containing 3.5 mL/L CAP or distilled water (control group) for 5 min. CAP induced fear-like responses during the exposure period in both populations. Fish were further euthanized, the brains were dissected out and the biochemical analyses were performed. Four brains were pooled for each independent experiment. Data were expressed as means \pm standard error of mean of four independent experiments ($n=4$) and analyzed by two-way ANOVA followed by Student-Newman Keuls multiple comparisons test, considering $p < 0.05$ as significant. **RESULTS:** Although CAP did not alter brain acetylcholinesterase activity in leo, it increased the enzyme activity in WT population ($p < 0.01$). Significant effects of population \times pheromone interaction ($F(1, 12) = 5.086$; $p = 0.0436$) and population ($F(1, 12) = 7.349$; $p = 0.0189$) were observed for ecto-5'-nucleotidase activity. We verified that WT showed a significant decrease in AMP hydrolysis when compared to its respective control. Moreover, basal endpoints between populations revealed enhanced acetylcholinesterase and reduced ecto-5'-nucleotidase activities in leo population. **CONCLUSION:** Considering the modulatory role of CAP in brain acetylcholinesterase and ecto-5'-nucleotidase activities and the basal differences between WT and leo, we suggest a potential role of cholinergic and purinergic systems in fear- and anxiety-like responses of zebrafish.

ETHANOL-INDUCED AGGRESSIVE BEHAVIOR IN ZEBRAFISH: PUTATIVE INVOLVEMENT OF SEROTONERGIC PATHWAY. TE Muller, PR Ziani, BD Fontana, J Canzian, FV Stefanello, ARS Santos and DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

INTRODUCTION: Alcoholism is a prevalent disease that has a significant negative impact on the patient and society. Alcohol abuse affects the levels of neurotransmitters as serotonin. However, the neurobiological processes underlying alcohol-induced behavioral changes are poorly understood. Zebrafish is gaining popularity in behavioral neuroscience due to the genomic conservation, the well-characterized neurotransmitter systems, and their extensive behavioral repertoire. Studies have shown that acute ethanol (EtOH) exposure induces behavioral changes and increases serotonin levels in zebrafish brain. Thus, the aim of this study was to verify the involvement of serotonergic pathway on aggressive behavior triggered by acute EtOH exposure in zebrafish. **METHODS:** Subjects were 120 adult zebrafish (Danio rerio, 50:50 male:female ratio, short fin strain). The tryptofan hydroxylase enzyme inhibitor (p-chlorophenylalanine) was administered for 2 days (a single i.p. injection, 300 mg/kg per day) prior to 1 h EtOH exposure at 0.25, 0.5 and 1.0% (v/v). Aggression was further evaluated using the inclined mirror-image

stimulus. Fish were able to explore the apparatus for 5 min and the following behaviors were quantified: transitions and time spent in the mirror area, number, duration and latency to aggressive attacks. **RESULTS AND DISCUSSION:** EtOH exposure did not alter transitions and time in the mirror area, but pCPA administration decreased the transitions to the mirror area at 1.0% EtOH. The number and duration of aggressive episodes increased at 0.25% EtOH. pCPA abolished aggressive behavior at 0.25% EtOH and decreased the number of aggressive episodes at 0.5% EtOH. Although EtOH did not alter the latency to attack the mirror, pCPA increased this endpoint at 0.25 and 1.0% EtOH. In summary, we suggest an involvement of serotonergic system in EtOH-induced aggressive behavior. **RESEARCH SUPPORT:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Amparo à Pesquisa do Rio Grande do Sul (FAPERGS), and Conselho Nacional de Pesquisa e Tecnologia (CNPq).

FEAR CONDITIONING RESPONSES TO THE CONSPECIFIC ALARM SUBSTANCE IN ZEBRAFISH. FV Stefanello, BD Fontana, NJ Mezzomo, DL Meinerz, C Maximino, MG Lima and DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

INTRODUCTION: Anxiety and stress-related disorders are severe psychiatric conditions that affect the human population. Conspecific alarm substance (CAS) is a complex pheromone-like mixture that induces fear responses in species. Fear conditioning involves learning the association of a neutral conditioned stimulus (CS) with an unconditioned stimulus (US), which serves as a threat signal. Re-exposure to the CS will elicit the expectancy of an aversive outcome and activates conditioned defensive responses. Here, we assess whether a single CAS exposure elicits aversive conditioning responses in zebrafish using the conditioned place aversion (CPA) paradigm. Moreover, we verify the stability of conditioned responses after different time intervals. **METHODS:** In the preconditioning test, the basal preference of each fish for a particular compartment in a white/yellow tank was tested. Later, animals were placed in their preferred chamber and then exposed to CAS for 5 min in the conditioning session. Changes in preference, as well as defensive behavior were tested on different post-conditioning days (1, 2, 3 and 7) after conditioning. **RESULTS AND DISCUSSION:** Zebrafish showed a slight basal preference for the white compartment of the CPA apparatus in the preconditioning phase. CAS increased freezing and erratic movements in the conditioning session. We also observed a reduced time spent in the conditioning side of the tank, as well as increased risk assessment, freezing and erratic movements up to 7 days post-conditioning. Both distance traveled and crossings did not alter in the sessions. Overall, we demonstrate a persistent aversive response of zebrafish after a single CAS conditioning session. **RESEARCH SUPPORT:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Amparo à Pesquisa do Rio Grande do Sul (FAPERGS), and Conselho Nacional de Pesquisa e Tecnologia (CNPq).

NICOTINE MODULATES CONTEXTUAL FEAR CONDITIONING INDUCED BY ALARM SUBSTANCE IN ZEBRAFISH. T Duarte, PR Ziani, TE Muller, FV Stefanello, BD Fontana, J Canzian and DB Rosemberg, Federal University of Santa Maria, Santa Maria, RS, Brazil

INTRODUCTION: Alarm substance (AS) is produced by fish epidermal cells and released after a predator attack, triggering aversive responses. Fear is an adaptive response of animals that may influence learning and memory processing. Acetylcholine (ACh) is a neurotransmitter that plays a key role in aversive memory via nicotinic receptors. At synaptic cleft, acetylcholinesterase (AChE) cleaves ACh into choline and acetate, controlling the cholinergic neurotransmission. Since previous data showed that AS elicits fear responses and modulates AChE activity after a single exposure, we investigated whether nicotine modulates contextual fear conditioning responses and alters AChE activity following alarm substance exposure. **METHODS:** Fish were exposed to 1 mg/L of nicotine or non-chlorinated water for 3 min. Later, animals were transferred to the

experimental tank (containing self-adhesive films of opaque plastic in black and white color stripes externally) in the absence or presence of 3.5 mL/L AS for 5 min (training session). Animals were reintroduced in the same context after 24 h in the absence of AS (post-training session). **RESULTS AND DISCUSSION:** In the training session, AS increased freezing and erratic movements. Nicotine had a preventive effect in the number and duration of erratic movements. In the post-training session, freezing bouts were elevated in fish previously exposed to AS and nicotine exacerbated freezing responses, as well as increased AChE brain activity. Therefore, we suggest an involvement of cholinergic signaling in associative learning and fear-like behaviors, as well as demonstrate a positive modulation of nicotine in the contextual fear conditioning responses of zebrafish. **RESEARCH SUPPORT:** Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Amparo à Pesquisa do Rio Grande do Sul (FAPERGS), and Conselho Nacional de Pesquisa e Tecnologia (CNPq).

ZNRC LECTURE 6: ZEBRAFISH MODELS OF CHRONIC STRESS. AV Kalueff, ISBS Fellow, ZENEREI Research Center, Slidell, LA, USA; Southwest University, Chongqing, China; St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia

Chronic stress is the major pathogenetic factor of human anxiety and depression. Zebrafish (*Danio rerio*) have become a novel popular model species for neuroscience research and CNS drug discovery. The utility of zebrafish for mimicking human affective disorders is also rapidly growing. Here, we present a new zebrafish model of clinically relevant, prolonged unpredictable strong chronic stress (PUCS). The 5-week PUCS induced overt anxiety-like and motor retardation-like behaviors in adult zebrafish, also elevating whole-body cortisol and proinflammatory cytokines - interleukins IL-1 β and IL-6. PUCS also elevated whole-body levels of the anti-inflammatory cytokine IL-10 and increased the density of dendritic spines in zebrafish telencephalic neurons. Chronic treatment of fish with an antidepressant fluoxetine (0.1mg/L for 8days) normalized their behavioral and endocrine phenotypes, as well as corrected stress-elevated IL-1 β and IL-6 levels, similar to clinical and rodent data. The CNS expression of the *bdnf* gene, the two genes of its receptors (*trkB*, *p75*), and the *gfap* gene of glia biomarker, the glial fibrillary acidic protein, was unaltered in all three groups. However, PUCS elevated whole-body BDNF levels and the telencephalic dendritic spine density (which were corrected by fluoxetine), thereby somewhat differing from the effects of chronic stress in rodents. Together, these findings support zebrafish as a useful in-vivo model of chronic stress, also calling for further cross-species studies of both shared/overlapping and distinct neurobiological responses to chronic stress (Song et al., 2017).

EFFECTS OF U-49900, A μ -OPIOID RECEPTOR AGONIST, ON ADULT MICE AND ZEBRAFISH. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: 3,4-dichloro-N-(2-(diethylamino)cyclohexyl)-N-methylbenzamide (U-49900) is a structural analogue opioid analgesic drug of U-47700. Effects and toxicity are only reported in drug user forums, and unsubstantiated by analytical confirmation. Little is known about U-49900's toxicoepidemiology, and no published studies exist for it due to the drug's recent emergence as a recreational drug. An online search for "U-49900" retrieved results as a "research chemical." Vendors listed U-49900 as a "hot-selling" item with effect stronger than U-47700. We have previously reported psychoactive action U-47700. Here, we characterize behavioral effects of U-49900 in adult mice in the open field test (OFT) and the elevated plus-maze test (EPM), and in adult zebrafish (*Danio rerio*) in the novel tank test. **METHODS:** A total of 40 white 4-month-old female mice were used for this study. The OFT and EPM were utilized to assess mouse behavior for 5 min in each of the following tests: a 30-min pretreatment with 50, 75 and 100 mg/kg U-49900

(n = 10 per group), scoring the latency, frequency and duration of locomotor activity, freezing, rearing and hole-poking behavior. 75 adult (6-month-old) wild type long-fin zebrafish (50:50 male: female ratio) were threatened by 1, 5, 10 and 25 mg/L of U-49900 and testes in the novel tank test. All fish were experimentally naïve and housed in groups of 15 fish per 20-L tank. The standard 20-min-pre-treatment was based on our prior experience with different drugs. We are registered the number and duration of freezing bouts, number of erratic movements, latency, duration and frequency of top entries. **RESULTS AND DISCUSSION:** The study showed that U-49 with acute administration at doses of 50, 75 and 100 mg/kg in mice does not change consciousness, characteristic for psychoactive substances. The course of acute behavioral stress response in experimental animals of the experimental group is within the limits of the norm of control animals. The substance does not exhibit psychoactive properties at low doses, however, when the dosage increased, twitching of limbs, convulsions, and shallow breathing are observed. In the Novel tank test, a decrease in the number of exits to the upper part of the tank at 25 mg/l was found vs. control group and 1 mg/l. These differences indicate the presence of weak anxiogenic-like properties in the tested compound. Thus, U-49900 does not cause a temporary change in consciousness similar to that of opioid analgesics, but it is toxic with one-time administration of high doses, and can be lethal. **RESEARCH SUPPORT:** Ural Federal University.

CONFERENCE PRESENTATION

SCHIZOPHRENIA: IMPACT ON FAMILY DYNAMICS. A Caqueo-Úrizar, M Rus-Calafell, TKJ Craig, M Irarrazaval, A Urzúa, L Boyer and DR Williams, Universidad de Tarapacá, Escuela de Psicología y Filosofía, Arica, Chile; Department of Health Service and Population Research, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; Departamento de Psiquiatría, Facultad de Medicina, Hospital Clínico Universidad de Chile, Instituto Milenio para la Investigación en Depresión y Personalidad, Santiago, Universidad Católica del Norte, Antofagasta, Chile, Aix-Marseille University Public Health, Chronic Diseases and Quality of Life Research Unit, Marseille, France, Department of Social and Behavioral Sciences, Harvard School of Public Health, Department of African and African American Studies, Harvard University, Cambridge, MA, USA

In many societies, family members are now the primary caregivers of mental health patients, taking on responsibilities traditionally under the purview of hospitals and medical professionals. The impact of this shift on the family is high, having both an emotional and economic toll. The aim of this presentation is to review the main changes that occur in family dynamics for patients with schizophrenia. The article addresses three central themes: i) changes in the family at the onset of the disorder; ii) consequences for family members because of their caregiver role; and iii) family interventions aimed at improving the complex dynamics within the family. After analyzing and discussing these themes, it is observed that despite advances in the field, the viability of taking care of a patient with schizophrenia by the family remains a challenge. Improving care will require commitments from the family, the mental health service system, and local and national governments for greater investments to improve the quality of life of society in general, and individuals with schizophrenia, in particular. **RESEARCH SUPPORT:** Universidad de Tarapacá through Proyecto Mayor de Investigación Científica y Tecnológica UTA n°3732-16.

INTERACTIVE POSTER: EFFECT OF TOLUENE CHRONIC EXPOSURE ON EXPLORATORY BEHAVIOR AND RECOGNITION MEMORY IN ADOLESCENT AND ADULT RATS. NO Pochkhidze, MG Zhvania, NJ Japaridze and MD Dashniani, Institute of Chemical Biology Ilia State University, I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Toluene and toluene-containing volatile substances are the most widely abused solvents with demonstrative addictive potential in humans. Several data indicate that as a result of toluene misuse alterations in learning and memory in organisms of different age take place. But because of differences in species, length of exposure, dose or rate of administration, it is not always possible to conclude whether adolescent experience results in changes in learning and memory are comparable to that seen in adults. The present study has been undertaken to determine whether toluene chronic exposure provokes immediate and/or persisting effect on exploratory behavior and recognition memory in open field in adolescent and adult rats. We exposed male Wistar rats at ages P 28-32 (adolescents) and P 70-75 (adults) to 2000 ppm inhaled toluene for 40 days. The immediate and persisting effects of toluene misuse (immediately after the end of toluene chronic inhalation and 90-day after the end of toluene chronic inhalation, correspondingly) were evaluated. Experimental protocol was approved by Animal Studies Committee of Beritashvili Center of Experimental Biomedicine. The major findings are: (1) toluene misuse alters exploratory activity and recognition memory in adolescent and adult rats; (2) the level of alterations depends upon the postnatal age of testing animals. In particular: in adolescent rats the most significant behavioral alterations were observed by the day following toluene chronic exposure. These alterations do not progress significantly during abstinence period: some altered parameters were almost the same as observed the day following immediately after toluene misuse and others were very close to observed in control animals. Therefore, in adolescent rats the most expressed was immediate effect of toluene misuse. In contrast, in adult rats most alterations significantly progress during the 90-d abstinence. Therefore, in these animals more substantial was persistent effect of toluene chronic exposure. Our data suggest that adolescent rats may show partial recovery from toluene toxic effect.

ART MEETS NEUROSCIENCE: AN ARTIST'S PERSPECTIVE. D Raytchev, London, UK

II GOTTESMAN ISBS LECTURES (ESTABLISHED IN 2016):

2016: RECOGNIZING THE ENDOPHENOTYPE CONCEPT IN BIOLOGICAL PSYCHIATRY OF STRESS. AV Kalueff, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; Research Institute for Marine Drugs and Nutrition, Guangdong Ocean University, Zhanjiang, China; ZENEREI Research Center, New Orleans, LA, USA

2017: STRESS ENHANCED MOTIVATION FOR HIGH CALORIC FOOD REWARDS IN SATIATED RATS: DEPENDENCE ON EXTRAHYPOTHALAMIC CRF NEUROTRANSMISSION, BUT NOT HPA AXIS ACTIVATION. X Liu, ISBS Fellow, L Armstrong, A Decoteau and A Covacevich, University of Mississippi Medical Center, Jackson, MS, USA

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DANIELA RAYTCHEV

'Progress not Perfection' and upcoming 'Capital' projects are centered around people who currently suffer or have dealt with their addictions, whole spectrum of them. Abstract portraits of the participants who come from all walks of life show their past experience, present state of mind and future ambitions. Graphic nature in some cases suggests altered state of reality as well as playful, honest and open-minded approach to discussing many times stigmatized issue. Expressive character of the artwork relates to the fluctuating emotions, often accompanied by anxiety and depression, that is juxtaposed against clean 'peaceful' linework. There is certain beauty in capturing the chaos and vulnerabilities. Paintings include personal narratives of the subjects who Raytchev interviews and studies over the period of several sittings before creating the final large scale pieces.





The International Zebrafish Neuroscience Research Consortium (ZNRC)

The main goal of ZNRC is to promote zebrafish neuroscience research. Created in February 2010, ZNRC offers excellent networking opportunities and peer support for active zebrafish labs.

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- Dominic Wright, Sweden
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- William Norton, UK
- Adam Michael Stewart, USA
- Lucas Noldus, Netherlands
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- and others

ZNRC is currently involved in inter-lab academic exchanges, zebrafish scholarly publications, and organizing zebrafish-related symposia and conferences.

If your lab is interested in joining ZNRC, please email your request and PI's CV to the ZNRC coordinator at info@stressandbehavior.com



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