

THE INTERNATIONAL STRESS AND BEHAVIOR SOCIETY (ISBS)

Program and Proceedings

11th International Regional (North America)
Neuroscience and Biological Psychiatry Conference

“Stress and Behavior”



Miami Beach, FL, USA
June 22-24, 2017

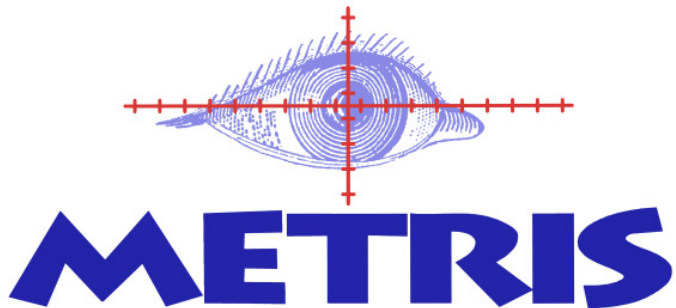


CELEBRATING 20 YEARS TO ISBS CONFERENCES!

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CONFERENCE PROGRAM

Day 1. Thursday, June 22, 2017

Celebration Room, Holiday Inn Miami Beach-Oceanfront, 4333 Collins Ave, Miami Beach, FL

09.30-17.00 REGISTRATION

MORNING SESSION

10.20-10.45 WELCOMING ADDRESSES: CELEBRATING 20 YEARS OF ISBS “STRESS AND BEHAVIOR” CONFERENCES

10.45-11.25 EDUCATION ROUNDS: TEACHING NEUROBIOLOGY IN PSYCHIATRY. S Sabbag and L Ajajji, Miller School of Medicine, University of Miami, Jackson Memorial Hospital, Miami, FL, USA

11.25-11.50 ISBS CLINICAL TALK: HARM-AVOIDANT INDIVIDUALS EXHIBIT ENHANCED LEARNING IN A PROBABILISTIC CATEGORY LEARNING TASK: FURTHER SUPPORT FOR A LEARNING DIATHESIS MODEL OF ANXIETY DISORDERS. MT Allen and CE Myers, University of Northern Colorado, Greeley, CO, Stress and Motivated Behavior Institute, Syracuse, NY, Department of Veterans Affairs, NJ Healthcare System, East Orange, NJ Medical School, Rutgers University, Newark, NJ, USA

11.50-12.15 ISBS PRE-CLINICAL TALK: PARTIAL REINFORCEMENT DURING SIGNED LEVER-PRESS AVOIDANCE TRAINING IS LESS DETRIMENTAL TO LEARNING IN BEHAVIORALLY INHIBITED WISTAR-KYOTO RATS COMPARED TO SPRAGUE DAWLEY RATS. DP Miller, BL Glaeser, TK Regetz, KL Nilles, DR Cook-Snyder and RJ Servatius, Carthage College, Kenosha, WI, Stress and Motivated Behavior Institute, Newark, NJ, Department of Veterans Affairs, NJ Healthcare System, East Orange, NJ Medical School, Rutgers University, Newark, NJ, USA

12.15-13.40 LUNCH BREAK (FREE TIME)

AFTERNOON SESSION

13.40-14.10 ISBS SPECIAL TALK: A COMPREHENSIVE INTERVENTIONAL DESIGN STRATEGY TO OPTIMIZE MULTI-GENERATIONAL LIVING ENVIRONMENTS. A Lawrence, S Percival, M Kolvenbach and D Wint, Interior Architecture + Healthcare Design, University of Nevada, Cleveland Clinic Ruvo Center for Brain Health Staff Neurologists, Psychiatrists and Physical Therapists, Las Vegas, NV, USA

14.10-16.40 ZUKOWSKA SYMPOSIUM ON STRESS NEUROSCIENCE
Chairs: AV Kalueff and CD Nichols (USA)

14.10-14.20 INTRODUCTION: PROFESSOR ZOFIA M ZUKOWSKA

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- 14.20-14.35 THE RELATION OF STRESS TO PLACEBO ANALGESIA.** MA Flaten, Norwegian University of Science and Technology, Trondheim, Norway
- 14.35-14.50 GLUTAMATERGIC NEUROTRANSMISSION IN THE SUPRAOPTIC NUCLEUS OF HYPOTHALAMUS MODULATES AUTONOMIC RESPONSES EVOKED BY ACUTE RESTRAINT STRESS IN RATS.** S Lopes-Azevedo, C Busnardo, AA Scopinho and FMA Corrêa, Department of Pharmacology of the School of Medicine of Ribeirao Preto, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil
- 14.50-15.10 MODULATION OF STRESS RESPONSE BY INTRANASAL OXYTOCIN AND BODY WEIGHT IN CHRONIC STRESS EXPOSED RATS.** D Önal, H Korkmaz, G Önal and B Pehlivanoglu, Hacettepe University Faculty of Medicine, Ankara, Turkey
- 15.10-15.45 ISBS TRANSLATIONAL TALK: PSYCHEDELIC DRUG ACTION IN MAMMALIAN BRAIN.** CD Nichols, Department of Pharmacology and Experimental Therapeutics, LSU Health Sciences Center, New Orleans, LA, USA
- 15.45-16.00 COFFEE BREAK**
- 16.00-16.20 STATUS OF WORK ON SELECTIVE MUTISM IN ITALY AND NEW PERSPECTIVES.** M Di Meo, AIMUSE - Associazione Italiana Mutismo Selettivo, Pescara, Italy
- 16.20-16.40 DEPRESSION AND STIGMA IN UNIVERSITY STUDENTS IN TAIWAN.** A Pendi, J Ashraf, F-J Tsai, C Liu, S Abou El Magd, SM Gohar, M Khalil and DA Baron, University of California Irvine, Irvine, University of Southern California, Los Angeles CA, USA; American University of the Caribbean, Cupecoy, St. Maarten; Taipei Medical University, Taipei, Taiwan; Cairo University, Cairo, Egypt
- 16.40-17.10 CONFERENCE PRESENTATION 1: BEHAVIORAL STUDY OF ANIMALS AND MULTI-DIMENSIONAL MEASUREMENT SYSTEMS (LABORAS, SONOTRACK, DSI TELEMETRY).** L Bachdasarian, R Bulthuis, E Molenwijk, M Boscaro, Metris B.V., Hoofddorp, The Netherlands, Data Sciences International, St. Paul, USA
- 17.10-17.30 ISBS OUTREACH EVENT 1: NEUROSCIENCE MEETS ARTS: AN ARTIST'S PERSPECTIVE.** D Raytchev, Daniela Raytchev Art, London, UK

Day 2. Friday, June 23, 2017

Celebration Room, Holiday Inn Miami Beach-Oceanfront, 4333 Collins Ave, Miami Beach, FL

09.30-17.00 REGISTRATION

MORNING SESSION

10.00-12.40 LAPIN SYMPOSIUM ON BIOLOGICAL PSYCHIATRY

Chairs: MT Allen and DP Miller (USA)

10.00-10.10 INTRODUCTION: PROFESSOR IZYASLAV P LAPIN

10.10-10.30 GLOBAL PERSPECTIVES ON HALLUCINOGENIC AGENTS IN BIOMEDICINE.

AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; School of Pharmaceutical Sciences, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

10.30-10.45 IMPAIRED PV AND PNN EXPRESSION IN CA1 HIPPOCAMPUS MAY UNDERLIE CONTEXTUAL RECALL DEFICITS AFTER AUDITORY FEAR CONDITIONING IN THE FMR1 KNOCKOUT MICE.

K Pendi, S Afroz, S Reinhard, Y Hanania, I Ethell and K Razak, University of California, Riverside, CA, USA

10.45-11.10 A CORTICOSTERONE RECEPTOR ANTAGONIST REDUCES SIGN TRACKING.

BA Rice, MA Prendergast and CK Akins, University of Kentucky, Lexington, KY, USA

11.10-11.30 NPAS4-DEFICIENT MICE LACK CELLULAR RESILIENCE AGAINST MILD STRESS IN ADOLESCENCE AND SHOW IMPAIRED COGNITIVE FLEXIBILITY IN ADULTHOOD.

CE Page, J Alexander and L Coutellier, Department of Neuroscience, Department of Psychology, Ohio State University, Columbus, OH, USA

11.30-12.00 COFFEE BREAK

12.00-12.20 PRE-OPERATIVE ANXIETY MANAGEMENT IN SPINE SURGERY.

A Pendi, JC Wang, FL Acosta Jr, R Movahedi, D Safani, A Shahbazi, A Melkonian and G Gucev, University of California Irvine, Irvine, University of Southern California, Los Angeles, CA, USA

12.20-12.40 DEPRESSION SEVERITY AND DEPRESSION STIGMA IN UNDERGRADUATE UNIVERSITY STUDENTS.

K Pendi, A Pendi, J Ashraf, KB Wolitzky-Taylor, D Lee, J Sugar, J Lee and DA Baron, University of California Riverside, Riverside, University of California Irvine, Irvine, University of Southern California, Los Angeles, CA, Virginia Commonwealth University, VA, USA; American University of the Caribbean, Cupecoy, St. Maarten

12.40-14.00 LUNCH BREAK (FREE TIME)

AFTERNOON SESSION

14.00-14.15 CONFERENCE PRESENTATION 2: WOLTERS KLUWER

14.15-17.00 INTERACTIVE POSTER SESSION

HEAT SHOCK PROTEIN HSPA1B IS OVEREXPRESSED IN THE MEDIAL PREFRONTAL CORTEX DURING THE LIFESPAN IN THE RAT EARLY-LIFE STRESS MODEL. A Solarz, I Majcher-Maślanka, K Wędzony and A Chocyk, Laboratory of Pharmacology and Brain Biostructure, Institute of Pharmacology Polish Academy of Sciences, Krakow, Poland

EFFECTS OF EARLY-LIFE STRESS ON CORTICOSTEROID BINDING GLOBULINS AND ALBUMIN LEVELS IN SERUM AND LIVER OF ADOLESCENT RATS. I Majcher-Maślanka, A Solarz, K Wędzony and A Chocyk, Laboratory of Pharmacology and Brain Biostructure, Institute of Pharmacology Polish Academy of Sciences, Kraków, Poland

THE PREVALENCE OF INTIMATE PARTNER VIOLENCE IN UNVERISTY STUDENTS AND ITS ASSOCIATION WITH ANXIETY AND DEPRESSION SEVERITY. K Pendi, A Pendi, AJ Valdez, D Lee, J Lee, KB Wolitzky-Taylor, JL Aguilar and D Safani, University of California Riverside, Riverside, University of California Irvine, Irvine, CA, Virginia Commonwealth University, Richmond, VA, University of California Los Angeles, CA, USA

DEPRESSION AND SOCIAL STIGMA IN EMIRATI STUDENTS. A Pendi, H Hussain, J Ashraf and DA Baron, University of California Irvine, Irvine, CA, USA; Amity University, Dubai, UAE; American University of the Caribbean, Cupecoy, St Maarten; University of Southern California, Los Angeles, CA, USA

DEPRESSION SEVERITY AND DEPRESSION STIGMA IN AMERICAN GRADUATE UNIVERSITY STUDENTS. K Pendi, A Pendi, J Ashraf, KB Wolitzky-Taylor, D Lee, J Sugar, J Lee and DA Baron, University of California Riverside, University of California Irvine, Irvine, CA, USA; American University of the Caribbean, Cupecoy, St. Maarten; University of California Los Angeles, University of Southern California, Los Angeles, CA, Virginia Commonwealth University, VA, USA

EFFECT OF AGE ON TRANSPORT STRESS IN COMMON PHEASANTS. E Voslarova, I Bedanova, V Vecerek, V Pistekova, P Forejtek, J Chloupek and L Plhalova, Department of Animal Protection, Welfare and Behaviour, Faculty of Veterinary Hygiene and Ecology, University of Veterinary and Pharmaceutical Sciences Brno, Brno, Czech Republic

EFFECT OF HEAT STRESS AND PROBIOTIC SUPPLEMENTATION ON PLASMA NEOPTERIN AND BIOPTERIN CONCENTRATIONS. V Vecerek, I Bedanova, E Voslarova, G Zelinska, L Plhalova, P Marsalek and J Chloupek, Department of Animal Protection, Welfare and Behaviour, Faculty of Veterinary Hygiene and Ecology, University of Veterinary and Pharmaceutical Sciences Brno, Brno, Czech Republic

BEHAVIORAL EFFECTS OF A SYNTHETIC CANNABINOID CBL-2201: MICE VS ZEBRAFISH. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

16.00-16.30 COFFEE BREAK

EFFECTS OF U-47700, A μ -OPIOID RECEPTOR AGONIST, ON ADULT RATS TESTED IN THE ELEVATED PLUS-MAZE AND THE FORCED SWIM TESTS. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

HEALTH CARE PROVIDER STRESS, STROKE AND RECOVERY: A COMPLICATED CASE REPORT WITH CLINICAL AND RESEARCH IMPLICATIONS. EA Hershberger, LG George and J Grewal, Florida International University, Miami, FL, USA

IS ACTIVITY ANOREXIA REALLY ANOREXIA? R Gonzalez and F Ernst, University of Texas Rio Grande Valley, Brownsville, TX, USA

AMINO ACID COMPOUND IN DIFFERENT BRAIN STRUCTURES IN EPILEPSY-PRONE KM RATS UNDERGOING EXPERIMENTAL AUDIOGENIC EPILEPSY. KN Zabegalov, MYu Bykova, EV Shulina, AD Solovyova, SA Krivopalov, TO Kolesnikova and Allan Kalueff, ISBS Fellow, Institute of Immunology and Physiology Ural Branch RAS, Ural Federal University, Ekaterinburg, Russia

EFFECTS OF CHRONIC AMITRIPTYLINE ADMINISTRATION ON BEHAVIORAL AND MONOAMINE METABOLISM-RELATED BIOMARKERS IN ZEBRAFISH. DA Meshalkina, EV Kysil, KA Antonova, EV Efimova, KA Demin, TO Kolesnikova, SL Khatsko and AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg University, St. Petersburg, Institutes of Chemical Technologies and Biological Sciences, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, New Orleans, LA, USA

Day 3. Saturday, June 24, 2017

Celebration Room, Holiday Inn Miami Beach-Oceanfront, 4333 Collins Ave, Miami Beach, FL

10.00-11.00 REGISTRATION

10.30-10.45 ISBS OUTREACH EVENT 2: WORLD THROUGH THE EYES OF A NEUROSCIENTIST - VIRTUAL PHOTO GALLERY. T Sotnikova, St. Petersburg State University, St. Petersburg, Russia

10.45-11.00 BIOETHICS ROUNDS

11.00-12.00 SESSION ON ALTERNATIVE MODELS IN BIOLOGICAL PSYCHIATRY: INTERNATIONAL ZEBRAFISH NEUROSCIENCE RESEARCH CONSORTIUM (ZNRC)

11.00-11.10 INTRODUCTION TO ZNRC

11.10-11.50 FUTURE OF ZEBRAFISH MODELS IN TRANSLATIONAL NEUROSCIENCE RESEARCH. AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; School of Pharmaceutical Sciences, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

11.50-12.05 EFFECTS OF NORIBOGAINE ON ADULT ZEBRAFISH REPEATED NICOTINE WITHDRAWAL. AV Kalueff, ISBS Fellow, A Kaluyeva and EL Maillet, DemeRx, Inc., R&D Laboratory, Miami, FL, ZENEREI Research Center, Slidell, LA, USA

12.05-12.15 GENERAL DISCUSSION

**12.15-12.30 CLOSING CEREMONY
ANNOUNCING FORTHCOMING ISBS CONFERENCES**

12.30-13.00 COFFEE BREAK

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 society, indeed, has a significant impact in these past 20 years - becoming one of the most influential

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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 PNIRSchina 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

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WHY STUDY STRESS, BRAIN AND BEHAVIOR? 20 YEARS AFTER

Today's translational neuroscience and stress biopsychiatry are entering an interesting, yet challenging, time. There are several major challenges in this field. First, we witness the ever-increasing utility and sophistication of various research tools, from complex genetic manipulations to cellular and whole-brain neuroimaging (many of which will be discussed here during the ISBS conference). Second, as these tools become available, there emerges a growing need in analyzing 'big data' – terabytes of information – that these tools generated. Third, although we recognize the significant societal burden of stress-related human brain disorders, we also know that the available drug therapies for them are often semi-efficient, and major classes of CNS drugs have not significantly improved in the last decades [1]. Fourth, brain pathogenesis is more often than not a poly-factorial process influenced by both genetic and environmental ('epigenetic' in a broad sense) factors [2]. Finally, there is a growing number of brain disorders that have developmental trajectories, and are associated with both early brain development and aging [3].

Clearly, to address this emerging complexity of clinical and basic stress neuroscience, many thorough studies are needed. However, the recognition that psychiatric disorders have fundamental underlying molecular processes [4, 5] becomes key for increasing our understanding of brain functioning, as well as treating (and, eventually, preventing) these disorders. Therefore, the ongoing and future studies need a good way to be conveyed to the research community. Surprisingly, there are very few neuroscience societies, journals and meetings that specifically address this important topic. Indeed, some conferences are overly 'physiological' or 'molecular', and less concerned about the behavior. Others are too focused on psychiatric or psychological aspects of stress, and do not seem to be interested in neurobiology of stress *per se*. Other excellent symposia tend to cover both topics, but are either clinical, or basic, but not both. Thus, we wanted to create a multidisciplinary platform (and the respective learned society) that would address these topic at once.

Twenty years ago, in 1997, this new STRESS AND BEHAVIOR conference series was expected to create its own niche and to provide a unique specialized media for experts in this filed. The goal of our STRESS AND BEHAVIOR community (which we later organized as the Society, ISBS) was to serve as a collaborative network. Today, this growing ISBS research community explores a wide range of subjects in the field of clinical and basic, as well as translational neuroscience, neurobehavioral sciences, biopsychology and biopsychiatry, with a particular focus on stress, stress-related neurobehavioral phenotypes, their neural, molecular and genetic mechanisms, as well as stress-evoked neuropsychiatric disorders. To reiterate, we would like to continue to bridge both clinical and basic science studies, and to provide a platform for improving translational dialogue between different disciplines and approaches (Fig. 1). Furthermore, we expect that the broad spectrum of STRESS AND BEHAVIOR's clinical, translational and basic (pre-clinical) topics in neuroscience, neuropsychiatry and biopsychology will continue attract a wide audience, also providing a dynamic balanced diversity of topics covered by this meeting series (Fig. 2).

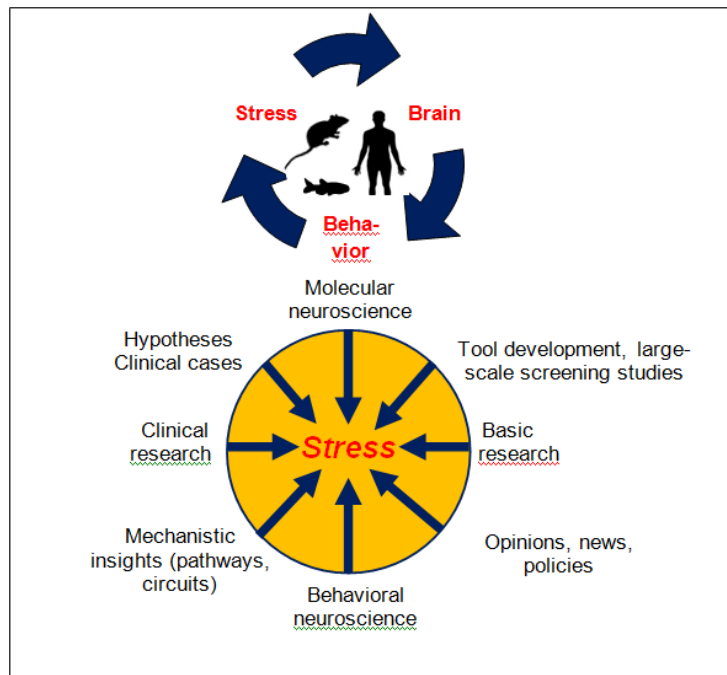


Figure 1. The proposed link between stress, brain and behavior: an ISBS perspective

ABSTRACTS

Day 1. Thursday, June 22, 2017

Celebration Room, Holiday Inn Miami Beach-Oceanfront, 4333 Collins Ave, Miami Beach, FL

MORNING SESSION

EDUCATION ROUNDS: TEACHING NEUROBIOLOGY IN PSYCHIATRY. S Sabbag and L Ajajji, Miller School of Medicine, University of Miami, Jackson Memorial Hospital, Miami, FL, USA

The relationship between psychiatry and neuroscience has been constantly evolving since the conception of our field. The past two decades have witnessed a steep rise in research related to neurobiology in psychiatry. Advances in neuroscience have made psychiatry residency programs steer towards a neuroscience based approach instead of the traditional focus. Despite increased advances and interest in neuropsychiatry, the Accreditation Council for Graduate Medical Education does not require neurobiology integration in psychiatry residency training programs. There are several difficulties residency programs face when attempting to teach neuropsychiatry, including having knowledgeable faculty available, knowing what to teach, and how to deliver the information. Psychiatrists across all levels of training are enthusiastic about learning more neuroscience. With the current advances in psychiatry, neurobiology needs to be integrated in the training and teaching of psychiatry residents. The approach of integration has to be transdiagnostic, clinically relevant and applicable to both trainees and psychiatry educators. Here, we will discuss the importance of teaching neurobiology in psychiatry residency programs, outline which specific areas we recommend teaching, and propose teaching strategies that may enhance learning by psychiatry residents. The neurobiology topics we recommend psychiatry programs to teach their residents include neuroscience literacy, neuroanatomy, neuroimaging, neuropathology, neural circuits and neurotransmitters, neuroendocrinology, neuroimmunology, neurophysiology, genetics and epigenetics, and neuropsychological testing. There are different strategies to teach residents that enhance adult learning, which include formal discussions, clinical case presentations, journal clubs, specialized neuroscience rotations, neuroanatomy modules, grand rounds and classes discussing neuropsychiatry topics in the media.

ISBS CLINICAL TALK: HARM-AVOIDANT INDIVIDUALS EXHIBIT ENHANCED LEARNING IN A PROBABILISTIC CATEGORY LEARNING TASK: FURTHER SUPPORT FOR A LEARNING DIATHESIS MODEL OF ANXIETY DISORDERS. MT Allen and CE Myers, University of Northern Colorado, Greeley, CO, Stress and Motivated Behavior Institute, Syracuse, NY, Department of Veterans Affairs, NJ Healthcare System, East Orange, NJ Medical School, Rutgers University, Newark, NJ, USA

INTRODUCTION: Anxiety vulnerable individuals have been found to exhibit enhanced classical eyeblink conditioning. One consistent finding from our work that fits with current theories of anxiety disorders (Grupe & Nitschke, 2013) is that enhanced learning is most evident in situations involving some degree of uncertainty. In the current study, we extended this work beyond Pavlovian associative learning to determine if harm avoidant individuals would exhibit enhanced learning in a probabilistic category learning task involving separate punishment and reward trials. Probabilistic category learning involves uncertainty in that an item is only in a particular category 80% of the time. Therefore, 20% of the time a correct categorization is scored as an incorrect response. Some trials involved reward where a correct response resulted in a gain in points while an incorrect response resulted in no points gained. On other trials, punishment takes place where an incorrect response resulted in a loss in points while a correct response resulted in no points lost. **METHODS:** One hundred participants completed paper and pencil inventories including the harm avoidance scale of the TPQ and the sensitivity to reward and punishment questionnaire along with the probabilistic category learning task. The total points and rates of optimal responding for reward and punishment trials were analyzed. **RESULTS AND DISCUSSION:**

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Overall, males and females did not differ in their performance on the quarters task ($p = 0.265$). Harm avoidant individuals had higher overall scores ($p < 0.05$) than non-avoidant individuals based on better performance on the punishment trials ($p < .005$), but not reward trials. Individuals sensitive to punishment had significantly higher total scores than non-punishment sensitive individuals ($p < 0.05$), but surprisingly this was due to better performance on reward trials rather than punishment trials. Individuals sensitive to reward had significantly lower scores than non-reward sensitive individuals ($p < 0.05$). These findings extend prior findings that harm avoidant individuals exhibit enhanced learning to a more cognitive probabilistic category learning task involving reward and punishment. **RESEARCH SUPPORT:** Stress and Motivated Behavior Institute and the University of Northern Colorado.

ISBS PRE-CLINICAL TALK: PARTIAL REINFORCEMENT DURING SIGNALLED LEVER-PRESS AVOIDANCE TRAINING IS LESS DETRIMENTAL TO LEARNING IN BEHAVIORALLY INHIBITED WISTAR-KYOTO RATS COMPARED TO SPRAGUE DAWLEY RATS. DP Miller, BL Glaeser, TK Regetz, KL Nilles, DR Cook-Snyder and RJ Servatius, Carthage College, Kenosha, WI, Stress and Motivated Behavior Institute, Newark, NJ, Department of Veterans Affairs, NJ Healthcare System, East Orange, NJ Medical School, Rutgers University, Newark, NJ, USA

INTRODUCTION: The behaviorally inhibited Wistar-Kyoto (WKY) strain has been studied extensively as a model for anxiety vulnerability. WKY rats acquire signaled lever-press avoidance more rapidly and they are resistant to extinguishing the avoidance response when compared to Sprague Dawley (SD) rats (e.g., Servatius et al, 2008). Recently it was demonstrated that learning in behaviorally inhibited humans was less affected by partial reinforcement during Pavlovian eye blink conditioning (Allen et al., 2014). In the present study we compared avoidance acquisition in female WKY versus female SD rats receiving either 100% paired tone-shock trials, or 50% paired trials with 50% tone only trials. **METHODS:** A total of 24 female WKY rats and 24 female SD rats received 20 1 min warning signal trials per session for 9 sessions. An avoidance leverpress during the warning signal resulted in no shock delivery. Failure to make an avoidance response resulted in 500 ms pulses of footshock which were terminated upon leverpress (and hence an escape response) or 20 shock pulses, whichever came first. One half of the rats received 100% paired tone-shock trials, and one half received 50% paired trials with 50% tone only trials. Avoidance responses were recorded. **RESULTS AND DISCUSSION:** WKY rats receiving 100% paired trials showed the highest levels of acquisition. SD rats receiving 50% paired trials showed very little avoidance acquisition. WKY rats receiving 50% paired trials showed levels of acquisition similar to but slightly higher than SD rats receiving 100% paired trials. Our results suggest that female WKY rats are extremely influenced by the tone shock contingency even when it is inconsistent. Such enhanced associative learning in vulnerable populations could be a major factor in the development of anxiety and stress disorders. To further study that relationship, we are performing ongoing immunohistochemical analysis in rat brain tissue from this study that aims to identify activated regions following avoidance training. **RESEARCH SUPPORT:** Stress and Motivated Behavior Institute, UMDNJ.

AFTERNOON SESSION

ISBS SPECIAL TALK: A COMPREHENSIVE INTERVENTIONAL DESIGN STRATEGY TO OPTIMIZE MULTI-GENERATIONAL LIVING ENVIRONMENTS. A Lawrence, S Percival, M Kolvenbach and D Wint, Interior Architecture + Healthcare Design, University of Nevada, and Cleveland Clinic Ruvo Center for Brain Health Staff Neurologists, Psychiatrists and Physical Therapists, Las Vegas, NV, USA

INTRODUCTION: A growing number of aging adults want to remain in multi-generational communities rather than relocating to retirement communities or, having to resort to an

institutional setting. To productively function in an environment where all generations interact and live well together, however, one's ability to manage diminishing cognitive and physical conditions precipitated by the aging process is a major factor that bears on everyone's quality of life. Because spatial qualities of the physical environment may act as stressors and frequently play a significant role in the occurrence of neurodegenerative disorders that involve biological changes, it is self-evident that design strategies for built environments intended to support the management of these symptoms on a daily basis must be integral to multicomponent intervention strategies and account for their biological and behavioral impact. **METHODS:** Pursuant to a systematic literature review and observational research, neurologists, psychiatrists and physical therapists were consulted to inform a highly structured developmental process of design strategies to serve as a knowledge base for the development of environmental design concepts. The Neuropsychiatric Inventory (Cummings) commonly used for assessing symptoms of dementia and other neurological disorders served as the conceptual framework for knowledge transfer and translation. The consultants reinforced the roles of specific features of the built environment as integral to one of three modalities - pharmacologic, behavioral, and environmental - for improving the quality of human life and health for people with dementia. Furthermore, they stressed the positive impact of environments that support higher-levels of functioning and well-being that will allow people to stay living in their homes longer. **RESULTS AND DISCUSSION:** To operationalize the concept of "aging at home", meaning a safe and stress-reducing environment for those experiencing functional changes related to aging, evidence was summarized for the development of translational neuroscience-informed design strategies that have the potential to support the management of neuropsychiatric symptoms, a common feature of all neurodegenerative dementias in the elderly. Given that there are no cures for the common dementias caused by progressive neurodegeneration, the design-research problem-solving methodological paradigm and the schematic design concepts presented may demonstrate best practices to optimize multi-generational living environments. **RESEARCH SUPPORT:** The Division of Research and Economic Development, University of Nevada, Las Vegas.

ZUKOWSKA SYMPOSIUM ON STRESS NEUROSCIENCE

Chairs: AV Kalueff and CD Nichols (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.

THE RELATION OF STRESS TO PLACEBO ANALGESIA. MA Flaten, Norwegian University of Science and Technology, Trondheim, Norway

INTRODUCTION: Placebo analgesia refers to the reduction in pain after information that a treatment against pain has been administered. It is hypothesized that providing information that a treatment is effective against pain, will induce an expectation in the patient or research volunteer that the pain will be reduced. A number of studies have shown that reported pain, pain-related behaviour, physiological reactions, and activity in pain-relevant areas in the brain are reduced following this type of information. Thus, placebo analgesia seems to involve subjective, behavioural, and physiological processes. The central element in placebo analgesia is the expectation of reduced pain. Without expectation in some form, placebo analgesic responses will not occur. However, the effect of expectations on pain may be mediated by subjective and physiological reactions. The present project investigated whether placebo analgesia is mediated by reduction in stress or negative emotions. **METHODS:** Pain was either induced experimentally by a thermode (heat and cold pain), by the submaximum tourniquet technique (ischemic pain), by electrical stimuli, or by dental procedures. Participants were healthy volunteers or dental patients. Subjective pain and stress was recorded by numerical rating scales. Physiological indexes of stress and pain were event-related potentials, heart rate variability, cortisol, and skin conductance responses. **RESULTS AND DISCUSSION:** Overall, the results showed that the effects of expectations on pain were partly mediated by a reduction in negative emotions and stress. However, there are also situations in which information was not found to be mediated by a reduction in stress, and more surprisingly, not by conscious expectations. Better ways of measuring expectations, and possibly subjective stress, should be developed. **RESEARCH SUPPORT:** Research Council of Norway, Bial Foundation of Portugal, University of Tromsø, Norway. Norwegian University of Science and Technology.

GLUTAMATERGIC NEUROTRANSMISSION IN THE SUPRAOPTIC NUCLEUS OF HYPOTHALAMUS MODULATES AUTONOMIC RESPONSES EVOKED BY ACUTE RESTRAINT STRESS IN RATS. S Lopes-Azevedo, C Busnardo, AA Scopinho and FMA Corrêa, Department of Pharmacology of the School of Medicine of Ribeirao Preto, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil

INTRODUCTION: Exposure of animals to acute restraint stress (RS) causes neuronal activation in the supraoptic nucleus of the hypothalamus (SON), indicating its involvement in the physiological responses to stress. This study aimed to test the hypothesis that SON glutamatergic neurotransmission mediates autonomic [mean arterial pressure (MAP), heart rate (HR) and tail skin temperature] responses to RS in rats. **METHODS:** Guide cannulas were implanted into the SON of male Wistar rats (250–270g). A catheter was introduced into femoral artery for MAP and HR recordings. Rats were submitted to a 60min session of RS, 10 min after the microinjection of drugs or vehicle into the SON. And it was studied the effect of the bilateral microinjection of selective non-NMDA or NMDA glutamate receptor antagonist, respectively, NBQX (2nmol/100nL) and DL-AP7 (10nmol/100nL) into the SON on pressor and tachycardiac responses and drop in tail temperature induced by RS. **RESULTS AND DISCUSSION:** The NBQX or DL-AP7 pretreatment of the SON significantly reduced the RS-evoked increase in MAP response (NBQX: $F_{1,77} = 42.7$; $P < 0.0001$, $n = 5$; DL-AP7: $F_{1,77} = 58$; $P < 0.0001$, $n = 5$), while the NBQX potentiated the tachycardiac response caused by RS and DL-AP7 did not change it (NBQX: $F_{1,77} = 26.8$; $P < 0.0001$, $n = 5$; DL-AP7: $F_{1,77} = 0.8$; $P > 0.05$, $n = 5$), when compared to animals treated with artificial cerebrospinal fluid (ACSF, vehicle, 100nL). Moreover, NBQX or DL-AP7 treatment of the SON significantly reduced the restraint-evoked decrease in tail skin temperature (NBQX: $F_{1,110} =$

4.7; $P < 0.05$, $n = 5$; DL-AP7: $F_{1,110} = 14.5$; $P < 0.001$, $n = 5$), when compared with ACSF-treated animals. These results showed that local SON glutamatergic neurotransmission participate in the neural pathway, which is involved with autonomic responses observed during RS. **RESEARCH SUPPORT:** FAPESP: 2014/22228-6.

MODULATION OF STRESS RESPONSE BY INTRANASAL OXYTOCIN AND BODY WEIGHT IN CHRONIC STRESS EXPOSED RATS. D Önal, H Korkmaz, G Önal and B Pehlivanoglu, Hacettepe University Faculty of Medicine, Ankara, Turkey

INTRODUCTION: Stress, via activation of stress system modulates various physiological parameters among which food intake and energy consumption can be named. Understanding the pathogenesis of obesity and mutual interaction between obesity and stress is of vital importance since obesity has become an important public health problem in today's stressful world. The role of oxytocin for control of these mechanisms because of its anxiolytic, anorexigenic effects and being the common ground concerning the hypothalamus cannot be disregarded. On this background we aimed to investigate the effect of intranasal oxytocin (INO) on stress response in obese and normal rats exposed to chronic stress. **METHODS:** Cold-immobilization stress was applied for 5 consecutive days to male Sprague-Dawley rats fed either with standard ($n = 20$) or high fat diet (HFD) ($n = 20$). Half of the animals in each group were administered INO. Stress response is evaluated via serum and saliva cortisol levels as well as elevated plus maze scores. Prefrontal cortex and hypothalamus oxytocin receptor (OxtR) protein levels were designated using western blot analysis. **RESULTS AND DISCUSSION:** Stress response of obese animals was higher when compared with control (non-obese) group. Anxiolytic effect of oxytocin was prominent in control group whereas the effect was found to be diminished for obese animals. While OxtR protein levels in prefrontal cortex was found to be invariable according to the bodyweight and exogenous oxytocin administration, levels for hypothalamus was found to be changing according to feeding type and oxytocin administration. Our results indicated that the peripheral and central effects of oxytocin, a well-known anxiolytic peptide, vary with body weight. However, obesity, probably reinforcing the stress condition via central receptors, masks the foretold anxiolytic effects of oxytocin. In conclusion, enlightening the central effect mechanisms of oxytocin is of vital importance and deserves further studies in order to cope with stress and growing problem of obesity and its modulation. **RESEARCH SUPPORT:** Hacettepe University Research Projects Coordination Unit (Project No: BAP- THD-2015-5714 and TBB-2015-8621).

ISBS TRANSLATIONAL TALK: PSYCHEDELIC DRUG ACTION IN MAMMALIAN BRAIN. CD Nichols, Department of Pharmacology and Experimental Therapeutics, LSU Health Sciences Center, New Orleans, LA, USA

The classic serotonergic hallucinogens (i.e. psychedelics) are known to produce their behavioral effects primarily through activation of cortical serotonin 5-HT_{2A} receptors (5-HT_{2A}R). These effects can include hallucinations, delusions, and detachment from reality. Several recent reports using imaging technologies have informed on the neural circuitry underlying these effects, which includes destabilization of the default mode network, and hyperconnectivity between brain regions. The key molecular and cellular mechanisms underlying these effects, however, remain unknown. To gain a better understanding of the effects of psychedelics on cellular, molecular, and genetic aspects of brain function we have performed several experiments in rats using the 5-HT_{2A} receptor agonist and psychedelic DOI. These involved flow cytometry, gene expression analysis, and immunofluorescence. We have found that psychedelics like DOI directly activate only small subpopulations of both excitatory and inhibitory neurons, as well as glial cells, including astrocytes. The small population of directly responding neurons was found to express significantly higher levels of HTR_{2A} mRNA than non-responding neurons. We have termed this the "Trigger Population", and hypothesize that their activation is necessary to produce down-stream behavioral

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effects. Interestingly, cells from different brain regions responded differently at the molecular level. In addition to the mPFC, high levels of activation were observed in the claustrum, one of the least understood brain regions, which recently was suggested to function by segregating attention between modalities and has been proposed to be the “seat of consciousness.” The effects of psychedelics at the cellular level are, therefore, mediated by a complex interaction not only between diverse cellular types but also discreet regions of the brain that together give rise to the observed behavioral effects. A better understanding of these interactions will likely inform on the etiology of several psychiatric diseases, such as schizophrenia, which have some symptoms that can resemble the effects of psychedelics.

STATUS OF WORK ON SELECTIVE MUTISM IN ITALY AND NEW PERSPECTIVES. M Di Meo, AIMUSE - Associazione Italiana Mutismo Selettivo, Pescara, Italy

INTRODUCTION: Selective Mutism is a rare, little known disorder, that mainly affects children, characterized by the inability to speak in some social contexts despite the development and understanding of language being normal. Selective Mutism is not a phenomenon due to some organic dysfunction or an inability related to development, but it is an attitude of response to a strong emotional state linked to anxiety. Actually, the Italian Association AiMuSe, is working to find out the right method to help children affected by Selective Mutism. In 2009 I was asked to work with those children and then asked to collaborate with association. **METHODS:** We decided to use case studies. My sample is actually consisting of 15 children, aged from 4 to 10 years old, 3 male and 12 female. I have developed a personal method that consists of several steps: Talks with family and school; Knowledge of the child and creation of the therapeutic alliance (3-6 months); Intervention at school, as a mediator and work with small groups, large groups and insertion of teachers with special games developed for therapy and adapted to each child (1 year); Support family and teachers; Follow up. **DISCUSSION:** The average time for therapy is 1 year and a half; 12 cases have been resolved, 2 cases are still under treatment and 1 case has not been solved. When there is adherence to treatment by the family and by teachers the treatment works better and faster. In follow up, I found out that this method works if adapted to each child; and children affected by Selective Mutism, at the end of the therapy, become overwhelmed and have difficulty in emotional self-regulation.

DEPRESSION AND STIGMA IN UNIVERSITY STUDENTS IN TAIWAN. A Pendi, J Ashraf, F-J Tsai, C Liu, S Abou El Magd, SM Gohar, M Khalil and DA Baron, University of California Irvine, Irvine, University of Southern California, Los Angeles CA, USA; American University of the Caribbean, Cupecoy, St. Maarten; Taipei Medical University, Taipei, Taiwan; Cairo University, Cairo, Egypt

INTRODUCTION: As the disability associated with depressive disorders continues to increase worldwide, social stigma remains a pervasive barrier to treatment-seeking behavior. Among university students characterized by low rates of mental healthcare utilization, depression-specific stigma is particularly concerning given the ubiquity of depressive disorders. The purpose of this cross-sectional study is to quantify depression stigma in university students and investigate the association between depression severity and depression stigma, personal and perceived, in Taiwanese university students. **METHOD:** An anonymous survey was disseminated via email to students at a university in Taiwan. The survey included a socio-demographic section, Patient Health Questionnaire-9 (PHQ-9), and Depression Stigma Scale (DSS). Depression severity was measured by the PHQ-9, depression stigma was determined by scores on the DSS subscales for personal and perceived stigma, and socio-demographic predictors of stigma were identified. Analyses were conducted using IBM® SPSS® Version 22 and Microsoft® Excel Mac Version 15.11.2. **RESULTS AND DISCUSSION:** Of 207 Taiwanese students that completed the survey, 21.3% met the criteria for moderate to severe depression (n=44); the rest exhibited mild

symptoms or none (n=163). Moderate to severe depression severity was linked to greater personal stigma (p=0.006) and perceived stigma (p=0.006). According to linear regression, alcohol use was associated with greater personal stigma (p<0.05) and non-heterosexual orientation was associated with greater perceived stigma (p=0.001). As a result, more depressed students were noted to exhibit more stigmatized beliefs, underscoring a need to reduce depression stigma on-campus. Moreover, stigma reduction programs may need to be demographic-specific given the variations in stigmatized beliefs among university students. **ACKNOWLEDGEMENT:** Presented in part at 29th Annual U.S. Psychiatric and Mental Health Congress on October 22-23, 2016 at San Antonio, TX, USA.

CONFERENCE PRESENTATION 1: BEHAVIORAL STUDY OF ANIMALS AND MULTI-DIMENSIONAL MEASUREMENT SYSTEMS (LABORAS, SONOTRACK, DSI TELEMETRY). L Bachdasarian, R Bulthuis, E Molenwijk, M Boscaro, Metris B.V., Hoofddorp, The Netherlands, Data Sciences International, St. Paul, USA

Current trends in the Pharmaceutical industry requires new translational approaches for pre-clinical test. Those aspects can be achieved by animal experiments in which not only one variable (e.g. behavior) at the time is analyzed but rather a multidimensional approach (physiology +behavior + Ultra Sounds Vocalization) is applied. Therefore, automation and integration of different measuring technologies become the crucial aspects in this process. Behavior = function {internal stimuli / external stimuli} Behavior = function {dynamic internal stimulus /from drug effects}; if external factors = constant. **Laboras system: Automated Behavior Classification:** freezing behavior is not immobility behavior; Hindlimb licking behavior is not Scratching; Wet Dog Shakes (WDS) behavior is not Head shakes; Head twitches behavior is not Head shakes; Laboras system and Automated Behavior Classification of 18 behaviors for mice and rats. **Sonotrack System: Automated Ultrasounds Call Classification:** Mice can generate 1000+ Vocalizations in less than 5 minutes; Manual Call Classification and analysis requires about 2 minutes per call for an experienced analyst. Long duration recordings (several hours or more) are therefore not manageable; Automated Call Classification is more consistent and provides more additional parameters of the vocalization; Only Automated Call Classification will enable use of USV for animal models in pharmaceutical research; Metris is the first company offering USV fully automated call classification (starting in May 2017). **Stress study and Fear Conditioning Protocol.** Metris BV proposes two special algorithms for automated Startle and Freezing detection. Having an automated detection system is not sufficient at the behavioral level for excluding false results (e.g. sleeping phases or immobility behavior → less movement confounded as freezing). Therefore, the behavioral response needs to be integrated and synchronized with physiological parameter (e.g. EEG,ECG, BP, Datasciences Int., The best way to do so would be using Laboras system (for behavioral study), DSI (for Physiological parameter) and Sonotrack (for ultrasounds vocalization study). LABORAS - system for fully automatic recognition, recording and analysis of the behavior and tracking of small laboratory rodents (rats, mice), based on the analysis of force and energy. SONOTRACK-system for recording, playback and visualization of ultrasounds vocalizations in laboratory animals (15KHz-125Khz). DSI - system for measuring physiological parameters remotely (without wire measuring pressure, temperature, ECG, EEG, EMG, identification, activity, respiration). Data Sciences is the leading manufacturer for implantable monitoring devices used in preclinical studies. The devices acquire cardiovascular, CNS and respiratory data from freely moving animals in a stress-free environment.

ISBS OUTREACH EVENT 1: NEUROSCIENCE MEETS ARTS: AN ARTIST'S PERSPECTIVE.
D Raytchev, Daniela Raytchev Art, London, UK

'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.

Day 2. Friday, June 23, 2017

Celebration Room, Holiday Inn Miami Beach-Oceanfront, 4333 Collins Ave, Miami Beach, FL

MORNING SESSION

LAPIN SYMPOSIUM ON BIOLOGICAL PSYCHIATRY

Chairs: MT Allen and DP Miller (USA)

INTRODUCTION: PROFESSOR IZYASLAV P LAPIN



Professor Izyaslav P. Lapin. This regular ISBS symposium is dedicated to Professor Izyaslav 'Slava' P. Lapin (1930-2012), a true pioneer of experimental neuropsychopharmacology 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 kynurenic acid 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 regular ISBS symposium will continue Lapin's scientific legacy in the field of biological psychiatry.

GLOBAL PERSPECTIVES ON HALLUCINOGENIC AGENTS IN BIOMEDICINE. AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; School of Pharmaceutical Sciences, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

Traditional hallucinogenic *psychedelic* drugs, such as lysergic acid diethylamide (LSD), mescaline and psilocybin, act mostly on serotonergic 5HT_{2A} receptors to exert profound effects on brain and behavior in both animals and humans. In addition to psychedelics, other hallucinogenic drugs include *dissociatives* - hallucinogens which distort perceptions and produce feelings of dissociation from the environment and self. Dissociatives, such as ketamine, phencyclidine and MK-801, act by inhibiting glutamatergic receptors, and can evoke general depressant effects, sedation, respiratory depression, analgesia, anesthesia, ataxia and cognitive/memory deficits. *Deliriant* hallucinogens represent another group, acting mostly as anticholinergic agents to induce specific behavioral effects, primary of which is delirium (as opposed to the more lucid states produced by other hallucinogens). Other hallucinogenic drugs include *opioid ligands*, such as ibogaine and Salvinorin A, and several hallucinogenic-related specific drugs, such as marijuana and ecstasy (3,4-Methylenedioxymethamphetamine, MDMA), which are not currently classified as classic

hallucinogens, but often cause similar behavioral effects. After decades of stagnation in studying these compounds globally (due to unjust overregulation and political oppression), hallucinogenic drugs are now again being tested as potential treatments for human intractable disorders. Preclinical research of such drugs complements human neuroimaging studies and pilot clinical trials, suggesting these compounds as promising treatments for addiction, depression, anxiety and other CNS conditions. Here, I will summarize recent preclinical and clinical data in this field of studying hallucinogenic drugs, discuss their pharmacological mechanisms of action, and outline critical areas for future studies of hallucinogenic drugs, with the goal of maximizing the potential benefits of their translational biomedicine to patients.

IMPAIRED PV AND PNN EXPRESSION IN CA1 HIPPOCAMPUS MAY UNDERLIE CONTEXTUAL RECALL DEFICITS AFTER AUDITORY FEAR CONDITIONING IN THE FMR1 KNOCKOUT MICE. K Pendi, S Afroz, S Reinhard, Y Hanania, I Ethell and K Razak, University of California, Riverside, CA, USA

INTRODUCTION: Fragile X Syndrome (FXS) is a genetic disorder characterized by a series of cognitive, social, and behavioral deficits found on the autism spectrum. The genetic basis of FXS is increased methylation of CGG repeats at the untranslated 5' promoter region of the Fragile X Mental Retardation Gene (FMR1). Expression of the FMR protein (FMRP) expression is consequently reduced in these individuals. This study aims to understand how FXS affects the fear and anxiety circuitry of mice following auditory fear conditioning and extinction. **METHOD:** Both WT and FMR1 KO were subject to a standardized fear conditioning protocol composed of habituation, training, and extinction with both conditioning and alternate contexts. Percent freezing behavior was measured using FreezeFrame and TopScan Lite software. This behavioral test was performed in conjunction with immunostaining techniques that stained for changes in the density of cell types within the CA1 and dentate gyrus: parvalbumin (PV) cells, perineuronal networks (PNN), and co-localization of PV and PNN. Staining was also applied to a control group to account for behavioral changes. **RESULTS AND DISCUSSION:** While there was no difference in freezing behavior between groups for tone recall, context recall exhibited a significant difference. Because freezing differences were only contextual, hippocampal regions were selected as the target for immunostaining. When compared to WT, FMR1 KO showed a pre-behavioral decrease in PV that persisted following protocol. While WT did experience a post-behavior decrease in PNN, a similar decrease was localized to the CA1 of FMR1 KO. Co-localized PV and PNN increased in WT but decreased in the CA1 of FMR1 KO. These findings together suggest that contextual deficits can be attributed to cell density imbalances within the CA1 region of the hippocampus. By investigating FXS with both behavioral and cellular approaches, we contribute to the framework necessary to improve current treatment options. **RESEARCH SUPPORT:** NIH grant 1U54HD082008-01. **ACKNOWLEDGEMENT:** Presented in part at the University of California, Riverside 11th Annual Undergraduate Research, Scholarship, and Creative Activity Symposium (May 3-4, 2017).

A CORTICOSTERONE RECEPTOR ANTAGONIST REDUCES SIGN TRACKING. BA Rice, MA Prendergast and CK Akins, University of Kentucky, Lexington, KY, USA

INTRODUCTION: Addiction is characterized as a chronic debilitating disease. One devastating feature of addiction is the susceptibility of relapse (40-60%) after stretches of abstinence. One theory that may account for relapse suggests addiction relevant cues (e.g., paraphernalia) may increase the stress hormone corticosterone (CORT), and this may prompt renewed drug seeking (i.e., relapse). Repeatedly pairing a neutral cue with a reward is commonly utilized to measure what subjects learn about a cue that is predictive of reward. Research has shown that animals that attend to a cue more (sign trackers) than to the reward are more vulnerable to drug addiction. Additionally, research has shown that sign tracking increases CORT. In the current experiment, it

was hypothesized that a CORT antagonist would reduce sign tracking after repeated doses compared to subjects given placebo. **METHODS:** In the current experiment, time spent (sec) at a cue that predicts reward (CS+) served as a measure of sign tracking, and PT 150 (or placebo) was administered following acquisition of sign tracking. A decrease in sign tracking was measured as reduced time spent at the CS+. **RESULTS AND DISCUSSION:** To investigate the hypothesis, an independent sampled t-test with mean time spent on the last day of conditioning was conducted. This test revealed a significant difference in time spent at the CS+ on day 15 of conditioning between subjects that received placebo and subjects that received PT 150 [$F=12.59$]. Subjects that received PT 150 following acquisition of sign tracking spent less time at the CS+. The current findings suggest that drug addiction behaviors like sign tracking may be associated with stress hormones. Specifically, a reduction in CORT may attenuate sign tracking. Given the devastating effects of drug addiction, identification of a potential pharmacological intervention in the reduction of relapse would be of great value. Therefore, future research is needed to validate the use of PT 150 in reducing behaviors associated with drug addiction. **RESEARCH SUPPORT:** Palisades Therapeutics, LLC (generous gift of PT 150), Pre-doctoral Fellowship of the USA NIH/NIDA National Institute on Drug Abuse (T32DA035200).

NPAS4-DEFICIENT MICE LACK CELLULAR RESILIENCE AGAINST MILD STRESS IN ADOLESCENCE AND SHOW IMPAIRED COGNITIVE FLEXIBILITY IN ADULTHOOD.

CE Page, J Alexander and L Coutellier, Department of Neuroscience, Department of Psychology, Ohio State University, Columbus, OH, USA

INTRODUCTION: The prefrontal cortex (PFC) relies on a balance of excitatory and inhibitory neurotransmission to integrate perceptions, memories, and emotions toward guiding goal-directed behavior. This excitatory/inhibitory (E/I) balance is largely established during early postnatal and adolescent development and depends on activity-dependent maturation of the GABAergic system. Genetic and/or environmental factors during adolescence can disrupt E/I balance and maturation and lead to cognitive and emotional dysfunction in adulthood. **METHODS:** The present study examined in mice the interaction between chronic mild stress (CMS) during adolescence [postnatal day – PND – 28-42] and deficiency of Npas4, a brain-specific, activity-dependent transcription factor that regulates the formation and maintenance of inhibitory synapses. Npas4 wild type (WT) and heterozygous (HET) mice were tested and brains were collected in adulthood [PND 63-68]. Anxiety behaviors were measured in the elevated plus maze and open field test, and PFC-dependent cognitive function was measured using the attentional set shifting task (ASST). **RESULTS AND DISCUSSION:** Behaviorally, adolescent CMS lead to increased anxiety in adulthood, an effect that was not mediated by Npas4. Only the Npas4 HET mice trended toward impaired cognitive flexibility in adulthood following adolescent stress, as observed by poor performance on the extradimensional set shift trial of the ASST. At the cellular level, adolescent stress increased the percentage of PV cells that were surrounded by perineuronal nets (PNNs) in WTs. HET mice, on the other hand, did not show this increase in PNNs. Preliminary data also show that adolescent stress may increase expression of inducible nitric oxide synthase (iNOS), a producer of nitric oxide and thereby a marker of oxidative stress. PNNs protect PV cells from oxidative damage, and decreases in PNNs and PV expression have been observed in the brains of schizophrenia patients. Further analyses will investigate whether a stress-induced increase in iNOS, together with a lack of PNN upregulation in HETs, impacts the PV cells of HET mice. These results suggest that WT mice are capable of exerting homeostatic compensatory changes in response to adolescent stress, such as increasing PNN coverage of PV cells, which protect against cognitive impairment in adulthood: an ability that Npas4 HET mice lack. This demonstrates a novel gene by environment interaction that influences E/I balance and resilience vs. vulnerability to stress, with implications for adolescent onset disorders like schizophrenia.

PRE-OPERATIVE ANXIETY MANAGEMENT IN SPINE SURGERY. A Pendi, JC Wang, FL Acosta Jr, R Movahedi, D Safani, A Shahbazi, A Melkonian and G Gucev, University of California Irvine, Irvine, University of Southern California, Los Angeles, CA, USA

INTRODUCTION: Pre-operative anxiety is experienced by the vast majority of patients undergoing spine surgery. Pre-operative anxiety, which is distinct from a prior diagnosis of anxiety (e.g. generalized anxiety disorder), is often overlooked during perioperative care. However, more anxious patients respond differently to anesthesia, consume more postoperative analgesics, and have a longer length of stay. Despite its ubiquity, pre-operative anxiety has not been extensively studied in spine surgery. **METHOD:** A cross-sectional survey was disseminated online to orthopaedic and neurological spine surgeons of AO Spine North America (AOSNA). The survey measured how surgeons measure pre-operative anxiety among their patients, which entities have responsibility for its management, and which management techniques are preferred. Analyses were performed with IBM® SPSS® Version 22 and Microsoft® Excel Mac Version 15.11.2. **RESULTS AND DISCUSSION:** Respondents were all male (n=35, 100.0%) with the majority in practice for 0-19 years (n=23, 65.7%) as orthopaedic spine surgeons (n=25, 71.4%). The majority did not ask patients about pre-operative anxiety (n=23, 65.7%) but would discuss it if mentioned by the patient (n=21, 91.3%). Pre-operative education about the procedure (n=27, 77.1%) and permitting family members to be present (n=18, 51.4%) were preferred by most surgeons to manage pre-operative anxiety. Pre-operative tours or information about perioperative care (n=15, 42.9%) and pre-operative visit from the anesthesiologist and/or perioperative care team (n=17, 48.6%) were also used. Traditional, complementary, and alternative medicine (n=2, 5.7%), cognitive behavioral therapy (n=4, 11.4%), anxiety medication (n=5, 14.3%), nurse-patient therapeutic relationships (n=7, 20.0%), referral to psychologist or psychiatrist (n=9, 25.7%), other technique (n=2, 5.7%), and no pre-operative management (n=5, 14.3%) were preferred by the minority. Surgeons assigned themselves major responsibility (n=20, 57.1%) to manage pre-operative anxiety. Anesthesiologists (n=17, 48.6%), nurse or perioperative care team (n=14, 40.0%), and patients themselves (n=14, 40.0%) were assigned major responsibility. Family members (n=26, 74.3%), other staff (n=20, 57.1%), and psychologists or psychiatrists (n=20, 57.1%) held some responsibility. Other entities were assigned no responsibility (n=9, 100.0%).

DEPRESSION SEVERITY AND DEPRESSION STIGMA IN UNDERGRADUATE UNIVERSITY STUDENTS. K Pendi, A Pendi, J Ashraf, KB Wolitzky-Taylor, D Lee, J Sugar, J Lee and DA Baron, University of California Riverside, Riverside, University of California Irvine, Irvine, University of Southern California, Los Angeles, CA, Virginia Commonwealth University, VA, USA; American University of the Caribbean, Cupecoy, St. Maarten

INTRODUCTION: As the global burden of depressive disorders continues to rise, the study of depression stigma constitutes an important area for research due to the influence of stigmatized beliefs upon treatment-seeking behavior. Among undergraduate students, the relationship between depression severity and depression stigma remains unclear. As a result, the purpose of this study was to determine the prevalence of depression among undergraduates, investigate the relationship between depression severity and depression stigma (personal and perceived), and identify demographic predictors of depression stigma. **METHOD:** A cross-sectional study was conducted at an institution in the USA. The online survey link was posted on social media pages, on websites, and in emails sent to student organizations. The survey contained a demographic questionnaire, PHQ-9 (Patient Health Questionnaire-9), and DSS (Depression stigma scale). Participants were sorted into more depressed and less depressed groups based on PHQ-9 scores and compared in terms of continuous scores on the personal and perceived subscales of the DSS. Analyses were performed with IBM® SPSS® Version 22. **RESULTS AND DISCUSSION:** Of 1080 completed responses, 36.3% screened positive for moderate to severe depression severity. This percentage is higher than the percentages previously reported. Notably, respondents with moderate to severe depression severity exhibited greater perceived stigma

($p=0.002$). Therefore, to be effective, on-campus efforts to reduce stigma should prioritize reduction of perceived stigma. In addition, females ($p<0.001$), LGBT students ($p<0.001$), upperclassmen ($p<0.001$), and those with non-Christian or no religious affiliation ($p<0.001$) were associated with greater depression severity. Also, male ($p<0.001$), heterosexual ($p<0.001$), unemployed ($p<0.05$), Caucasian ($p<0.001$), older ($p<0.05$), and single-race students ($p<0.05$) were linked to greater personal stigma. **ACKNOWLEDGEMENT:** Presented at 29th Annual U.S. Psychiatric and Mental Health Congress on October 22-23, 2016 at San Antonio, TX, USA.

AFTERNOON SESSION

CONFERENCE PRESENTATION 2: WOLTERS KLUWER

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INTERACTIVE POSTER SESSION

HEAT SHOCK PROTEIN HSPA1B IS OVEREXPRESSED IN THE MEDIAL PREFRONTAL CORTEX DURING THE LIFESPAN IN THE RAT EARLY-LIFE STRESS MODEL. A Solarz, I Majcher-Maślanka, K Wędzony and A Chocyk, Laboratory of Pharmacology and Brain Biostructure, Institute of Pharmacology Polish Academy of Sciences, Krakow, Poland

INTRODUCTION: According to clinical and epidemiological studies early-life stress (ELS) is an important factor in etiology of mood and anxiety disorders. The medial prefrontal cortex (mPFC) is a key brain structure that is highly implicated in pathophysiology of mentioned disorders. Moreover, the mPFC is especially vulnerable to stress due to its prolonged developmental trajectory. *Recently, our cDNA microarray screening study has revealed that ELS, modeled by maternal separation (MS) procedure, strongly upregulated the expression of genes engaged in endoplasmic reticulum (ER) stress and chaperones functioning in the mPFC of juvenile rats (on postnatal day (PND) 15). ER stress is induced by accumulation of unfolded/misfolded proteins. In such conditions ER activates unfolded-protein response (UPR) which acts via chaperones induction and elimination of misfolded proteins. ER stress and UPR are strong regulators of cell survival. The limited knowledge about the engagement of these processes into primary mechanisms of ELS, prompted us to direct our research on molecular chaperons family of heat shock proteins 70 (HSP70).* **METHODS:** To model ELS we applied MS procedure in Wistar rats. Briefly, pups were isolated from dams for 3 hours each day, during the first two weeks of their life (PND 1-14). Expression of one of the most abundant representatives of HSP70, i.e., HSPA1B was measured in the mPFC by RT-qPCR, Western blot and immunohistochemistry. **RESULTS AND DISCUSSION:** MS upregulated mRNA and protein expression of HSPA1B in the mPFC of juveniles (3 and 24 h after the last MS). Our immunohistochemical experiments showed that HSPA1B protein was present in glial cells and in blood vessels within the mPFC of MS juveniles. Moreover, we found that HSPA1B was overexpressed on mRNA level in all stages of development from juvenile, through adolescent (PND 35) to adult rats (PND 70). Since HSPA1B is engaged in ER stress and UPR processes, these observation suggests that ELS may potentially affect apoptosis or cell survival during mPFC maturation and, in consequence, lead to its lifelong dysfunction. **RESEARCH SUPPORT:** Statutory activity of the Institute of Pharmacology, Polish Academy of Science.

EFFECTS OF EARLY-LIFE STRESS ON CORTICOSTEROID BINDING GLOBULINS AND ALBUMIN LEVELS IN SERUM AND LIVER OF ADOLESCENT RATS. I Majcher-Maślanka, A

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Solarz, K Wędzony and A Chocyk, Laboratory of Pharmacology and Brain Biostructure, Institute of Pharmacology Polish Academy of Sciences, Kraków, Poland

INTRODUCTION: Adolescence is a developmental time when individuals show enhanced response to stress. The experience of early-life stress (ELS) during childhood can additionally influence adolescent reaction to stressful events, what in turn may lead to stress-related psychopathologies, i.e., anxiety and mood disorders. Stress response is mediated by glucocorticoids (GCs) action in a target tissue. Tissue concentration of GCs is highly regulated by serum corticosteroid binding globulins (CBGs) and albumin which act as buffers and control the amount of biologically active GCs. CBGs and albumin are synthesized and stored in the liver. Little is known about the role of CBGs and albumin in ELS-induced alterations in the response to stress. Therefore, we decided to study the effect of ELS on serum corticosterone (CORT), CBGs and albumin levels in adolescent rats. Moreover, we examined the gene and proteins expression of CBGs and albumin in the liver. **METHODS:** As a model of ELS we used maternal separation (MS) procedure in rats based on 3h daily separation of pups from the dams on postnatal days 1-14. The final experimental procedures were performed during adolescence period i.e., on postnatal day 35 in male subjects. Serum levels of CORT, CBGs and albumin were measured by the enzyme linked immunosorbent assay (ELISA). To investigate mRNA expression of CBGs and albumin in the liver we applied RT qPCR procedure, whereas their protein levels in the liver were measured by Western blot technique. **RESULTS AND DISCUSSION:** MS decreased serum CORT levels in adolescent rats, accompanied by lower serum levels of CBGs and albumin. However, our studies did not reveal significant changes in either mRNA or protein expression of albumin and CBGs in the liver. The results imply that ELS may modulate the response to stress in adolescents by its impact on the secretion and/or degradation of CBGs and albumin but not on their synthesis. Low serum levels of these proteins may enhance CORT clearance and, in consequence, affect its activity and availability in a target tissue. **RESEARCH SUPPORT:** Grant Preludium 2015/17/N/NZ4/02800 from National Science Centre, Kraków, Poland.

THE PREVALENCE OF INTIMATE PARTNER VIOLENCE IN UNVERISTY STUDENTS AND ITS ASSOCIATION WITH ANXIETY AND DEPRESSION SEVERITY. K Pendi, A Pendi, AJ Valdez, D Lee, J Lee, KB Wolitzky-Taylor, JL Aguilar and D Safani, University of California Riverside, Riverside, University of California Irvine, Irvine, CA, Virginia Commonwealth University, Richmond, VA, University of California Los Angeles, CA, USA

INTRODUCTION: While previous studies have recognized the association between Intimate Partner Violence (IPV) and mental illness within various populations, the prevalence of IPV among college students remains unreported. Moreover, the relationship between IPV and the severity of anxiety and depression in this population has not been examined. Therefore, the purpose of this study is to investigate the prevalence of IPV and its association with anxiety and depression severity in university students. **METHOD:** A cross-sectional study of university students in the United States was conducted to assess IPV prevalence, anxiety severity, and depression severity. The survey contained the Hurt, Insult, Threaten, and Scream (HITS) screening tool to determine IPV prevalence, the Generalized Anxiety Scale 7 (GAS-7) to determine anxiety severity, and the Patient Health Questionnaire 9 (PHQ-9) to determine depression severity. Individuals that screened positive for IPV were compared in terms of their GAS-7 and PHQ-9 scores using a two-tailed t-test and assuming unequal variances. Analyses were performed with IBM® SPSS® Version 22 and Microsoft® Excel Mac Version 15.11.2. **RESULTS AND DISCUSSION:** Our results and analyses are derived from a total of 396 respondents. From this total, 5% were positive for IPV (n=18). IPV-positive individuals were associated with both a greater anxiety severity (10.83 ± 5.711 versus 6.23 ± 5.355 ; $p=0.003$) and a greater depression severity (12.06 ± 6.384 versus 7.34 ± 6.266 ; $p=0.007$). As a result, targeted screenings for anxiety and depression may be useful for students experiencing IPV. In order to better manage the mental health of their student populations, student health services need to

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recognize this association. **RESEARCH SUPPORT:** This work was partially supported by National Institutes of Health grant UL1 TR001414 from the National Center for Advancing Translational Sciences. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. **ACKNOWLEDGEMENT:** Presented in part at 10th Annual Meeting of Social & Affective Neuroscience Society (March 16-18, 2017) at University of California, Los Angeles.

DEPRESSION AND SOCIAL STIGMA IN EMIRATI STUDENTS. A Pendi, H Hussain, J Ashraf and DA Baron, University of California Irvine, Irvine, CA, USA; Amity University, Dubai, UAE; American University of the Caribbean, Cupecoy, St Maarten; University of Southern California, Los Angeles, CA, USA

INTRODUCTION: The social stigma surrounding depression remains a barrier to treatment-seeking behavior among university students worldwide. As the burden of depression rises among university students, the relationship between depression and stigmatized beliefs has important implications for the management of depressive disorders. As a result, the purpose of this study was to investigate the relationship between depression severity and depression stigma in a population of Emirati university students. **METHOD:** An anonymous survey was disseminated via email to students at a university in the United Arab Emirates. The survey consisted of three components: a socio-demographic questionnaire, Patient Health Questionnaire-9 (PHQ-9), and Depression Stigma Scale (DSS). The PHQ-9 was used to measure depression severity and the DSS was used to determine the degree of stigmatized beliefs in two domains: personal and perceived beliefs. More depressed students were compared to their counterparts in terms of depression stigma via t-test, twotailed, and assuming unequal variances. A series of linear regressions were performed to identify independent predictors of depression severity, personal stigma, and perceived stigma. Analyses were carried out using IBM® SPSS® Version 22. **RESULTS AND DISCUSSION:** Of 134 respondents, 39.6% self-reported moderate-to-severe depression severity (n=53). Compared to students who experienced minimal to no depression severity (n=81), more depressed students exhibited lower personal stigma (15.91 ± 7.29 vs 17.31 ± 5.75 , $p=0.240$) and greater perceived stigma (22.55 ± 7.46 vs 20.74 ± 6.20 , $p=0.147$), though neither of these comparisons was considered statistically significant. Sexual orientation ($p=0.019$) and smoking status ($p=0.003$) were each identified as predictors of depression severity. No socio-demographic predictors of depression stigma, personal or perceived, were identified. These findings indicate a higher prevalence of depression among university students than previously reported. Although there was no significant association between depression severity and stigmatized beliefs, students exhibited highly stigmatized beliefs on average compared to American counterparts. **ACKNOWLEDGEMENT:** Presented in part at 10th Annual Meeting of Social & Affective Neuroscience Society (March 16-18, 2017) at University of California, Los Angeles.

DEPRESSION SEVERITY AND DEPRESSION STIGMA IN AMERICAN GRADUATE UNIVERSITY STUDENTS. K Pendi, A Pendi, J Ashraf, KB Wolitzky-Taylor, D Lee, J Sugar, J Lee and DA Baron, University of California Riverside, University of California Irvine, Irvine, CA, USA; American University of the Caribbean, Cupecoy, St. Maarten; University of California Los Angeles, University of Southern California, Los Angeles, CA, Virginia Commonwealth University, VA, USA

INTRODUCTION: Recent evidence suggests that the burden of depressive disorders is increasing worldwide. Depression remains a commonly encountered mental illness among graduate university students. Unfortunately, depression-specific stigma may be experienced differently by students who exhibit greater depression severity. Differences in the stigmatized beliefs among depressed students have implications for successful efforts to prevent, screen for,

and treat depressive disorders in graduate students. Therefore, a cross-sectional study was conducted to determine the following: the prevalence of depression in American graduate students and the relationship between depression severity and stigmatized beliefs. **METHOD:** An anonymous survey of graduate students was conducted online by posting the survey to websites and social media pages and requesting student organizations to forward an email containing the survey to members. Patient Health Questionnaire-9 (PHQ-9) was used to measure depression severity, with a score of 0-9 indicating minimal to no depression severity and a score of 10-29 indicating moderate to severe depression severity. Depression Stigma Scale (DSS), which contained personal and perceived stigma subscales, was used to determine the degree of stigmatized beliefs. Based on PHQ-9 scores, respondents were divided into more and less depressed groups and compared in terms of continuous scores on the personal and perceived DSS subscales using t-test, two-tailed, and assuming unequal variances. Analyses were conducted by IBM® SPSS® Version 22. **RESULTS AND DISCUSSION:** 231 responses were obtained from graduate students, the majority of which were female (n=159, 68.8%), over the age of 23 years (n=203, 87.9%), and heterosexual (n=203, 87.9%). Most participants consumed alcohol (n=188, 81.4%) but did not smoke (n=199, 86.1%). Over one-third of respondents self-reported moderate-to-severe depression severity (n=79, 34.2%). This group was associated with a greater personal depression stigma (11.06 ± 5.642 versus 9.61 ± 6.276 , $p=0.076$) and significantly greater perceived depression stigma (23.65 ± 5.700 versus 21.09 ± 6.132 , $p=0.002$).

EFFECT OF AGE ON TRANSPORT STRESS IN COMMON PHEASANTS. E Voslarova, I Bedanova, V Vecerek, V Pistekova, P Forejtek, J Chloupek and L Plhalova, Department of Animal Protection, Welfare and Behaviour, Faculty of Veterinary Hygiene and Ecology, University of Veterinary and Pharmaceutical Sciences Brno, Brno, Czech Republic

INTRODUCTION: In many countries, a large number of common pheasants are reared artificially every year in rearing facilities and subsequently released into the wild in late summer with the aim of increasing the number of birds available for the autumn hunting season. This practice means that pheasants are routinely transported over varying distances from the rearing facility to the pheasantry which represents considerable stress for the birds. **METHODS:** The aim of this work was to assess the intensity of stress quantified by the concentration of plasma corticosterone in common pheasants (*Phasianus colchicus*) aged 8 and 16 weeks transported for 2 hours in transport containers or merely placed in transport containers for 2 hours and exposed to ambient stir (visual contact with people walking past, human communication, movements of the container) and to evaluate a difference in the stress response of younger and older birds to determine the appropriate period of transportation of pheasants from the rearing facility to the pheasantry or to the site of their subsequent release prior to hunting. Both young (n = 40) and older pheasants (n = 40) were divided into 3 groups: Control (n = 10), Container 2h (n = 10), and Transport 2h (n = 20). Plasma corticosterone concentration was measured on the principle of photometric detection using a commercial Corticosterone Enzyme Immunoassay Kit. The results were analyzed using the statistical package Unistat 5.1. **RESULTS AND DISCUSSION:** The corticosterone concentration was significantly higher in 16-week pheasants irrespective of group. The highest corticosterone level was found in pheasants of both age groups that were crated for 2 h. However, older birds showed a significantly higher corticosterone level than younger birds. No significant difference in corticosterone level was found between pheasants transported for 2 h at the age of 8 and 16 weeks. It can be said in conclusion that the level of plasma corticosterone is statistically significantly higher, regardless of the treatment used in the experiment, in older pheasants (aged 16 weeks) than in younger pheasants (aged 8 weeks). The greatest stress associated with pheasant transport is the handling of the birds and close contact with man, and this stress load is higher in older pheasants than in younger birds. A smaller stress load is represented by transport itself, an area in which no statistically significant difference was proven between older and younger birds.

EFFECT OF HEAT STRESS AND PROBIOTIC SUPPLEMENTATION ON PLASMA NEOPTERIN AND BIOPTERIN CONCENTRATIONS. V Vecerek, I Bedanova, E Voslarova, G Zelinska, L Pilhalova, P Marsalek and J Chloupek, Department of Animal Protection, Welfare and Behaviour, Faculty of Veterinary Hygiene and Ecology, University of Veterinary and Pharmaceutical Sciences Brno, Brno, Czech Republic

INTRODUCTION: In recent years, a possibility to use neopterin and biopterin as indicators of stress and activation of the immune system in animals and also a possibility to use probiotics to stimulate the immune system in birds have been investigated. The aim of the study was to determine the level of plasma neopterin and biopterin and the effect of probiotic supplementation in broiler chickens exposed to thermal stress. **METHODS:** In the experiment, a total of 80 ROSS 380 broiler-type chickens were used. Chickens were divided into 4 groups (20 broilers in each group): 1) control group, 2) group supplemented with probiotics, 3) group exposed to heat stress without probiotics supplementation and 4) group exposed to heat stress with probiotics supplementation. On the day 42 of age, chickens in groups 3 and 4 were exposed to increased ambient temperature of 33 ± 1 °C for 24 h. On the day 43, blood was taken from all chickens (n = 80). The measurement of neopterin and biopterin concentrations was based on high-performance liquid chromatography with fluorometric detection. Plasma corticosterone concentration was measured on the principle of photometric detection using a commercial Corticosterone Enzyme Immunoassay Kit. The total leukocyte counts were determined by means of the flask method of dilution and counting corpuscles using the Bürker chamber, proportions of individual leukocyte types (in 200 cells) were computed from blood smears panoptically stained according to Pappenheim with a use of microscope with an immersion lens. The results were analyzed using the statistical package Unistat 5.1. **RESULTS AND DISCUSSION:** The results show that the level of plasma neopterin, biopterin and corticosterone was higher ($p < 0.05$) in chickens exposed to thermal stress compared with the control group. A positive correlation ($p < 0.01$) was found between the concentration of corticosterone and concentrations of neopterin and biopterin in all groups. Probiotic supplementation resulted in increased levels of plasma neopterin. Heterophile to lymphocyte ratio was higher ($p < 0.05$) in chickens supplemented with probiotics and a positive correlation ($p < 0.05$) was found between heterophile to lymphocyte ratio and plasma levels of neopterin and biopterin.

BEHAVIORAL EFFECTS OF A SYNTHETIC CANNABINOID CBL-2201: MICE VS ZEBRAFISH. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: A growing number of new synthetic drugs with modified chemical structure are being abused globally. Synthetic cannabinoids are among the most popular psychoactive substance, often sold online as smoke mixtures ('spice') which evoke increased heart rate, agitation, hallucinations, anxiety, paranoia and heart attacks in human. Withdrawal symptoms from these drugs include headaches, anxiety, depression and irritability. CBL-2201 is a cannabinoid CB1 and CB2 receptor agonist, widely used in manufacturing illegal drugs. Here, we characterized acute behavioral effects of CBL-2201 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 30 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 test following a 30-min pre-treatment with 2 and 20 mg/kg of CBL-2201 (n=10 per group), scoring the latency, frequency and duration of locomotor activity, freezing, rearing and hole-poking behavior. 60 adult (6-month-old) wild type long-fin zebrafish (50:50 male:female ratio) were threat by 1, 10 and 20 mg/L of CBL-2201 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 registered the number and duration of freezing bouts, number of erratic

movements, latency, duration and frequency of top entries. **RESULTS AND DISCUSSION:** Overall, CBL-2201 in dose 2 and 20 mg/kg significantly reduced frequency and duration of mouse exploratory activity and wall-leaning behavior compared with control in the OFT. Increased of freezing duration was noted for 20 mg/kg in both OFT and EPM. Also, the drug decreased locomotor activity in the EPM in both open and closed arms, and decreased frequency and duration of vertical wall-leaning behavior in the closed arms. At the 20-mg/L dose, CBL-2201 significantly decreased the number of entries in closed arms of EPM. In the fish novel tank test, CBL-2201 did not change any parameters in 1, 10 and 20 mg/L, but caused stereotypic-like side-to-side swimming in the bottom part of the tank, and ataxia. Thus, CBL-2201 likely has a shared sedative and/or anxiogenic-like psychotropic properties in mice and zebrafish models in-vivo, which can be used to further characterize the available, and screen for novel putative, synthetic cannabinoid drugs. **RESEARCH SUPPORT:** Ural Federal University, Ekaterinburg, Russia.

EFFECTS OF U-47700, A μ -OPIOID RECEPTOR AGONIST, ON ADULT RATS TESTED IN THE ELEVATED PLUS-MAZE AND THE FORCED SWIM TESTS. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: 3,4-dichloro-N-[(1R,2R)-2-dimethylamino)cyclohexyl]-N-methylbenzamide (U-47700) was developed by Upjohn in 1978 as a strong morphine-like analgesic agent. U-47700 acts as a selective agonist of the μ -opioid receptor, with an approximately 10x stronger potency in animal models than morphine. However, the abuse of U-47700 has led to its current ban in various countries. We have previously reported psychoactive action of this drug in zebrafish (Kolesnikova et al., 2017). Here, we characterize acute behavioral effects of U-47700 in adult mice in the elevated plus-maze test (EPM) and forced swim test (FST). **METHODS:** 50 white outbred 6-month old male mice were used for this study. The EPM test was used to assess mice behavior for 5 min following a 60-min pre-treatment with U-47700, given by intraperitoneal injection at 1, 5, 10 and 25 mg/kg (n=10 per group). We counted number, duration and latency of entries in open and closed arm, freezing, rearing and wall-leaning behavior. Immediately after testing in EPM, we examined mice in the FST for 6 min, recording the frequency, latency and duration of passive swimming. **RESULTS AND DISCUSSION:** We found that in dose 25 mg/kg mice were disoriented and could not assess the limits of EPM open arms (these data were not included in further analyses). U-47700 in 1 mg/kg did not change any behavioral parameters, except for the latency of entries in open arms of EPM. In dose 5 mg/kg, the drug significantly decreased the number of entries into closed arms, but increase freezing frequency and duration (as in dose of 10 mg/kg). Also, in 5 and 10 mg/kg, the agent significantly reduced locomotor activity, frequency and duration of wall-leaning behavior. In the FST, animals receiving the 25 mg/kg dose were not able to respond adequately to placing them in a situation of unavoidable despair and swim properly (these results were also not included in further analyses). The drug did not change any FST parameters at other (lower) doses tested, but also caused catalepsy-like freezing state that resembled characteristic morphine-evoked catalepsy. Taken together, these findings confirm U-47700 as a potent psychoactive drug with pronounced sedative-like properties in rodents, with a similar profile earlier noted in zebrafish.

HEALTH CARE PROVIDER STRESS, STROKE AND RECOVERY: A COMPLICATED CASE REPORT WITH CLINICAL AND RESEARCH IMPLICATIONS. EA Hershberger, LG George and J Grewal, Florida International University, Miami, FL, USA

INTRODUCTION: Health care providers often find themselves in situations where demands exceed resources, a situation well established to induce high levels of stress. The purpose of this presentation is to heighten awareness of the clinically very complicated interactions that arise between stress, pre-existing physical and behavioral reactions, stroke and recovery. **METHOD:**

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Using the experiential approach of a case study rather than attempting to limit the variables as would be done for a research design, this study broadens the variables in order to highlight the complicated relationship between stress and health that many of us face in our practices on an almost daily basis. **RESULTS AND DISCUSSION:** For those of us who are health care providers or who find ourselves in highly demanding professions this is a story that will add to our professional, personal and clinical wisdom and practice. For those of us who are researchers the case presentation will emphasize the multiplicity of variables that must be taken into consideration to design a meaningful research study.

IS ACTIVITY ANOREXIA REALLY ANOREXIA? R Gonzalez and F Ernst, University of Texas Rio Grande Valley, Brownsville, TX, USA

A number of studies have examined the phenomenon of activity anorexia (AA) in rats (Gutierrez, 2013), first demonstrated by Routtenberg & Kuznesof (1967) and replicated by Cheney & Epling (1968). AA is a paradoxical self-starvation emerging within days of a diet restricted to a 1-3 h/day serving of food with access to a running wheel during all but the feeding hour(s). It is thought that the loss of interest in food (anorexia) is a product of increased interest in running. We questioned whether the phenomenon is truly an anorexic one or simply an inability to consume enough food to support the energy expenditure of increasingly desperate attempts to locate food. We hypothesized that rats should reveal a decrease in food consumption as excessive running emerges within days of starting the protocol if anorexia is the key process. Twenty female Sprague-Dawley rats were acquired at 23 days of age from Charles River Laboratories and were housed in pairs with ad libitum Purina rat chow and tap water. At 60 days of age, rats were weighed and moved in groups of eight, seven, and five to individual housing in Med Associates running wheel home cages. Room temperature was controlled at a constant 22.2 C during a 12-h light cycle. Rats were then run in a 4-day baseline with unlimited running wheel access and ad libitum rat chow. On Day 5, Day 1 of the AA protocol was initiated in which food was removed for 23 h and returned for 1 h. During the 1-h feeding period, the door between the living area and the running wheel was closed, preventing entry to the running wheel. This protocol was continued for 9 days during which food was weighed and revolutions were recorded from counters. Repeated-measures ANOVA confirmed a statistically significant increase in food consumption from 3.35 g/day to an asymptote of 7.5 g/day across the 9 days of the AA protocol ($p < 0.05$) after stabilizing at 13-14 g/day of food during baseline. Activity in the running wheel increased linearly across the 9 days ($p < 0.05$) following stabilization during baseline. These findings were revealed in both group and individual reversal design analyses. All rats lost significant amounts of body weight ($p < 0.05$) across the protocol as activity increased beyond the energy balance between food consumed and energy expended by the running. These data suggest that the critical phenomenon in the AA process is not anorexia, because food consumption increased from the first to the last day of the protocol. In the last few days of the AA protocol, rats ate fully one-half of what a rat will typically consume in ad libitum conditions with over a twenty-fold increase in the amount of time food is available. The findings indicate that the primary factor affecting life-threatening weight loss in the AA animal model is activity-related and not related to self-starvation. We named this phenomenon "treximomania": addiction to running. Currently we are following up on these findings by 24-hr video-taping to determine if running appears purposeful, i.e., direction is changed when unsuccessful checks on food availability occur. We are also comparing conditions in which the running wheel is or is not locked during the 1-hr feeding period of the protocol.

AMINO ACID COMPOUND IN DIFFERENT BRAIN STRUCTURES IN EPILEPSY-PRONE KM RATS UNDERGOING EXPERIMENTAL AUDIOGENIC EPILEPSY. KN Zabegalov, MYu Bykova, EV Shulina, AD Solovyova, SA Krivopalov, TO Kolesnikova and Allan Kalueff, ISBS Fellow, Institute of Immunology and Physiology Ural Branch RAS, Ural Federal University, Ekaterinburg, Russia

11th Regional "Stress and Behavior" ISBS Conference, June 22-24, 2017, Miami Beach, FL, USA

INTRODUCTION: Free amino acids play an important role in epileptic pathogenesis, acting as CNS neuromediators, essential metabolites and regulatory molecules. Here, we examine the composition of neuronal amino acids in hippocampus, frontal cortex and medulla oblongata in selectively bred, audiogenic seizure-prone rats undergoing experimentally evoked epilepsy. **METHODS:** Experiments utilized a total of 24 adult rats of the Krushinsky-Molodkina (KM) line (12 males and 12 females) with and without a series of 5 evoked epileptiform seizures. Seizures were assessed as 4 points according to the Krushinsky scale, showing maximal tonic convulsions with extension of all limbs. Amino acid qualitative and quantitative analyses was performed using HPLC. **RESULTS AND DISCUSSION:** Total amino acid content varied significantly in different brain regions. Of the three brain regions tested here, the largest total amino acid content was found in the hippocampus (showing high glutamate and aspartate levels), likely due to abundance of excitatory glutamatergic and aspartatergic synapses in this area. The KM rat females showed lower total amino acid content than males, likely due to higher metabolic rate and nervous impulse transmission rate in female brain. After a series of audiogenic epileptiform seizures, both male and female KM rats significantly reduced total amino acid content in the frontal cortex. The total number of amino acids was reduced in males in medulla oblongata, mainly affecting the inhibitory amino acids glycine, taurine and GABA. Such differences may be associated with anticonvulsive action of female sex hormones, which modulate female organism's susceptibility to seizures. Despite some differences in free amino acid total content in the brain of females vs males observed here, there was a similar dynamics for individual amino acids. For example, the frontal cortex and the hippocampus of both sexes showed lower levels of inhibitory amino acids (glycine, taurine and GABA), which are critical for dampening epileptogenic excitation in the CNS. In addition, a significantly reduced aspartate levels in the frontal cortex suggest the inclusion of this amino acid in the Krebs cycle, necessary for energy recovery after seizures. Furthermore, epileptiform activity of male and female KM rats reduced leucine levels in the hippocampus, and lysine levels in frontal cortex. Such differences are likely associated with anticonvulsive effect of these amino acids. **CONCLUSION:** We found a generally lower total content of free amino acids in female brains, although the dynamics of individual amino acids in both sexes was generally similar. However, the medulla oblongata of the KM female rats after experimentally evoked epileptiform seizures did not show altered content of inhibitory amino acids, which may be due to a lower predisposition of female organism to epileptiform activity (e.g., related to neuroprotective effects of female sex hormones). **RESEARCH SUPPORT:** Ural Federal University, Ekaterinburg, Russia.

EFFECTS OF CHRONIC AMITRIPTYLINE ADMINISTRATION ON BEHAVIORAL AND MONOAMINE METABOLISM-RELATED BIOMARKERS IN ZEBRAFISH. DA Meshalkina, EV Kysil, KA Antonova, EV Efimova, KA Demin, TO Kolesnikova, SL Khatsko and AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg University, St. Petersburg, Institutes of Chemical Technologies and Biological Sciences, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, New Orleans, LA, USA

INTRODUCTION: A commonly used CNS drug, amitriptyline is a tricyclic antidepressant with a strong serotonin transporter-inhibiting activity, but rather minor norepinephrine transporter-inhibiting action. Amitriptyline is currently facing the resurgence of interest to it as to a drug with a wide range of CNS effects, including not only major depressive and bipolar disorders, but also for attention deficit hyperactivity disorder and Parkinson's disease. **METHODS:** Here, we utilized two chronic doses of amitriptyline (10 and 50 $\mu\text{g/L}$) for two weeks in short-fin wild-type zebrafish ($n = 8$ per group). Behavior in the novel tank was recorded for 6 min, and analyzed with Ethovision XT 11.5 (Noldus IT, Netherlands). Whole-brain preparations were extracted on ice, sonicated in 0.1 M perchlorate solution and subjected to HPLC on the CA-5ODS column (Eicom, USA) for monoamine quantification. For tyrosine hydroxylase analysis, whole-brain preparations were lysed in low RIPA buffer and subjected to Western blot with sc-14007 antibodies (Santa Cruz). The data

were analysed with Kruskal-Wallis rank sum test with post-hoc multiple comparison Dunn's test. **RESULTS AND DISCUSSION:** Amitriptyline-exposed zebrafish showed overt behavioral changes, including hypolocomotion (shorter distance travelled, 767 ± 109 vs 1713 ± 154 cm $p=0.00089$ at maximal dose) and latency to the top (2.69 ± 0.7 vs 106.97 ± 11.5 s, $p=0.00099$), but more time in the top (273 ± 10 vs 101 ± 18 s, $p=8.90E-05$) and transitions to the top (3.7 ± 1.5 vs 11.5 ± 2.9 , $p=0.0095$). Analysis of the neurotransmitter levels in the brains of exposed zebrafish revealed a prominent decrease of serotonin turnover, assessed by 5-HIAA/5-HT ratio (0.180 ± 0.012 at $10 \mu\text{g/L}$ and 0.179 ± 0.014 at $50 \mu\text{g/L}$ vs 0.296 ± 0.009 in control, both $p=0.00179$) and significant increase in norepinephrine levels (865 ± 42 pg/mg of tissue vs 668 ± 58 pg/mg, $p=0.03789$), which was predictable, given the established amitriptyline binding to corresponding serotonin and norepinephrine transporters. Notably, acute and chronic drug effects share a common diad of hypolocomotion and top swimming (surfacing), which both correlate with enhanced serotonergic levels, and have been suggested earlier (Stewart et al., 2013) to reflect 'hyperserotonergic' serotonin toxicity-like phenotype, relevant to human serotonin toxicity syndrome. Interestingly, while earlier acute amitriptyline exposure studies (Demin et al., 2017) revealed altered serotonin (but not norepinephrine) neurotransmission in zebrafish, the present chronic exposure study yielded significant norepinephrine changes (suggesting the drug's sufficient action on norepinephrine transporter upon chronic exposure). Furthermore, CNS dopamine level was also significantly elevated in the exposed zebrafish (335 ± 20 vs 254 ± 10 pg/mg, $p=0.03969$), suggesting a potential additional (indirect) action of the drug on dopaminergic signalling/tone in-vivo. To explore this possibility further, we examined the level of the key enzyme in dopamine synthesis, tyrosine hydroxylase (TH), noting a significant increase in its level (121.9 ± 6.3 % from control, $p=0.03913$), that may underlie higher dopamine and norepinephrine brain contents reported here. Overall, zebrafish high sensitivity to chronic effects of amitriptyline can help improve our understanding of complex monoamine-modulating psychopharmacological profiles of this compound (and the related CNS drugs), and may also contribute further to the development of aquatic experimental animal models of human toxidromes. **RESEARCH SUPPORT:** Laboratory zebrafish maintenance utilized the SPbSU Environmental Safety Observatory Bioelectronic complex and Ural Federal University Drug screening platform. The research was supported by the Russian Foundation for Basic Research (RFBR) grant 16-04-00851A.

Day 3. Saturday, June 24, 2017

Celebration Room, Holiday Inn Miami Beach-Oceanfront, 4333 Collins Ave, Miami Beach, FL

SESSION ON ALTERNATIVE MODELS IN BIOLOGICAL PSYCHIATRY: INTERNATIONAL ZEBRAFISH NEUROSCIENCE RESEARCH CONSORTIUM (ZNRC)

INTRODUCTION TO ZNRC

FUTURE OF ZEBRAFISH MODELS IN TRANSLATIONAL NEUROSCIENCE RESEARCH. AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; School of Pharmaceutical Sciences, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

Neuropsychiatric diseases represent a difficult biomedical problem, both in their treatment and investigation. Additionally, many affected CNS phenotypes (e.g., social deficits in autism or cognitive deficits in schizophrenia) lack efficient approved treatments, and the success rate for new drugs remains extremely low, despite the rapidly growing body of relevant biological information. Based on the premise of targeting evolutionarily conserved (and, therefore, *core*) disease phenotypes and mechanisms, this strategy highlights the value of novel model organisms, such as zebrafish (*Danio rerio*), in translational neuroscience research. Native to South-East Asia, the zebrafish is a small tropical fish inhabiting streams, canals, ponds and rice fields. A popular aquarium species, it has also been long used in developmental, genetic, and, more recently, neuroscience research. Recent sequencing of the zebrafish genome reveals high similarity to other vertebrates, with ~71.4% of human genes having at least one zebrafish ortholog. However, zebrafish underwent an additional round of teleost-specific whole-genome duplication and also contain multiple deletions, inversions and duplications, compared to the human genome. A clear advantage of using zebrafish models is the non-invasive drug administration, since water-soluble substances added directly to water can be rapidly absorbed via gills and skin. Zebrafish may also be subjected to systemic (e.g., intraperitoneal or oral) drug administration, which can not only reduce the amount of drug used, but ensure a better dose control and enable direct dose comparisons with rodents (note, however, that immersional substance introduction helps avoid the injection stress, replacing it with a less intense restraint). Approximate generation time of zebrafish is 3-4 month, and females can spawn every 2-3 days producing ~200 eggs in each clutch. Zebrafish eggs are relatively large (0.7 mm in diameter), and their larvae are optically transparent during first days post fertilization, enabling easy neonatal manipulations through all developmental stages. Fast reproduction, relatively high genetic homology to humans and low cost have made zebrafish a convenient and cost-effective tool for genetics, embryology, neurophysiology and high-throughput drug or toxicity screening. Zebrafish also represent an emerging organism for modeling of complex brain diseases. Although some of zebrafish models (e.g., anxiety-, depression- and addiction-related) are relatively well-established, others are less recognized (e.g., autism- and obsessive-compulsive-like states) and appreciated. In summary, mounting data indicate that a wide spectrum of CNS diseases can be modeled in adult zebrafish, as will be discussed here using selected brain disorders as examples. Here, we summarize recent findings utilizing the zebrafish as an exciting novel tool to study complex CNS functions and dysfunctions. We also discuss model limitations and challenges, as well as outline future directions of research in this relatively 'young' (and, therefore, currently less established/supported), but highly promising field.

EFFECTS OF NORIBOGAINE ON ADULT ZEBRAFISH REPEATED NICOTINE WITHDRAWAL. AV Kalueff, ISBS Fellow, A Kaluyeva and EL Maillet, DemeRx, Inc., R&D Laboratory, Miami, FL, ZENEREI Research Center, Slidell, LA, USA

Noribogaine is a pharmacologically active primary metabolite of a hallucinogenic drug ibogaine. The activity profile of noribogaine includes modulation of opioid receptors, the serotonin transporter, and nicotinic cholinergic receptors. Recent evidence suggests using ibogaine and/or noribogaine as a novel potential therapeutic approach to treat various brain disorders, including addiction. Here, we tested psychotropic effects of noribogaine in adult zebrafish (*Danio rerio*) in a clinically relevant, repeated nicotine withdrawal model. In addition to behavioral testing in the novel tank test, whole body endocrine (cortisol) levels were assessed in all four groups. While repeated nicotine withdrawal produced overt anxiogenic behavioral, motor and cortisol responses in zebrafish, we found that acute noribogaine markedly alleviated these behaviors and blunted cortisol responses. Collectively, our findings demonstrate that noribogaine potently affects zebrafish behavior and physiology in models relevant to drug abuse, anxiety and the modulation of central cholinergic system. These results provide further support for developing novel psychoactive medication based on noribogaine, to treat comorbid drug abuse and affective disorders.

PROGRAM AND SELECTED LECTURES

**The International Neuroscience and Biological Psychiatry
ISBS/USBP Symposium
"TRANSLATIONAL BIOLOGICAL PSYCHIATRY"**



Kiev, Ukraine

May 23, 2017

**Program of the International Neuroscience and Biological Psychiatry
ISBS Symposium "TRANSLATIONAL BIOLOGICAL PSYCHIATRY", May
23, 2017**

Welcoming remarks: 20 years to ISBS Conferences – bridging “Biological” and “Psychiatry”

Prof. Allan V Kalueff (USA), ISBS and USBP President
Prof. Anatoliy P. Chuprikov (Ukraine)
Prof. Mykola Yu. Makarchuk (Ukraine)
Prof. Galina Ya. Pilyagina (Ukraine)

STRESS AND ITS OVERCOMING IN THE FAMILIES WITH THE CHILDREN WITH DEVELOPMENT AND BEHAVIOR DEVIATIONS. TV Chorna, AP Chuprikov, VD Mishiiiev, IV Kuznetsov. International Academy of Personnel Management, Shupyk National Medical Academy of Postgraduate Education, Kiev, Ukraine

ACTUAL SOCIAL STRESS, MENTAL DISTURBANCIES AND SELF-DESTRUCTIVE BEHAVIOUR IN UKRAINE. G Pyliagina, Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine

OLFACTION IN HUMANS: NEW INSIGHTS. MYu Makarchuk, Taras Shevchenko Kiev National University, Kiev, Ukraine

MILD COGNITIVE DEFICITS AND ALZHEIMER’S DISEASE. VA Kholin, NYu Bachinskaya, KN Poletaeva, Institute of Gerontology NAMS of Ukraine, Kiev, Ukraine

COFFEE BREAK

THE ROLE OF STRESS IN THE DEVELOPMENT OF ANXIETY DISORDERS - PROSPECTS OF MODERN PSYCHIATRIC RESEARCH IN THEORY AND PRACTICE (2014 UKRAINIAN POPULATION DATA). I Frankova, Bogomolets National Medical University, Kiev, Ukraine

PERSPECTIVES ON PSYCHEDELIC BIOMEDICAL RESEARCH. AV Kalueff, ISBS Fellow, ZENEREI Research Center, New Orleans, USA, St. Petersburg State University, St. Petersburg, Ural Federal University, Yekaterinburg, Southwest University, Chongqing, China

ZEBRAFISH MODELS OF HUMAN BRAIN DISORDERS AV Kalueff, ZENEREI Research Center, New Orleans, USA, St. Petersburg State University, St. Petersburg, Ural Federal University, Yekaterinburg, Southwest University, Chongqing, China

ROUND TABLE: ETHICS IN BIOMEDICINE

PRESENTATIONS OF ISBS AND THE UKRAINIAN SOCIETY FOR BIOLOGICAL PSYCHIATRY (USBP)

CONCLUDING REMARKS

11th Regional “Stress and Behavior” ISBS Conference, June 22-24, 2017, Miami Beach, FL, USA

STRESS AND ITS OVERCOMING IN THE FAMILIES WITH THE CHILDREN WITH DEVELOPMENT AND BEHAVIOR DEVIATIONS. TV Chorna, AP Chuprikov, VD Mishiiiev and IV Kuznetsov, International Academy of Personnel Management, Shupyk National Medical Academy of Postgraduate Education, Kiev, Ukraine

The number of children with developmental and behavioral deviations is growing globally. The families with special needs children are subjected to constant stress. Many researchers have examined psycho-traumatizing and crisis factors in such families. However, little is known on how to help the parents. Misunderstanding by close relatives and other people force such families to limit their communication with people. High unplanned expenses for the treatment and correction of the child's behavior condemn the family to considerable restrictions of the expenses for their own needs. Financial problems in the family often are the reason of quarrels between parents. The father, as a rule, spends the most time at work trying to earn more money for the family (or pretends doing so, and spends as little as possible time at home). Thus, the mother is in constant contact with a special needs child, and is a subject of nervous exaltation. Breaking the habitual way of life, the lack of necessary information on help to the child, isolation from society, feeling of doom and loneliness, bring the whole family into the condition of chronic stress. Besides a serious psycho-emotional state, many mothers feel physical pain as well. Many of them experienced a difficult delivery, the organism did not fully restore, and the child requires special attention. The psycho-trauma and household physical load cause psychosomatic disorders in young women, including back pain, constant headaches, pain in the neck and arms. Such serious intra-domestic environments can become a reason for family separation. Only in few families, the fathers are ready to share all the burdens of upbringing of the child with developmental and behavioral deviations with their spouses. The psycho-emotional state of parents influences not only the relationship between them, but also affects the focus and activity of helping the child (Chernaia, 2014; Dushka, 2016). Thus, help and support of the parents of children with developmental and behavioral problems became an object of research of Kiev-based psychologists and child psychiatrists. The system of help to such families has been developed to include not only psychological consultation of parents, but also Complex Game Kinesiotherapy (CGKT, 2013). Along with the child, the parents are offered to undergo manual massage typically performed on their children during rehabilitation. With quiet and slow movements of fingers, it is possible to help the parents to feel relaxed and calmed. After that, it is best to apply head massage, which helps to relieve fatigue and headaches. Several minutes are usually enough for parents to feel well-rested and full of strength. Many subjects note unusual feelings and unusual state following such influences. Therefore, under such easy and game-like massage (performed at the same time on both the parent and the child), they experience unusual feelings together: their facial expression and mood change, and the mutual understanding between them increases. After several sessions of the "game", it is easy to involve the parent into ball game and other active games with the child. Also, a positive impact on the parents' psycho-emotional condition is achieved by body-focused techniques and elements of yoga, as well as respiratory gymnastics (breath/exhalation and breath-holding). After such respiratory therapy, it is best to perform a relaxation session - a kinesthetic 'trance', during which the person realizes the events, mentally fixes his attention on body feelings and independently tries to cooperate with therapeutic correction of the body area which (in his opinion) is a problem. Thus, the parents learn to cope with fatigue and pain independently, without any intervention in their mentality by psychotherapists. The results of such interactions strongly affect the quality of help given to such children. Parents gain the valuable experience and an ability to relieve their fatigue, stresses and pains, also gaining more strength for spending time caring for their child, thereby indirectly improving the child's well-being and prognosis.

ACTUAL SOCIAL STRESS, MENTAL DISTURBANCIES AND SELF-DESTRUCTIVE BEHAVIOUR IN UKRAINE. GYa Pyliagina, Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine

INTRODUCTION: Social stress is any long period of social and economic instability that encompasses the whole population of the country or its large subgroups. It causes essential and rapid changes in social stereotypes and a significant transformation of social values, accompanied by a great deterioration of living standards for the majority of the population, a strong maladaptation due to irreversible lifestyle changes. Long-term, severe psycho-emotional overloads form mental disorders as serious public consequences social stress. Unfortunately, there is no direct way to measure the impact of social stress. Indirectly it is possible to assess of it on the population subgroups by the specificity of mental disorders, prevalence trends of them, and suicide rate as well. **METHODS:** Analysis of long-term statistic data about suicide rate,

traffic accidents death rate and mortality by cardio-vascular diseases (myocardial infarction as example) in Ukraine was used to assess the impact of actual social stress. **RESULTS AND DISCUSSION:** The population of Ukraine experienced major social stresses every 10-15 years throughout the 20th century. They were wars and drastic social change accompanied by enormous human casualties, strong economic troubles and forced violent or compelled migration of large masses of the population as well. One of the most serious consequences of social stress is an increasing of various mental disorders in a population. The period 2014–2017 includes the Revolution of Dignity and the three-year war conflict continuing in Donbass area should be considered as a new actual chronic social stress for Ukraine population. **CONCLUSIONS:** Our analyses show that the main psycho-traumatic factors are the duration of stress influence (first of all, the conserved war conflict); the *feeling* of immutability of a situation; essential, in many cases irreversible changes of life; continuing deterioration of economic troubles. Main impact target-groups of social stress: those who are in the deep of war conflict (active participants or unwitting victims of events) and those who believe that they are outside the situation. Main consequences of chronic social stress are pathopsychological problems (social and personal maladaptation, especially unemployment, marital conflicts and/or delinquent behavior) and mental disturbances (increasing alcohol abuse (F1), depressions (F32, F34), adjustment disorders (F43) and conduct disorders (F92)). The latter have essential gender differences. For these last three years, several stages of alternating main stressors have passed. Accordingly, we note significant changes in the specification of mental disorders in the main target groups following social stress. There is also indirect evidence that Ukrainian population may adapt to the current stressful situation.

THE ROLE OF STRESS IN THE DEVELOPMENT OF ANXIETY DISORDERS. PROSPECTS OF MODERN PSYCHIATRIC RESEARCH IN THEORY AND PRACTICE (UKRAINIAN POPULATION 2014 DATA). I Frankova, Bogomolets National Medical University, Kyiv, Ukraine

BACKGROUND: Overwhelming traumatic experience (mass murder scenes, international, civil wars, natural, man-made disasters, serious accidents, terrorist attacks, incarceration, sexual assaults and serious illness) or sudden change in social circumstances (multiple bereavement and forced relocation) that became a reality in Ukraine in 2014, leads to mental disorders, including anxiety, stress related disorders. **OBJECTIVE:** To summarize current theoretical and research data, analyze practical problems associated with views on anxiety disorders in Ukrainian population. **METHODS:** Based at Psychoneurology Department of the First Railway Clinical Hospital (Kyiv, Ukraine), we conducted pilot follow-up study of medical records. Study focus included data collected from 25 persons with traumatic experience, divided into 5 subgroups: 1) displaced persons, who left/lost homes (32%), 2) captives (8%), 3) regular soldiers (36%), 4) National Guard volunteers (12%), and 5) social workers, volunteers coping with injured soldiers, refugees (12%). **RESULTS:** Main syndromes, diagnoses, assigned medication and psychotherapy were identified for all 5 subgroups. Common diagnoses for all subgroups were adjustment disorders, acute stress reaction, neurasthenia. Prevalent for subgroup 1 were depressive disorders, for subgroups 2-4 - PTSD with comorbid post-contusion syndrome. Antidepressants, anxiolytics, hypnotics, antipsychotics, anticonvulsants were prescribed, based on comorbid diagnoses, targeting specific symptoms rather than diagnosed illnesses. **CONCLUSION:** Current endophenotypic approach applied to DSM-V divided anxiety and stress-related disorders into different groups. The era of modern diagnostic capabilities and neuroimaging clearly indicates that the strategy and the treatment of stress-related disorders at different stages after traumatic event must be reconsidered. According to results of the present pilot study, recommendations can be made to optimize the management of patients with stress-related anxiety disorders.



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.

ZNRC currently includes the following labs/PIs:

- Allan Kalueff, USA/Russia/China
- Georgianna Gould, USA
- Oliver Braubach, Canada/Korea
- Anderson Manoel Herculano, Brazil
- Caio Maximino, Brazil
- David Echevarria, USA
- Joseph Schroeder, USA
- Jason Warnick, USA
- Dominic Wright, Sweden
- Carla Denise Bonan, Brazil
- Mônica Ryff Moreira Roca Vianna, Brazil
- Wei Weng, USA
- Bally-Cuif, France
- Julian Pittman, USA
- Denis Rosemberg, Brazil
- Diogo Onofre Souza, Brazil
- Diogo Losch de Oliveira, Brazil
- Raul Bonne Hernandez, Brazil
- William Norton, UK
- Adam Michael Stewart, USA
- Lucas Noldus, Netherlands
- Jeremy Ullmann, Australia
- 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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'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.



INVITATION LETTER



Dear Colleagues and Friends,

It is my privilege to invite you to attend the 7th Mind-Body Interface (MBI) International Symposium, to be held at China Medical University, Taichung, Taiwan on Nov. 3 & 4, 2017.

The MBI Int'l Symposium has been vigorously promoting a global agenda of translational medicine by encouraging interdisciplinary research, and integrating biomedical discovery and development focused on patients, to provide better care and service in the field of mental health. This year, the main theme is *"From Molecule to Mind: Bridging the Gap between Research and Practice in Mental Health"*. The symposium will comprise keynote speech, plenary sessions from international researchers and clinician worldwide, and poster sessions. Bursaries for overseas participants are provided. Abstract for oral and poster presentations, as well as symposium sessions, are welcome. Submission deadline is July 15, 2017.

With the emerging and compelling evidence for nutrition as a crucial factor in the high prevalence and incidence of mental disorders, it is suggested that diet is as important to neuroscience as it is to other fields of medicine. This year, the symposium is featured with a broad spectrum of research, including basic science and the biological processes and factors underlying the links between diet, nutrition and mental health, including immunology, metabolic processes and molecular science as well as the brain-gut-microbe axis. Furthermore, there will be a strong focus on neuroimaging, personalized medicine, lifestyle intervention, health promotion and disease management, and epidemiology and population studies in mental health for different age groups.

Finally, we are delighted to welcome our academic partners to actively take part in this symposium, including International Stress and Behavior Society (ISBS), International Society for Omega-3 Research (ISOR), Japan Society for Lipid Nutrition (JSLN) and Psychoneuroimmunology Research Society (PNIRS-Asia Pacific). With the inspiration, intimate interaction and our great hospitality during the conference, the 7th MBI Int'l Symposium is guaranteed to be a wonderful event like it has been in the previous years.

We look forward to greeting a group of multidisciplinary participants, including biomedical researchers, psychiatrists, psychologists, dietitians, and other health professionals in Taichung, Taiwan in November.

Sincerely yours,

Kuan-Pin Su, M.D., Ph.D.

Chairman, 7th MBI Int'l Symposium

Director, Mind-Body Interface Laboratory (MBI-Lab)

President, Taiwanese Society for Nutritional Psychiatry Research



THE INTERNATIONAL STRESS AND BEHAVIOR SOCIETY (ISBS)

Established in 2007

President: Allan V. Kalueff, PhD (2015-2017)

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www.stress-and-behavior.com

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ISBS is the international society of experts working with a wide range of topics in the field of translational neuroscience, neurobehavioral sciences, biopsychology and biopsychiatry, with a particular focus on stress, stress-related neurobehavioral phenotypes, their neural, molecular and genetic mechanisms, as well as stress-evoked neuropsychiatric disorders.

Anyone with an interest in stress-related human or animal behaviors, neurobehavioral disorders and their mechanisms, wishing to join ISBS, can do so by paying dues. Payment can be made following sending the e-mail form and payment request to the ISBS Secretariat at info@stressandbehavior.com. Once the form and the payment have been received, you will receive a membership confirmation.

Membership:

Regular membership dues are \$100.00 for the period of three years, or \$60.00 for the period of one year. Student (undergraduate and graduate) membership dues are \$60.00 for the period of three years.

- Regular membership benefits include a \$50.00 discount for registration for any of the ISBS Conferences, symposia, workshops and summer schools.
- Student members will benefit from a \$25.00 discount for registration for any of the ISBS Conferences, symposia, workshops and summer schools.
- Membership cycle starts January 1st. ISBS Members benefit from reduced STRESS, BRAIN & BEHAVIOR journal subscription fees: \$70.00 (regular member), \$55.00 (student member).

ISBS Membership application form (please fill in and send by e-mail to the ISBS Secretariat at info@stressandbehavior.com, with the subject 'ISBS Membership request')

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Fellows of ISBS:

The ISBS Fellowship (with Life membership) is the highest honor bestowed by the International Stress and Behavior Society. It is awarded annually to international scholars, in recognition of their contribution to clinical or translational neuroscience, biological psychiatry and stress physiology research and/or education, as well as for their long-standing support of the ISBS mission and its national, regional or international programs.

Dr. Mikhail Aghajyanov (Yerevan Medical University, Armenia), 2015
Dr. Elliott Beaton (University of New Orleans, USA), 2015
Dr. Jean Martin Beaulieu (Laval University, Canada)
Dr. Marcus Day (Caribbean Drug and Alcohol Research Institute, St. Lucia), 2016
Dr. David Diamond (University of South Florida, USA), 2015
Dr. Evgeniy Budygin (Wake Forest Medical Center, USA), 2014
Dr. David Echevarria (University of Southern Mississippi, USA), 2014
Dr. Alexey Egorov (Sechenov Institute, Russia), 2014
Dr. Irina Ekimova (Sechenov Institute, Russia), 2013
Dr. Philippe Fauquet-Alekhine (Chinon Nuclear Power Plant, France), 2017
Dr. Raul Gainetdinov (Italian Institute of Technology, Italy), 2013
Dr. Allan Kalueff (ZENEREI Institute, USA), ISBS President, 2013
Dr. Victor Klimenko (Institute of Experimental Medicine, Russia), Vice-President, 2013
Dr. Mamiko Koshiba (Tokyo University of Agriculture and Technology, Japan), 2014
Dr. Dusko Kozic (University of Novi Sad, Serbia), 2016
Dr. Shun Nakamura (Tokyo University of Agriculture and Technology, Japan), 2014
Dr. Xiu Liu (University of Mississippi Medical Center, USA), 2016
Dr. Tatyana Nevidimova (National Mental Health Institute, Russia), 2014
Dr. Louis Newman (Destiny Medical School, St. Lucia), 2016
Dr. Yuriy Pastuhov (Sechenov Institute, Russia), 2013
Dr. Ghanshyam Pandey (University of Illinois at Chicago, USA), 2017
Dr. Mikhail Pletnikov (Johns Hopkins University, USA), 2015
Dr. Vsevolod Rozanov (Odessa University, Ukraine), 2017
Dr. Urban Seraphin (Allied Health Council, St. Lucia), 2016
Dr. Tatyana Sollertinskaya (Sechenov Institute, Russia), 2013
Dr. Adam Stewart (ZENEREI Institute, USA), 2015
Dr. Petr Shabanov (Institute of Experimental Medicine, Russia), 2016
Dr. Cai Song (Guangdong Ocean University, China), 2016
Dr. Tatyana Strelkova (Maastricht University, Netherlands), 2014
Dr. Gilbertha St. Rose (Eden Herbs, St. Lucia), 2015
Dr. Oleg Syropiatov (UAPO, Ukraine), 2013
Dr. Sergei Tsikunov (Institute of Experimental Medicine, Russia), 2014
Dr. Jason Warnick (Arkansas Tech University, USA), 2014

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Dr. James Erskine (St George's University of London, UK), 2018



THE INTERNATIONAL STRESS AND BEHAVIOR SOCIETY (ISBS)

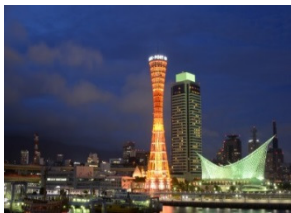
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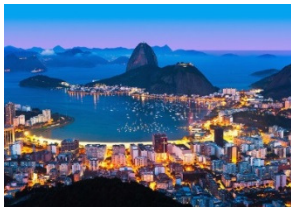
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ISBS is the international society of experts working with in the field of clinical and translational neuroscience, neurobehavioral sciences, biopsychology and biopsychiatry, with a particular focus on stress, stress-related neurobehavioral phenotypes, their neural, molecular and genetic mechanisms, as well as stress-evoked neuropsychiatric disorders. Anyone with an interest in stress-related human or animal behaviors, neurobehavioral disorders and their mechanisms, wishing to join the International Stress and Behavior Society can do so by paying dues of \$100.00 regular member or \$60.00 student member for a three-year term. To join please send membership application request to the ISBS Secretariat at info@stressandbehavior.com.

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



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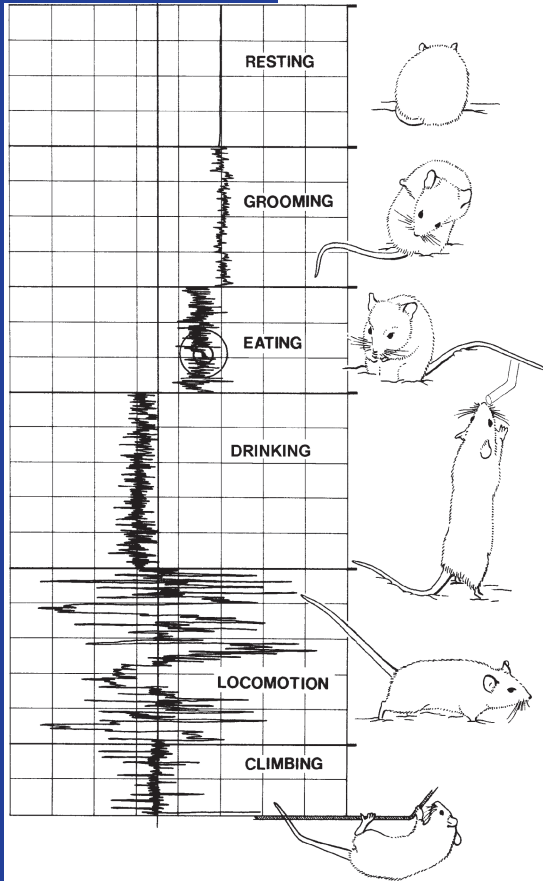


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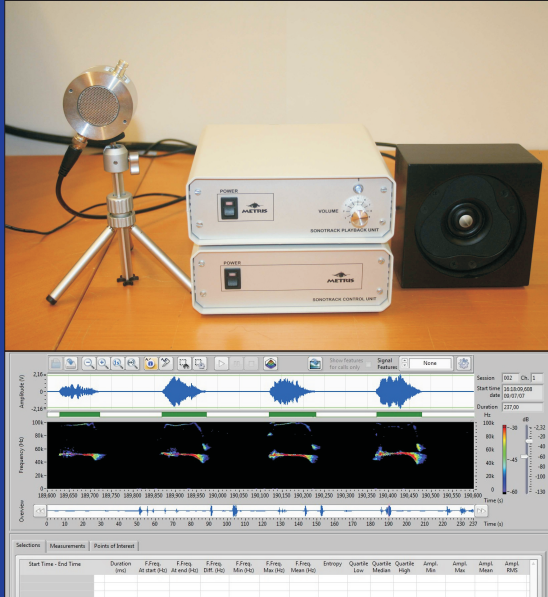


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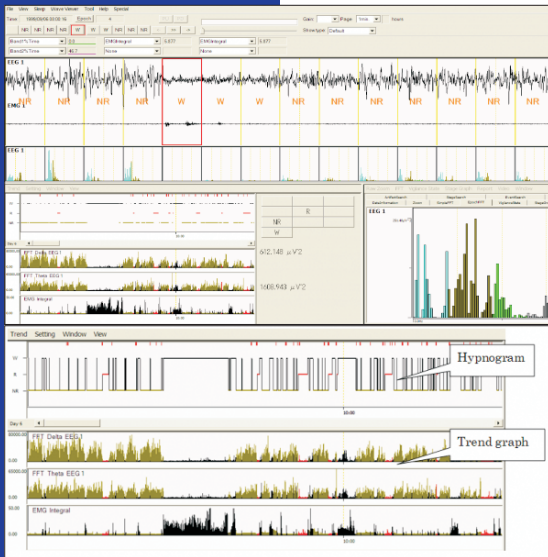


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