The International Stress and Behavior Society (ISBS)

Program and Proceedings

4th Caribbean Biomedical Research Days CBRD-2017

Rodney Bay, St. Lucia
January 16-18, 2017

CONFERENCE PROGRAM:

DAY 1, Monday, January 16, 2017

Dolphins Conference Center, Bay Gardens Beach Resort & Spa, Rodney Bay, St. Lucia

09.00 – 10.00	**Registration**
10.00 – 10.20	**CONFERENCE OPENING REMARKS. BRIEF INTRODUCTION TO THE HISTORY OF ISBS AND CBRD. WELCOMING ADDRESSES**
10.20 – 11.35	**ISBS Special Opening Lecture: BEHAVIORAL SCIENCE DETERMINANTS – ISBS DISCOURSE.** U Seraphin, ISBS Fellow, Saint Lucia Allied Health Practitioners Association (AHPA), St. Lucia, WI
11.35 - 12.30	**ISBS Presidential Lecture: ENDOPHENOTYPES AND RESEARCH DOMAINS IN BIOLOGICAL PSYCHIATRY - A TRIBUTE TO IRV GOTTESMAN.** AV Kalueff, ISBS Fellow, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, Slidell, LA, USA; Guangdong Ocean University, Institute of Marine Drugs and Nutrients, Zhanjiang, China
12.30 – 02.00	***Lunch Break (free time)***
02.00 - 02.35	**DIFFERENTIAL EFFECTS OF OPIOID RECEPTOR ANTAGONISM ON NICOTINE REINFORCEMENT AND CONDITIONED INCENTIVE EFFECT OF NICOTINE-ASSOCIATED CUES.** Y Gong, C Jernigan, L Biswas, E Harrison, R Avusula and X Liu, ISBS Fellow, University of Mississippi Medical Center, MS, USA
02.35 - 03.00	**EFFECTS OF BISPHENOL A AND HOP EXTRACTS EXPOSURE DURING ADOLESCENCE ON ANXIETY, DEPRESSION-LIKE BEHAVIORS, MEMORY AND SOCIAL INTERACTION IN ADULT MALE RATS.** L Van de Beeck, N Chapados and H Plamondon, University of Ottawa, Ottawa, ON, Canada
03.00 - 03.25	**THE SELECTIVE TRKB ANTAGONIST, ANA-12, REDUCES STRESS-INDUCED CORTICOSTERONE SECRETION AND SUPPORT SEX DIFFERENCES IN BDNF/TRKB SIGNALING.** I Azogu and H Plamondon, Behavioral Neuroscience Group, Department of Psychology, University of Ottawa. Ottawa, ON, Canada
03.25 – 03.50	***Coffee Break***
03.50 - 04.30	**ISBS Special talk: BENEFITTING FROM HERBAL MEDICINE.** G St. Rose, ISBS Fellow, Eden Herbs, Creative Health Center, St. Lucia, WI

04.30 - 04.45 **GENERAL DISCUSSION AND CONCLUDING REMARKS**

04.45 - 05.00 **VIDEO-PRESENTATION: ART MEETS SCIENCE.** D Raytchev, D Raytchev Art, London, UK

DAY 2, Tuesday, January 17, 2017

Dolphins Conference Center, Bay Gardens Beach Resort & Spa, Rodney Bay, St. Lucia

9.30 – 10.00 **Registration**

10.00 – 10.50 **ISBS Plenary Lecture: EXPRESSION OF HPA AXIS GENES AND THEIR METHYLATION IN TEENAGE AND ADULT SUICIDE.** GN Pandey, ISBS Fellow Inductee, Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA

10.50 - 11.15 **NOVEL BUTTERFLY DERIVATIVES OF FINGOLIMOD REDUCE DISEASE SYMPTOMS OF EXPERIMENTAL AUTOIMMUNE-INDUCED ENCEPHALO-MYELITIS IN MICE INDEPENDENT OF SPHINGOSINE KINASE 2 BY A DIRECT ENHANCEMENT OF BLOOD-BRAIN BARRIER FUNCTION.** A Huwiler, F Imeri, S Schwalm, B Engelhardt, A Zivkovic, H Stark and J Pfeilschifter, Institute of Pharmacology, Inselspital, University of Bern, Theodor-Kocher Institute, University of Bern, Switzerland; Pharmazentrum Frankfurt/ZAFES, University Hospital, Goethe University Frankfurt am Main, Institute of Pharmaceutical and Medicinal Chemistry, Heinrich-Heine-University Düsseldorf, Germany

11.15 - 11.30 **MANUAL LYMPHATIC DRAINAGE EFFECT ON CORTISOL CIRCADIAN RHYTHMICITY IN HEALTHY YOUNG MEN AND WOMEN.** MSM Pires-de-Campos, EAM Camargo, AL Souza, PC Silva, Rodrigues, LL and Grassi-Kassisse, Faculty of Health Sciences (FACIS), Methodist University of Piracicaba (UNIMEP), Piracicaba, São Paulo, Brazil, Institute of Biology, University of Campinas (UNICAMP), Campinas, São Paulo, Brazil

11.30 - 11.45 **DISCUSSION**

11.45 – 01.00 ***Lunch Break (free time)***

01.00 - 01.20 **UPDATE ON CANNABIS NEUROBIOLOGY.** M Fraites, St. Lucia, WI

01.20 - 01.50 **ISBS Special lecture: OVERCOMING THE NEGATIVE – CANNABIS AS MEDICINE: WILL IDEOLOGY OR SCIENCE BE OUR GUIDE?** M Day, ISBS Fellow, Caribbean Drug and Alcohol Research Institute (CDARI), St. Lucia

01.50 - 02.00 **DISCUSSION**

02.00 – 02.30 ***Coffee Break***

02.30 - 03.20 **ROUNDTABLE I: PERSPECTIVES AND CHALLENGES OF BIOMEDICINE AND BIOMEDICAL EDUCATION IN THE CARIBBEAN.** Moderators: AV Kalueff, USA and M Day, St. Lucia

03.20 - 04.00 **OCD NEW CLASSIFICATION AND MANAGEMENT.** RG Swamy, St. Jude's Hospital and Bay Medical Center, V/Foil, St Lucia

04.00 - 04.20 **ISBS BOOK CLUB: PROF. STEPHEN P. HINSHAW'S "ANOTHER KIND OF MADNESS. A JOURNEY THROUGH THE STIGMA AND HOPE OF MENTAL ILLNESS", ST. MARTIN'S PRESS, NY, 2017**

DAY 3, Wednesday, January 18, 2017

Dolphins Conference Center, Bay Gardens Beach Resort & Spa, Rodney Bay, St. Lucia

10.00 - 11.00 **INTERACTIVE GUIDED POSTER MINI-SYMPOSIUM**

CRH R1 and HPA AXIS ACTIVATION UPON A GLOBAL ISCHEMIA AFFECTS NEUROENDOCRINE REGULATION, BRAIN PLASTICITY AND RECOVERY OF FUNCTIONS AT DELAYED SURVIVAL INTERVALS. H Plamondon, PB de la Tremblaye, M Milot, J Raymond, N Narvaez-Linares and S Shock, University of Ottawa, Ottawa, ON, Canada

INFLUENCE OF OMEGA-3 AND ENRICHED ENVIRONMENT DURING THE ADOLESCENCE PERIOD ON SUBSEQUENT STRESS REACTIVTY IN FEMALE AND MALE RODENTS. Raymond J and Plamondon H, University of Ottawa, Ottawa, ON, Canada

UTILIZING ZEBRAFISH MODELS IN REHABILITATION MEDICINE. MK Poudel and AV Kalueff, ISBS Fellow, ZENEREI Research Center, Slidell, LA, USA

ZEBRAFISH BEHAVIORAL PHENOMICS AND CNS DRUG DISCOVERY. AV Kalueff, ISBS Fellow, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, Slidell, LA, USA; Guangdong Ocean University, Institute of Marine Drugs and Nutrients, Zhanjiang, China

11.00 – 11.20 *Coffee Break*

11.20 - 11.50 **ROUNDTABLE II: ETHICS IN BIOLOGY AND MEDICINE**

11.50 - 12.00 **ROUNDTABLE III: ANIMAL MODELS IN BIOMEDICAL RESEARCH: FROM LOGIC TO BIOETHICS**

12.00 - 12.15 **OFFICIAL CLOSING OF THE CONFERENCE**

ANNOUNCING FUTURE ISBS AND CBRD CONFERENCES

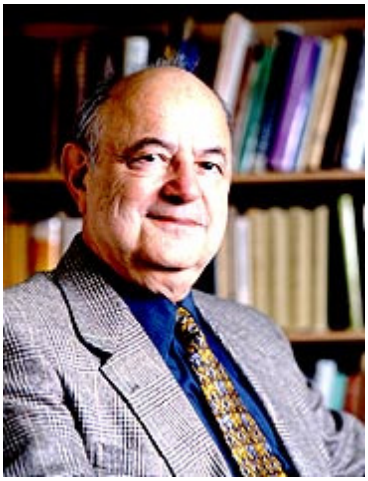
ABSTRACTS

DAY 1, Monday, January 16, 2017

BEHAVIORAL SCIENCE DETERMINANTS – ISBS DISCOURSE. U Seraphin, ISBS Fellow, Saint Lucia Allied Health Practitioners Association (AHPA), St. Lucia, WI

The multiple influences in our cultivation and interest in behavioral investigation cannot be considered in isolation. Therefore, dispositions and concern, care, warmth and unconditional acceptance that we develop towards a person has unlimited potential for actualization. To be effective, attention must be given to the different schools of psychological thought, to provide insight into the basis of behavior. Behavioral science is an integrative effort, and psychiatry cannot fully address clinical behavioral science, due to the ongoing overlapping in the scope and management of behavioral abnormalities. The scope of behavioral science today requires a great volume of knowledge of other basic medical sciences, in order to enable clinicians and students in this field to evaluate the diversified dimensions of behavior function and dysfunctions. It also largely depends mainly upon the personal nature and personality. Here, we will discuss basic concepts to explain the correlation of determinants of normal and abnormal human behavior. The emphasis will be placed on pragmatic data with theories of the pathogenesis of behavioral dysfunctions to reflect the multifactorial nature of mental disorders. The following theories of behavioral science determinants personality theory will be discussed: Client centered; Existential; Psychoanalytic; Gestalt; Transactional analysis; Individual psychology; Rational emotive theories; Strategic and Multi-model; Reality therapy; Repressive therapies, and others. The theories, within each category, share many similar propositions regarding the nature of humanity, the nature of dysfunctional behavior, the therapy goals, the counselor's role, the treatment techniques, the treatment components and the nature of psychological wellness.

ENDOPHENOTYPES AND RESEARCH DOMAINS IN BIOLOGICAL PSYCHIATRY - A TRIBUTE TO IRV GOTTESMAN. AV Kalueff, ISBS Fellow, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, Slidell, LA, USA; Guangdong Ocean University, Institute of Marine Drugs and Nutrients, Zhanjiang, China



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

"endophenotypes", proposed (with J. Shields) in their 1972 book, Schizophrenia and Genetics. Specifically, they posited that the genetic basis of psychiatric disorders could be better understood, and specific genes more readily identified, by the discovery of biological characteristics that lie a step closer to DNA/genes than the clinically observable symptoms and signs ('exophenotypes'), by which disorders are defined. Irv continued to elaborate the endophenotype concept over ensuing years and it provoked thousands of papers by others (McGuffiun, 2016). Today, Gottesman's endophenotype concept remains one of the most influential thoughts in biological psychiatry. Irving was also a good friend of ISBS, advising our members and enthusiastically contributing to many ISBS publications. Recognizing his critical impact on the field, this Special ISBS Lecture will discuss the developing utility of endophenotypes in neurobiology, the potential role of the interplay of endophenotypes in brain pathogenesis, their conceptual integration into the NIH's Research Domains Criteria (RDOC) framework, and the emerging promising new areas of research in this direction.

DIFFERENTIAL EFFECTS OF OPIOID RECEPTOR ANTAGONISM ON NICOTINE REINFORCEMENT AND CONDITIONED INCENTIVE EFFECT OF NICOTINE-ASSOCIATED CUES. Y Gong, C Jernigan, L Biswas, E Harrison, R Avusula and X Liu, ISBS Fellow, University of Mississippi Medical Center, MS, USA

INTRODUCTION: Opioid neurotransmission has been implicated in the mediation of reward and its associated learning/memory processes. However, it remains unclear whether activation of opioid receptors plays a role in mediating the motivational/reinforcing effects of nicotine and its associated environmental cues. This study investigated the effect of pharmacological blockade of opioid receptors on nicotine self-administration and cue-induced reinstatement of nicotine-seeking behavior. **METHODS:** Male Sprague-Dawley rats were trained in daily 1h sessions to self-administer nicotine (0.03 mg/kg/infusion, free base, iv) on an FR5 schedule and associate a conditioned stimulus (CS) with each nicotine delivery. In subsequent extinction sessions, there was no availability of nicotine and its associated cues. In the final reinstatement tests, responses resulted in re-presentation of the cues without nicotine delivery. Opioid antagonists were administered prior to the test sessions. **RESULTS AND DISCUSSION:** Pretreatment with the non-selective opioid antagonist naltrexone (0, 0.25, 1, 2 mg/kg, sc) dose-dependently attenuated the cue-induced reinstatement of extinguished lever responding. In contrast, naltrexone (both acute and chronic treatment) did not change lever responses for nicotine self-administration. However, pretreatment with antagonist selective for μ1 receptors (naloxanazine: 0, 5, 15 mg/kg, ip) but not δ receptors (naltrindole: 0, 0.5, 5 mg/kg, ip), or κ receptors (GNTI: 0, 0.25, 1 mg/kg, ip) suppressed nicotine self-administration responses. These results indicate that opioid neurotransmission is involved in mediating the conditioned incentive properties of nicotine cues, suggesting a clinical potential of the non-selective opioid antagonists for preventing cue-triggered relapse of tobacco craving. These results also indicate that the μ1 subtype rather than δ or κ subtype of opioid receptors plays a role in mediating the primary reinforcement of nicotine, suggesting that opioid neurotransmission via the μ1 receptors would be a promising target for the development of opioid ligands for curbing nicotine intake and stopping tobacco use. **RESEARCH SUPPORT:** NIH grants R01DA017288 & R01DA037277 and California TRDRP grant #12KT-0188.

EFFECTS OF BISPHENOL A AND HOP EXTRACTS EXPOSURE DURING ADOLESCENCE ON ANXIETY, DEPRESSION-LIKE BEHAVIORS, MEMORY AND SOCIAL INTERACTION IN ADULT MALE RATS. L Van de Beeck, N Chapados and H Plamondon, University of Ottawa, Ottawa, ON, Canada

INTRODUCTION: Bisphenol A (BPA), an organic compound and constituent of plastic, acting as an endocrine disruptor mimicking estrogens, has been involved in various health and behavioral conditions in humans. For instance, increased anxiety and depressive responses have been reported following BPA exposure, with greater effects during developmental periods. On the other hand, hop extract, a natural constituent of beer, is known for sedative actions on brain processes and beneficial effects on health. Our study assessed effects of juvenile BPA and hop extract administration on anxiety, depression-like behaviors, recognition memory and social interaction in adulthood. **METHODS:** Wistar juvenile male rats (n=10/group) were separated into 4 groups: control (Corn oil 40 mg/kg – the vehicle used to mix hop and BPA), BPA (BPA 40mg/kg), HOP (hop extracts 50mg/kg) and BPA-Hop (BPA 40mg/kg + hop extracts 50mg/kg). Solutions were administered by oral gavage for 20 consecutive days from PND28 to PND48. Animals were tested in the elevated plus maze (EPM) on PND54, the social interaction and preference test (SIT and SP) on PND55, the object recognition test on PND57 & 58, and the forced swim test (FST) on PND60. **RESULTS AND DISCUSSION:** Our findings revealed heightened anxiety and a tendency toward depressive-like behavior in the BPA exposed compared to the HOP exposed animals. Hop extract also enhanced retention at the longer 24 h retention interval, an effect mitigated in BPA-Hop exposed rats. The current study supports long-term effects on cognitive and emotional processes from exposure to these compounds at a critical brain maturation period along with possible interaction in regulating behaviors. This research underlies the importance of acquiring increased knowledge of brain and behavior mechanisms affected from exposure to unregulated environmental agents such as BPA; and encourages increased awareness of beneficial impact of nutraceuticals on those mechanisms. **RESEARCH SUPPORT:** NSERC discovery grants to HP and NC.

THE SELECTIVE TRKB ANTAGONIST, ANA-12, REDUCES STRESS-INDUCED CORTICOSTERONE SECRETION AND SUPPORT SEX DIFFERENCES IN BDNF/TRKB SIGNALING. I Azogu and H Plamondon, Behavioral Neuroscience Group, Department of Psychology, University of Ottawa. Ottawa, ON, Canada

INTRODUCTION: Adverse early life experience can have negative impacts on neuronal plasticity, behavior and stress response later in life. Stress-induced alterations in the signaling of brain-derived neurotrophic factor (BDNF) has emerged as a major component in the vulnerability to mood disorders in adulthood. In the current study, the selective tyrosine-related kinase B (TrkB) receptor antagonist, ANA-12, proven effective in reducing anxiety and depression-like behaviors, was used to determine the role of BDNF/TrkB signaling in mediating stress-induced corticosterone secretion in male and female juvenile rodents. **METHODS:** Adolescent male and female Wistar rats, aged 26 old, were exposed to a 10-day heterotypic stress paradigm (alternating 30 min restraint stress and 15 min forced swim stress on odd and even numbered days, respectively) in order to assess sex differences in stress responses and the relationship of these changes to TrkB signaling and endogenous corticosterone (CORT) secretion in early life. 30 min prior to the start of the stress or no stress sessions on days 1, 4, 7 and 10 of the paradigm, rats either received intraperitoneal injections (0.5 mg/kg) of ANA-12 or a vehicle solution (20% HP-β-Cyclodextrin in 0.9% saline) in 10ml/kg injection volume. CORT samples were collected via tail venipuncture on days 1, 5 and 10 and concentrations (pg/ml) determined using an enzyme-

linked immunosorbent assay (ELISA) protocol. **RESULTS AND DISCUSSION:** Both sexes showed a robust post stress increase in CORT levels. Sex differences were noted as females on average had higher CORT levels than males, i.e. CORT remained significantly higher in female compared to male rats on days 1, 5 and 10, except for the 30 and 60 min intervals on day 10 in which males showed elevated CORT levels compared to females. ANA-12 treatment lowered CORT levels in stressed males and females on day 1. On day 5, ANA-12 treatment received on day 4 had protracted effects to lower CORT levels immediately following stress cessation and 30 mins later in males but not in females. On day 10, CORT levels were significantly attenuated in ANA-12 treated males at 30 and 60 mins post stress compared to vehicle treated counterparts. Our findings support a relationship between TrkB receptor activation and stress-induced CORT secretion in both sexes. Using a combinatory stress model shown to steadily activate the hypothalamic-pituitary-adrenal (HPA) axis, we further show evidence of lasting dysregulation affecting basal CORT secretion in juvenile rats exposed to this paradigm. Sex specific effects of ANA-12 on endocrine responses suggest that modulating BDNF/TrkB levels could have therapeutic implications when considering depression and other mood related disorders. Future studies should investigate sex differences in TrkB bioavailability and determine ANA-12 dose-response profile in regulating HPA axis activation in the juvenile and adult period. **RESEARCH SUPPORT:** The Natural Sciences and Engineering Research Council of Canada grant (NSERC-RG203596-13) to HP.

BENEFITTING FROM HERBAL MEDICINE. G St. Rose, ISBS Fellow, Eden Herbs, Creative Health Center, St. Lucia, WI

Herbal medicines have been successfully used for centuries in all parts of the world. The putative mechanisms of action of these herbal medicines are known to be synchronized into the normal existing metabolic and biochemical processes to maintain internal harmony in the body while effecting healing and/or maintaining optimum health. In western herbal medicine, we consider the aspects of balancing internal bodily functions of stimulation and sedating and also contracting and relaxing as being the foundations for effecting metabolic and biochemical processes for maintenance of health and towards restoration from disease states. Modern phytotherapy has advanced to validate these pharmacological activities by laboratory evaluation of phytonutrients. As clinicians, we welcome the demonstration of efficacy as we see the positive results when using these herbs in the treatment of our patients. Several specific examples of herbs which demonstrate therapeutic properties will be discussed here, to support this notion.

ART MEETS SCIENCE. D Raytchev, D 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’ line-work. 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, Tuesday, January 17, 2017

EXPRESSION OF HPA AXIS GENES AND THEIR METHYLATION IN TEENAGE AND ADULT SUICIDE. GN Pandey, ISBS Fellow Inductee, Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA

INTRODUCTION: An impaired hypothalamic-pituitary-adrenal (HPA) axis response has been linked to depression and increased risk of suicide. Some studies also suggest epigenetic regulation of HPA axis genes in suicide, specifically related to early life adversity (ELA). Glucocorticoid receptors (GR) and mineralocorticoid receptors (MR) play an important role in observed abnormal HPA axis in depression and suicide. **METHODS:** We have examined GR, MR and FK506 binding protein 5 (FKBP5) expression and methylation status in the prefrontal cortex (PFC) of 24 adult and 24 teenage suicide victims and 24 matched normal controls (NC). Protein was determined by Western blot and mRNA was determined by real-time PCR. We also determined the methylating enzymes DNA (cytosine-5)-methyltransferase 1 (DNMT1) and DNMT3A and DNMT3B. **RESULTS AND DISCUSSION:** We found that the mRNA and protein expression of GR was significantly decreased, FKBP5 significantly increased, and no change in mRNA expression of MR in the PFC of teenage suicide victims compared with NC subjects. Although GR and MR levels did not differ between adult control and suicide subjects the expression of a GR transcript, GR1F, was significantly decreased in adult suicide subjects compared with NC subjects. FKBP5 was significantly increased in the PFC of both teenage as well as adult suicide subjects. The methylating enzymes DNMT1 and DNMT3A were significantly increased in both teenage and adult suicide victims. When we compared DNA methylation between groups we found that GR1F promoter region showed a greater increase in methylation in teenage suicide compared with adult subjects, and decreased methylation of FKBP5 in suicide. We also observed that GR methylation was increased in those subjects who had a history of ELA. These studies show abnormalities of GR and FKBP5 expression and methylation in both teenage, as well as adult suicide victims and that this increased methylation may be related to ELA. **RESEARCH SUPPORT:** RO1MH106565 grant from the US National Institutes of Health (NIH).

NOVEL BUTTERFLY DERIVATIVES OF FINGOLIMOD REDUCE DISEASE SYMPTOMS OF EXPERIMENTAL AUTOIMMUNE-INDUCED ENCEPHALO-MYELITIS IN MICE INDEPENDENT OF SPHINGOSINE KINASE 2 BY A DIRECT ENHANCEMENT OF BLOOD-BRAIN BARRIER FUNCTION. A Huwiler, F Imeri, S Schwalm, B Engelhardt, A Zivkovic, H Stark and J Pfeilschifter, Institute of Pharmacology, Inselspital, University of Bern, Theodor-Kocher Institute, University of Bern, Switzerland; Pharmazentrum Frankfurt/ZAFES, University Hospital, Goethe University Frankfurt am Main, Institute of Pharmaceutical and Medicinal Chemistry, Heinrich-Heine-University Düsseldorf, Germany

INTRODUCTION: The immunomodulatory drug FTY720 (Fingolimod) is presently approved for the treatment of relapsing-remitting multiple sclerosis. It is a prodrug that requires activation by sphingosine kinase 2 (SK-2) and in its active phosphorylated form, it acts as a functional antagonist on the sphingosine-1-phosphate receptor 1 (S1P1) to induce T cell homing to secondary lymphoid tissue. In this study, we have developed two novel butterfly derivatives of FTY720 (ST-968 and ST-1071) and have investigated their therapeutic effect and dependency on SK-2 in experimental autoimmune-induced encephalomyelitis (EAE) in mice. **METHODS:** EAE was induced by immunization of mice with a myelin oligodendrocyte glycoprotein peptide (MOG35-55). Clinical symptoms were determined daily. Molecular changes on mRNA and protein

level were analysed in brain and spinal cord tissue by PCR and immunofluorescent staining of sections. **RESULTS AND DISCUSSION:** We show that ST-968 and ST-1071 reduced the clinical symptoms of EAE comparable to FTY720 either by prophylactic or therapeutic treatment. In SK-2-deficient mice, the protective effect of FTY720 on EAE was abolished, while the non-prodrug compounds were still fully active and strongly reduced disease symptoms. Protection was paralleled by reduced numbers of T-lymphocytes in blood and a reduced blood-brain-barrier (BBB) leakage. This correlated with reduced mRNA expression of ICAM-1, VCAM-1, but enhanced expression of PECAM-1. In summary, the data suggest that these novel compounds could have considerable implication for future therapies of multiple sclerosis and other autoimmune diseases, and they may be a valuable alternative to FTY720 under conditions where SK-2 activity is limited. **RESEARCH SUPPORT:** The Swiss Society of Multiple Sclerosis, the Swiss National Science Foundation, and the German Research Council.

MANUAL LYMPHATIC DRAINAGE EFFECT ON CORTISOL CIRCADIAN RHYTHMICITY IN HEALTHY YOUNG MEN AND WOMEN. MSM Pires-de-Campos, EAM Camargo, AL Souza, PC Silva, Rodrigues, LL and Grassi-Kassisse, Faculty of Health Sciences (FACIS), Methodist University of Piracicaba (UNIMEP), Piracicaba, São Paulo, Brazil, Institute of Biology, University of Campinas (UNICAMP), Campinas, São Paulo, Brazil

INTRODUCTION: Cortisol a steroid hormone is considered an important marker of responses to stress. Its secretion in humans follows the circadian cycle with the highest concentration in the morning, during the last stages of sleep and in the moment of awakening, while the lowest concentration occurs during the night. Manual lymphatic drainage (MLD) aims to restore or maintain the water-electrolyte balance, the function of the lymphatic system and, consequently, human health. In addition to these effects, some research has shown that MLD has other systemic effects, as in the endocrine system. We aimed evaluate the effect of acute treatment of manual lymph drainage on concentrations of cortisol (CC), its rhythmicity (CCR) in healthy young men and women. **METHODS:** 40 healthy and sedentary volunteers, 7 men (22.6±1.1 years; BMI 23.2±1.2 Kg/m2), 33 women (18 non-users and 15 users oral contraceptive, 21.5±0.5 years; BMI 21.5±0.4 Kg/m2) were assessed. The experiments were carried out in an environment with temperature and relative humidity controlled, always in the morning. Samples were collected on two different days: control (C) and MLD. Saliva samples for CC (ng/mL) were collected on both days at: 6 a.m., noon, 6 p.m., and 10 p.m., and analyzed by ELISA. MLD was applied in the lower limbs and abdomen during 45 min. **RESULTS AND DISCUSSION:** MLD did not alter the total daily production of CC neither there were difference between sex (MC: 204+30.7vs MDLM: 216+42.6; WC: 198.7+13.5 vs WDLM: 181.3+9.5). The amounts of CC at 6 a.m. were the same between sex (MC: 17.6+3.3 vs WC: 13.9+1.4). CCR was preserved in men and women in day C, i.e. there were a significantly decrease in cortisol levels during the day. The DLM induces no decrease in CC in men. In women there is decrease in noon CC values in DLM day (WC: 15.8+1.6 vs WDLM: 12.1+0.9, p=0.01). The MLD abolish the cortisol rhythmicity in men, however in women DLM induced a decrease in CC noon values. **RESEARCH SUPPORT:** Fapesp (2013/20510-3), Faepex – Unicamp, and FAP – Unimep.

UPDATE ON CANNABIS NEUROBIOLOGY. M Fraites, St. Lucia, WI

I will outline the earliest known history of cannabis and some of the most significant studies and discoveries made in this field, showing that humans have long been inextricably linked with

cannabis. The first isolation of the THC molecule from cannabis was a breakthrough that led to the discovery and understanding of the endocannabinoid system. However, we have insight, but not a full understanding, of how the endocannabinoid system can be used to prevent, diagnose and treat a disease, defect or symptom of illness. The endocannabinoid system is comprised of receptors, their endogenous ligands, and the proteins synthesized to degrade them. Research has identified various cannabinoid receptors in the brain and immune cells which respond to agonists or inverse agonists which may be endogenous, synthetic or phyto-derived. The cannabinoid receptors are abundant in the mammalian brain. Appropriate levels of cannabinoids appear to be required to support pregnancy, and breast milk contains cannabinoids for the development and growth of the newborn. With a firm understanding of the endocannabinoid system and the 60+ cannabinoids, we can prevent or eliminate the few negative possible outcomes of Cannabis use and maintain optimum health.

OVERCOMING THE NEGATIVE – CANNABIS AS MEDICINE: WILL IDEOLOGY OR SCIENCE BE OUR GUIDE? M Day, ISBS Fellow, Caribbean Drug and Alcohol Research Institute (CDARI), St. Lucia

The use of medical marijuana or therapeutic cannabis is gaining wider acceptance in the medical community. The findings of the CARDIA study (JAMA Intern Med. 2016, 176, 352-361) has shown that long term use of cannabis has a minimal impact. Much of the early research protocols submitted for support were designed to investigate the negative impact of cannabis on the body. Research findings were often reported in a way that highlighted the most negative aspects of findings with beneficial or therapeutic qualities minimized US Government-funded cannabis research has had an ideological foundation rooted in a war on drugs mentality where criminal justice sanctions replaced health based interventions. The wider acceptance of the body of evidence that demonstrates the therapeutic value of cannabis has given rise to the necessity to examine the influence of ideological influences on the science in order to mitigate their influence. In this presentation, we will explore cannabis as medicine will ideology or science be our guide?

OCD NEW CLASSIFICATION AND MANAGEMENT. RG Swamy, St. Jude's Hospital and Bay Medical Center, V/Foil, St Lucia.

OCD until recently has been considered as a relatively rare disorder with poor prognosis. Currently, OCD is considered to be among the most common psychiatric disorders. New treatments have spurred the development of considerable clinical, epidemiological and biological research in this field. OCD classification with comorbidity, and new management methods, will be discussed.

ISBS BOOK CLUB: PROF. STEPHEN P. HINSHAW'S "ANOTHER KIND OF MADNESS. A JOURNEY THROUGH THE STIGMA AND HOPE OF MENTAL ILLNESS", ST. MARTIN'S PRESS, NY, 2017

In *Another Kind of Madness*, Hinshaw explores the burden of living in a family "loaded" with mental illness, and debunks the stigma behind it, explaining that in today's society, mental health problems can result in a loss of a driver's license, inability to vote or run for office, ineligibility for jury service, or automatic relinquishment of child custody. With a moving personal narrative and shocking facts about how America views mental health conditions in the 21st century, *Another Kind of Madness* is a passionate call to arms regarding the importance of destigmatizing mental

illness. The author, Stephen Hinshaw, is a professor of psychology at UC Berkeley and the Vice-Chair for Psychology at UC San Francisco, USA. Prof. Hinshaw is the author The Mark of Shame: Stigma of Mental Illness and an Agenda for Change (Oxford, 2007), the first book in the U.S. on mental illness stigma. His research has been covered in *The New York Times, The Washington Post, Time, The Economist, The Wall Street Journal*, among others. He lives in Berkeley, CA. This ISBS Book Club will continue the series of ISBS events dedicated to latest books published by members of our research community, and targeting mental issues in a format understandable to a wide readership audience, from general public to psychologists and psychiatrists.

DAY 3, Wednesday, January 18, 2017

INTERACTIVE GUIDED POSTER MINI-SYMPOSIUM

CRH R1 and HPA AXIS ACTIVATION UPON A GLOBAL ISCHEMIA AFFECTS NEUROENDOCRINE REGULATION, BRAIN PLASTICITY AND RECOVERY OF FUNCTIONS AT DELAYED SURVIVAL INTERVALS. H Plamondon, PB de la Tremblaye, M Milot, J Raymond, N Narvaez-Linares and S Shock, University of Ottawa, Ottawa, ON, Canada

INTRODUCTION: Cognitive deficits observed in rodents subjected to forebrain ischemia (mimicking the cerebral ischemia observed following cardiac arrest) are generally interpreted as produced by neuronal degeneration to discrete regions of the brain, principally the hippocampus. Challenging this view, the presence of ischemia-induced neuronal damage is not always associated with manifestations of cognitive impairment, or conversely, impairments post-reperfusion can originate at times when neuronal damage has yet to occur. The current work assess whether the impairing effects of ischemia on cognitive functioning and neurochemistry might in part be attributable to endogenous alterations of emotional systems regulating anxiety, stress, and/or arousal, thus not exclusively to discrete neuronal damage. **METHODS:** The four vessel occlusion model was used to induce 10 min global cerebral ischemia in male Wistar rats. Sham rats acted as controls. Rats received either an intracerebroventricular injection of the CRH type 1 receptor antagonist Antalarmin (2µg/2µl), a systemic injection with the glucocorticoid inhibitor metyrapone (175 mg/kg; s.c.), or a vehicle solution 30 min before ischemia or sham occlusion. Behavioural testing was initiated 7 days post ischemia and determined anxiety, memory and depressive-like behaviors using the elevated-plus maze, the Barnes maze and the Forced swim test. We used ELISA,RIA immunohistochemistry, Western blot and qPCR to assess the impact of ischemia and drug treatment on plasticity markers (BDNF, TrkB), HPA axis activation (CRH, CRHR1 and CORT) and microglial (IBA1) and TNFα expression 30 days following reperfusion. **RESULTS AND DISCUSSION**: Our data demonstrates that cerebral ischemia is a significant stressor having lasting impact on HPA axis reactivity, effects associated to spatial memory impairments and emotional/mood impairments at delayed post-reperfusion intervals. Ischemia led to persistent increase in GR-, CRH- and CRHR1-in the hypothalamic paraventricular nucleus while reduced expression of the same markers was present in the hippocampus; reduced and elevated BDNF and TrkB expression were observed in the hippocampus and VTA/Nucleaus accumbens, respectively, which alterations were regularized by CRH-R1 blockade. Antalarmin also partially blocked ischemia-induced microglial and TNF-α activation at the hippocampus. Together, our findings support beneficial effects of therapeutic approaches targeting hyper activation of neuroendocrine systems following cardiac arrest or myocardial infarction. **RESEARCH SUPPORT:** Discovery grant from the National Science and Engineering Research Council of Canada (NSERC) and internal funding from the University of

Ottawa to HP. PBT was supported by a postgraduate fellowship from NSERC and is now a postdoctoral fellow at the University of Pittsburgh, USA.

INFLUENCE OF OMEGA-3 AND ENRICHED ENVIRONMENT DURING THE ADOLESCENCE PERIOD ON SUBSEQUENT STRESS REACTIVTY IN FEMALE AND MALE RODENTS. J Raymond and H Plamondon, University of Ottawa, Ottawa, ON, Canada

INTRODUCTION: A rich omega-3 diet is necessary for many biological processes including neuronal growth, synapse function, neuroplasticity and learning, and appears to be especially important during discrete developmental periods. Omega-3 deficiency from the diet has been associated with reduced cognitive performance and physical abilities as well as cardiovascular disease and mental health problems. The adolescence is known to be a vulnerable period to stressful events exposure, the 'late blooming' prefrontal cortex developing well after puberty. Different external and internal factors are capable of modifying and/or improving brain plasticity during this period, including diet and environment. An enriched environment plays an important role in optimizing brain functions by conferring a stimulating environment and space for exercise. These elements have been shown to improve cognitive, sensory and motor function as well as social interaction. **METHODS:** Animals and conditions: 64 post-weaning Wistar rats (n=32 males; n=32 females) were randomly assigned to one of the 4 experimental upon arrival. Control animals received a soybean oil (C-SO, presenting a balance n-6/n-3 ratio) and the experimental groups received menhaden fish oil supplement (FO, n-3 PUFA rich condition; containing 300 mg/kg/day DHA) daily. Diet supplements (FO or C-SO) were provided by gavage (0.3ml/100g body weight) during the entire early and mid-adolescence period (from PD28-47). Half of the experimental and control groups were housed in an enriched environment (EE) for 31 days (PD28-58). On day 63 (PD90), rats were expose to the modified version of the Forced Swim Test for a period a 15 minutes on the first day and for 4 sessions of 6 min, 24 hours later. Behavioral testing: Assessment of anxiety-like behavior and fear avoidance mechanism was performed using the Open Field Test (PD93) and Y Maze (PD95). **RESULTS AND DISCUSSION:** Our findings revealed that omega-3-supplemented male rats exposed to an enriched environment surprisingly showed greater anxiety response compared to the control group. In contrast, males and females fed a CSO supplement and housed in an EE showed elevated locomotion in the testing area, a sign of reduced stress fostering increased exploration. These results indicate that a short-term omega-3 supplementation during the adolescence failed to affect significantly behavior in adulthood was not as beneficial as anticipated, especially in male rats. Further investigation is needed to explore these unexpected findings and the possibility of sex-specific effects. **RESEARCH SUPPORT:** Discovery grant from the National Science and Engineering Research Council of Canada (NSERC).

UTILIZING ZEBRAFISH MODELS IN REHABILITATION MEDICINE. MK Poudel and AV Kalueff, ISBS Fellow, ZENEREI Research Center, Slidell, LA, USA

Zebrafish (Danio rerio) models of human pathologies are significantly cheaper to maintain and easier and faster to perform. The utility of this model organism (including its developing embryo and larvae) as a vertebral model organism is rapidly growing in biomedical preclinical studies. Numerous human genetic disorders were found to be modeled in zebrafish because of high genetic homology with humans, and the availability of its complete genome sequence. The exceptional regenerative potential of muscle, skeletal, nervous and cardiac cells of this fresh-water fish was also distinctly discussed in the literature. In this literature review, the focus of

zebrafish models within rehabilitation medicine research studies was mostly found to be on regenerative medicine, neuropathies, myopathies, spinal cord injury, traumatic brain injury, wound healing, imaging studies, neuropsychology, muskuloskeletal disorders, cancers, neurodevelopmental disorders, neurodegenerative diseases and electromyogram studies. A number of publications was on drug discovery and various therapeutics (pharmacological, heat therapy, cryotherapy and electrical stimulation therapy) including the study on botulinum. However, there was the lack of extensive studies related to rehabilitation medicine which would utilize zebrafish and/or its embryo and larval models to establish strong foundation for preclinical mammalian studies, clinical studies and phase trials in this field. **CONCLUSIONS:** Since translational research is critical to PM&R specialty survival as a filed, and for improving practice and rehabilitation outcomes, we emphasize the need of extensive utilization of zebrafish as an important vertebrate model organism in PM&R. Specifically, PM&R scientists can explore more strongly the role of this model organism in regenerative medicine and the complex pathologies related to the nervous, musculoskeletal and cardiovascular systems, including the newer drug discovery and therapeutics based on utilizing the zebrafish and/or its embryo and larvae.

ZEBRAFISH BEHAVIORAL PHENOMICS AND CNS DRUG DISCOVERY. AV Kalueff, ISBS Fellow, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, Slidell, LA, USA; Guangdong Ocean University, Institute of Marine Drugs and Nutrients, Zhanjiang, China

Zebrafish (Danio rerio) are rapidly emerging as an important model organism for neuropharmacology and toxicology research. The behavioral/phenotypic complexity of zebrafish allows for thorough dissection of complex human brain disorders and drug-evoked pathological states. As numerous zebrafish models become available with a wide spectrum of behavioral, genetic, and environmental methods to test novel drugs, here we discuss recent zebrafish phenomics methods to facilitate drug discovery, particularly in the field of biological psychiatry. Additionally, behavioral, neurological, and endocrine endpoints are becoming increasingly well-characterized in zebrafish, making them an inexpensive, robust and effective model for toxicology research and pharmacological screening. Here, we also critically evaluate the limitations of utilizing this model organism, and outline future strategies of research in the field of zebrafish phenomics and drug discovery.

THE INTERNATIONAL "STRESS AND BEHAVIOR" SOCIETY (ISBS)

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')

Name, Family name:
Position/Title:
Institute/Company:
Category - please select one:
• Regular member, 3-year term ($ 100.00)
• Regular member, 1-year term ($ 60.00)
• Student member, 3-year term ($ 60.00)
Address (affiliation): City: Postal code: State: Country:
Phone, Fax:
E-mail address: www:

---

www.stress-and-behavior.com
info@stressandbehavior.com

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 Aghajanov (Yerevan Medical University, Armenia), 2015
Dr. Elliott Beaton (University of New Orleans, USA), 2015
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. 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. Mikhail Pletnikov (Johns Hopkins University, USA), 2015
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 Strekalova (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

ISBS Fellow Nominees:

Dr. Ghanshyam Pandey (University of Illinois at Chicago, USA), 2017
Dr. Vsevolod Rozanov (Odessa University, Ukraine), 2017

THE INTERNATIONAL STRESS AND BEHAVIOR SOCIETY (ISBS)

Please join our 2017-2018 ISBS conferences:

5th Caribbean Biomedical Research Days
CBRD-2018
January 16-18, 2018, Rodney Bay, St. Lucia

24th International Neuroscience and Biological Psychiatry Conference "STRESS AND BEHAVIOR"
May 16-19, 2017, St. Petersburg, Russia

International Neuroscience and Biological Psychiatry ISBS Symposium "TRANSLATIONAL NEUROSCIENCE OF STRESS"
May 23, 2017, Kiev, Ukraine

11th International Regional Neuroscience and Biological Psychiatry Conference "STRESS AND BEHAVIOR" (North America)
June 22-24, 2017, Miami Beach, FL, USA

12th International Regional Neuroscience and Biological Psychiatry Conference "STRESS AND BEHAVIOR" (Asia)
July 24-25, 2017, Yokohama, Japan

E-mail: info@stressandbehavior.com
www.stress-and-behavior.com