STRESS, BRAIN AND BEHAVIOR

Program and Proceedings of the 24th Multidisciplinary International Neuroscience and Biological Psychiatry Conference "Stress and Behavior"

St-Petersburg, Russia
May 16-19, 2017

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The Ukrainian Society for Biological Psychiatry (USBP)

Program and Proceedings

24th Multidisciplinary International Neuroscience and Biological Psychiatry Conference "Stress and Behavior"

St-Petersburg, Russia
May 16-19, 2017

CONFERENCE PROGRAM

Day 1. Tue, May 16, 2017

Venue: Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

9.00-09.30 **CONFERENCE OPENING CEREMONY**
WELCOMING ADDRESSESS.
WHY STUDY STRESS, BRAIN AND BEHAVIOR? 20 YEARS AFTER
INDUCTION OF NEW ISBS FELLOWS

09.30-10.00 **OPENING PLENARY LECTURE – THE IRVING I. GOTTESMAN 2017 LECTURE: ETHOLOGICAL AND EVOLUTIONARY ASPECTS OF SUICIDE – IMPLICATIONS FOR UNDERSTANDING STRESS IN ANIMALS AND HUMANS.** VA Rozanov, ISBS Fellow, Odessa National Mechnikov University, Odessa, Ukraine

10.00-10.30 **ISBS PRESIDENTIAL LECTURE: THE FUTURE OF HALLICINOGENIC BIOMEDICINE.** AV Kalueff, ISBS Fellow, St Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, New Orleans, LA, USA

10.30-11.00 **ISBS SPECIAL TALK 1: AGEING AND INTRUSIVE THOUGHTS.** JAK Erskine and GJ Georgiou, St George's University of London, London, University of Hertfordshire, UK

11.00-12.00 **LUNCH BREAK**

12.00-14.20 **SYMPOSIUM 1. ADVANCES IN GPCR BIOLOGY AND PHARMACOLOGY**
Chair: RR Gainetdinov (Russia)

12.00-12.30 **HIGH-THROUGHPUT SCREENING AND VALIDATION OF NOVEL LIGANDS OF THE HUMAN SEROTONIN RECEPTOR 5-HT$_{2C}$.** YM Xu, iHuman Institute, Shanghai Tech University, Shanghai, China

12.30-13.00 **GSK3B/FXR1P PATHWAY REGULATES HOMEOSTATIC SYNAPTIC SCALING.** JM Beaulieu, A Evstratova, Departments of Psychiatry and Neuroscience, Faculty of Medicine, Université Laval-CRULRG, Québec, Québec, University of Toronto, Toronto, Canada

13.00-13.30 **UNDERSTANDING OF NEURONAL FUNCTIONS OF TRACE AMINE-ASSOCIATED RECEPTORS: FOCUS ON TAAR5.** S Espinoza, I Sukhanov, A Gerasimov, TD Sotnikova, D Leo and RR Gainetdinov, ISBS Fellow, Fondazione Istituto Italiano di Tecnologia, Genoa, Italy; Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Skolkovo Institute of Science and Technology, Skolkovo, Russia

13.30-14.00 **THE ROLE OF TAAR1 IN MECHANISMS OF DRUG ADDICTION.** I Sukhanov, A Dorotenko, A Dolgorukova, M Dorofeikova, L Mus and RR Gainetdinov, ISBS Fellow, First St. Petersburg State Medical University, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Skolkovo Institute of Science and Technology (Skoltech), Skolkovo, Russia

14.00-14.20 **GENERAL DISCUSSION**

14.20-14.40 **ISBS FELLOW TALK: SOCIAL CONFORMITY AS AN INFLUENCE FACTOR ON THE ETHANOL PREFERENCE IN RATS**. EV Filatova, AA Orlov, AY Egorov, ISBS Fellow, and SV Afanas'ev, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

14.40-15.10 **CONFERENCE PRESENTATION 1: INVESTIGATING RODENT BEHAVIOR IN AN AUTOMATED HOMECAGE SYSTEM INCREASES DATA REPRODUCIBILITY.** J Fehmer, TSE Systems GmbH, Bad Homburg, Germany; LLC Alfa Mobili (the official representative of TSE Systems in Russia), St. Petersburg, Russia

15.10-15.30 **COFFEE BREAK**

15.30-17.00 **SYMPOSIUM 2: IRVING GOTTESMAN TRANSLATIONAL NEUROSCIENCE SYMPOSIUM**
Chairs: MI Aghajanov (Armenia), D Kozic (Serbia)

15.30-16.00 **ISBS SPECIAL TALK 2: NEUROCHEMICAL SHIFTS IN NONSPECIFIC ULCERATIVE COLITIS, INDUCED BY DEXTRAN SODIUM SULFATE.** MI Aghajanov, ISBS Fellow, AG Guevorkian, NCh Alchujyan, AA Aghababova and MR Hovhanniasyan, Heratsi Yerevan State Medical University, Buniatyan Institute of Biochemistry NAS, Yerevan, Armenia

16.00-16.25 **ISBS SPECIAL TALK 3: MODERN IMAGING MODALITIES IN DETECTION OF ALZHEIMER DISEASE AND OTHER TYPES OF DEMENTIA.** D Kozic, ISBS Fellow, R Semnic, M Semnic, B Srdic-Galic, V Turkulov, S Stojanovic, O Nikolic, A Spasic, A Todorovic and N Boskov, University of Novi Sad Faculty of Medicine, Novi Sad, General Hospital Djordje Joanovic, Zrenjanin, Serbia

16.25-16.45 **DECREASE IN PERCENTAGE OF GREY MATTER DURING PREGNANCY IN HEALTHY CONTROLS.** J-M Le Melledo, A Ghuman, AM McEwen, DTA Burgess, CC Hanstock, P Seres, P Khalili, C Newman, GB Baker, ND Mitchell, J Khudabux-Der and PS Allen, University of Alberta, Alberta, Canada

16.45-17.00 **ASSOCIATION OF THE GALANIN GENE POLYMORPHISM WITH THE PSYCHOLOGICAL CORRELATES OF STRESS RESISTANCE.** VI Lioudyno, OE Zubareva, SG Tsikunov, ISBS Fellow, VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia

17.00-17.30 **CONFERENCE PRESENTATION 2: MULTI-FUNCTIONAL MEASUREMENT SYSTEMS APPLICATION IN PRECLINICAL DRUG RESEARCH (LABORAS, SONOTRACK, DSI-TELEMETRY).** GA Piavchenko, L Bachdasarian, R Bulthuis and VI Nozdrin, J-SC Retinoids, Preclinical Research Center, Moscow, Medical Institute, Histology, Cytology and Embryology Department, Orel State University, Orel, Russia; Metris B.V., Hoofddorp, The Netherlands

17.30-17.45 **ISBS BOOK CLUB: PRESENTING "HEALTH OF MAN (FROM THE POINT OF VIEW OF MODERN STRESSOLOGY)".** AS Tadevosian and AA Muradyan, Heratsi Yerevan Medical State University, Yerevan, Armenia

17.45-19.00 **SOCIAL EVENT 1: RECEPTION AND MUSIC CONCERT -** CO-SPONSORED BY THE ISBS AND THE INTSTITUTE OF TRANSLATIONAL BIOMEDICINE (ITBM) OF ST. PETERSBURG STATE UNIVERSITY

PRESENTATION OF ITBM: 2 YEARS OF SUCCESS. RR Gainetdinov, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

19.00-22.00 **SOCIAL EVENT 2: BUS CITY TOUR (admissions)**

Day 2. Wed, May 17, 2017

Venue: Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

09.00-17.00 **REGISTRATION**

09.30-13.00 **SYMPOSIUM 3: ZOFIA ZUKOWSKA STRESS NEUROSCIENCE SYMPOSIUM**
Chairs: VM Klimenko (Russia), S Salim (USA)

09.30-09.40 **INTRODUCTION**

09.40-10.10 **ISBS SPECIAL TALK 4. PSYCHOLOGICAL STRESS AND OXIDATIVE STRESS: CAUSE OR CONSEQUENCE?** S Salim, Department of Pharmacological and Pharmaceutical Sciences, College of Pharmacy, University of Houston, Texas, USA

10.10-10.25 **PSYCHOLOGICAL IMPACT OF TRAFFIC-RELATED AIR POLLUTION: INSIGHTS FROM AN ANIMAL MODEL.** A Salvi, G Patki, H Liu and S Salim, University of Houston College of Pharmacy, Houston, Texas, USA

10.25-10.45 **LOSS OF ALPHA2 SUBUNIT OF GLYCINE RECEPTORS AFFECTS MATURATION OF CORTICO-STRIATAL CIRCUITRY.** SM Molchanova, J Comhair, D Karadurmus, SN Schiffmann, J-M Rigo, D Gall and B Brone, Laboratory of Neurophysiology, Université Libre de Bruxelles, BIOMED Research Institute, University of Hasselt, Belgium; Neuroscience Center, University of Helsinki, Finland

10.45-11.00 **THE EXPRESSION FORECAST OF POST-TRAUMATIC STRESS DISORDER IN FEMALE RATS.** NK Apraksina, TV Avaliani, SG Tsikunov, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg, Russia

11.00-11.15 **MECHANISMS AND CONSEQUENCES OF THE DELAY IN BRAIN DEVELOPMENT IN RATS SUBJECTED TO THE PRENATAL HYPOXIC STRESS.** DS Vasilev, NL Tumanova, NM Dubrovskaya and IA Zhuravin, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg State Pediatric Medical University, St. Petersburg, Russia

11.15-11.35 **DISTURBED VOCAL COMMUNICATION IN COMMON MARMOSET FAMILY WITH AN AUTISM-MODEL CHILD.** K Mimura, K Nakagaki and N Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan

11.35-12.00 **COFFEE BREAK**

12.00-12.15 **THE IMPACT OF EARLY LIFE STRESS ON DISTRIBUTION OF H3K4ME3 HISTONE MODIFICATION IN MURINE PREFRONTAL CORTEX: THE ROLE IN GENE EXPRESSION.** VV Reshetnikov, AA Lepeshko, NI Ershov, YuA Ryabushkina, AA Studenikina, NP Bondar and TI Merkulova, Institute of Cytology and Genetics SB RAS, Novosibirsk State University, Novosibirsk State Medical University, Novosibirsk, Russia

12.15-12.30 **CHANGES IN ADULT NEUROGENESIS IN TWO PARADIGMS OF STRESS IN RATS.** VA Aniol, NA Lazareva, AA Yakovlev, AO Manolova and NV Gulyaeva**,** Institute of Higher Nervous Activity and Neurophysiology, Moscow, Russia

12.30-12.45 **THE IMPORTIN OF ANXIETY-RELATED BEHAVIORS.** N Panayotis, A Sheinin, SY Dagan, F Rother, G Volpert, MM Tsoory, E Hartmann, M Bader, AH Futerman, I Michaelevski and M Fainzilber, Departments of Biomolecular Sciences, and Veterinary Resources, Weizmann Institute of Science, Rehovot, Sagol School of Neuroscience, Department of Biochemistry and Molecular Biology, Tel Aviv University, Tel Aviv, Israel; Max-Delbrück-Center for Molecular Medicine, Berlin, Center for Structural and Cellular Biology in Medicine, Institute of Biology, University of Lubeck, Lubeck, Germany

12.45-13.00 **PREFRONTAL MRNA EXPRESSION OF SHORT AND LONG D2 DOPAMINE RECEPTOR ISOFORMS AND COGNITIVE IMPAIRMENTS IN RATS FOLLOWING CHRONIC, EARLY-LIFE INTERLEUKIN-1β TREATMENT.** AP Schwarz, AN Trofimov, VI Lioudyno, DS Antonov, OE Zubareva and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry, Peter the Great St. Petersburg Polytechnic University, St. Petersburg, Russia

13.00-14.30 **LUNCH BREAK**

14.30-15.00 **CONFERENCE PRESENTATION 3: STATE OF THE ART IN BEHAVIORAL NEUROSCIENCE – ADVANCES IN VIDEO TRACKING, GAIT ANALYSIS AND OTHER TECHNIQUES.** A Willemsen, A Biarslanova, Noldus Information Technology, Wageningen, The Netherlands

15.00-15.30 **CONFERENCE PRESENTATION 4: BREAKING BOTTLENECKS: AUTOMATED AND AFFORDABLE SYSTEMS FOR BEHAVIORAL MONITORING AND COGNITIVE EXPERIMENTS.** JM Daggett, Zantiks Ltd, Cambridge, UK

15.30-15.45 **NEUROSCIENCE MEETS ARTS: AN ARTIST'S PERSPECTIVE.** D Raytchev, Daniela Raytchev Art, London, UK

15.45-18.00 **SYMPOSIUM 4: MODERATED POSTER SESSION**

DIFFERENTIAL EFFECT OF BERBERINE AND MINOCYCLINE, THE INHIBITORS OF TRYPTOPHAN–KYNURENINE METABOLISM, ON NEGATIVE GEOTAXIS OF DROSOPHILA MELANOGASTER. VV Navrotskaya and G Oxenkrug, Karazin Kharkiv National University, Kharkiv, Ukraine; Tufts University, Tufts Medical Center, Boston, USA

FEAR CONDITIONING ACTIVATES BASOLATERAL AMYGDALA COMPLEX IN INDUCIBLE TPH2 KNOCKOUT (ICKO) MICE. B Aboagye, K-P Lesch, S Popp and W Jonas, Division of Molecular Psychiatry, ZEP, University of Wurzburg, Wurzburg, Germany; Department of Psychiatry and Psychology, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands

COMPARING EARLY- AND LATE-ONSET ANOREXIA NERVOSA: A PEEK INTO THE STRESS-BEHAVIOR CORRELATE. SM Tan, V Kwok, A Loh, KA Zainal and HY Lee, Singapore General Hospital, Singapore

SEX DIFFERENCES IN ACUTE STRESS EFFECTS ON SPATIAL MEMORY AND HIPPOCAMPAL FUNCTION. VN Luine, RE Bowman, JL Gomez and PA Serrano, Hunter College of CUNY, New York, NY, Sacred Heart University, Fairfield, CT, USA

NEUREXAN® INFLUENCES STRESS-INDUCED ACTIVITY OF THE ANTERIOR CINGULATE CORTEX AND ASSOCIATED BRAIN REGIONS. A Kühnel, Y Fan, L Fensky, V Teckentrup, M Schultz and M Walter, Clinical Affective Neuroscience Laboratory, Magdeburg, Department of Psychiatry, CBF, Charité, Berlin, Department of Psychiatry and Psychotherapy, University of Tübingen, Tübingen, Leibniz Institute for Neurobiology, Magdeburg, Biologische Heilmittel Heel GmbH, Baden-Baden, Germany

EFFECTS OF NEUREXAN® ON EMOTIONAL BRAIN RESPONSE. L Fensky, V Teckentrup, A Kühnel, M Schultz, Y Fan and M Walter, Department of Psychiatry and Psychotherapy, University of Tübingen, Leibniz Institute for Neurobiology, Clinical Affective Neuroimaging Laboratory, Magdeburg, Biologische Heilmittel Heel GmbH, Baden-Baden, Department of Psychiatry, Charité, CBF, Berlin, Germany

THE EFFECTS OF 2-[4-(TRIFLUOROMETHYL)PHENYL]-5,6-DIHYDRO-4H-PYRROL-[1,2-C] TRIAZOLO-7-IUM-3-OLATE IN ADULT ZEBRAFISH IN THE NOVEL TANK TEST. TO Kolesnikova, SL Khatsko, AV Zhdanov, TV Gluhareva, YuI Nein, AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

SOCIODEMOGRAPHIC CHARACTERISTICS OF BOSNIAN WAR VETERANS WITH ENDURING PERSONALITY CHANGE AFTER CATASTROPHIC EXPERIENCE DIAGNOSIS. S Sarkic-Bedak, A Hrnjica, I Lokmic-Pekic, S Bise, B Kurtovic and M Ahmic, Cantonal Psychiatric Hospital Sarajevo, Sarajevo, Bosnia and Herzegovina

DIFFERENTIAL FOREBRAIN c-FOS EXPRESSION INDUCED BY NOVELTY AFTER CHRONIC STRESS. AI Bulava, OE Svarnik and YI Alexandrov, Laboratory of Psychophysiology, Institute of Psychology RAS, Moscow, Russia

THE INFLUENCE OF INTRA-UTERINE HALOPERIDOL INTRODUCTION ON THE POSTNATAL SLEEP – WAKEFULNESS CYCLE (SWC) FORMATION IN RATS. EA Aristakesyan, VV Kuzik, IY Morina and EP Stankova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INVESTIGATION OF DEPRESSIVE SYMTOMS AND NEURODEGENERATION IN MESOLYMBIC SYSTEM IN A RAT MODEL OF A PRECLINICAL STAGE OF PARKINSON'S DISEASE. AR Gazizova, DV Plaksina and IV Ekimova, ISBS Fellow, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

NEUROPROTECTIVE EFFECTS OF CHAPERONE GRP78 IN A RAT MODEL OF PARKINSON'S DISEASE. MB Pazi, DV Plaksina, LE Nitsinskaya and IV Ekimova, ISBS Fellow, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

AMPHETAMINE AFFECTS BEHAVIORAL PATTERNS OF OBSESSIVE-COMPULSIVE AND ADDICTIVE GAMBLING IN IN THE RAT MARBLE BURYING TEST. ND Yakushina, AG Pshenichnaya, VA Lebedev, ER Bychkov, KE Gramota, YuN Bessolova, KA Privalov, AM Potapkin and PD Shabanov,

ISBS Fellow, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

DOPAMINE REINFORCING AND OREXIGENIC EFFECTS DURING ELECTRICAL STIMULATION OF THE LATERAL HYPOTHALAMUS IN RATS. YuN Bessolova, OA Yakovlev, AA Lebedev, ER Bychkov, VA Lebedev and PD Shabanov, ISBS Fellow, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

TAUREPAR PROTECTS THE ISCHEMIC RAT BRAIN AGAINST OXIDATIVE STRESS AND BEHAVIOR DISORDERS. VV Bulion, EN Selina and IB Krylova, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

DERIVATIVE OF FLUORENCARBONIC ACID PREVENTS DEPLETION OF MONOAMINES LEVELS IN THE BRAIN OF DEPRESSED RATS. LK Khnychenko, EE Yakovleva and_ER Bychkov, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

BEHAVIORAL EFFECTS OF TILETAMINE, A NON-COMPETITIVE N-METHYL-D-ASPARTATE (NMDA) RECEPTOR ANTAGONIST, IN ADULT RATS IN THE OPEN FIELD TEST. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov, YuYu Morzherin and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

EFFECTS OF U-47700, A μ- OPIOID RECEPTOR AGONIST, IN ADULT MICE IN THE OPEN FIELD AND THE TAIL-FLICK TEST. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

ANTISTRESS PROPERTIES OF "A" AND "B" COMPOSITIONS. AF Safonova, Institute of Experimental Medicine, St. Petersburg, Russia

ACUTE EFFECT OF MANUAL LYMPHATIC DRAINAGE IN MEN AND WOMEN ON STRESS BIOMARKERS. MSM Pires-de-Campos, EAM Camargo, AL Souza, PC Silva, DM Marcorin, LL Rodrigues, and DM Grassi-Kassisse, Methodist University of Piracicaba, State University of Campinas, Campinas, Brazil

EFEECTS OF AGRP ON NOREPINEFRINERGIC BRAIN NEURONS. LO Saveleva, AL Mihrina and IV Romanova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

20.00-22.00 SOCIAL EVENT 3: CITY BOAT TRIP (admissions)

Day 3. Thur, May 18, 2017

Venue: Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

09.00-17.00 REGISTRATION

09.30-10.55 SYMPOSIUM 5: WORK STRESS
Chair: Ph Fauquet-Alekhine (France)

09.30-09.40 INTRODUCTION: UNDERSTANDING WORK STRESS

09.40-10.10 MODELING HEART RATE VS SHORT-TERM MENTAL STRESS INDICATORS. Ph Fauquet-Alekhine, L Rouillac, J Berton and JC Granry, Department of Psychological and Behavioral Sciences, London School of Economics and Political Science, London, UK; Laboratory for Research in Science of Energy, France and Germany, Nuclear Power Plant of Chinon, Avoine, University Hospital of Angers, France

10.10-10.35 EXPERIMENTAL METHOD FOR THE ASSESSMENT OF HUMAN REACTIONS IN MICROSTRESS. V Ababkov, St. Petersburg State University, St. Petersburg, Russia

10.35-10.55 STRESS ASSESSMENT USING EXPERIENCE SAMPLING: CONVERGENT VALIDITY AND CLINICAL RELEVANCE. T Vaessen, M van Nierop, U Reininghaus and I Myin-Germeys, Department of Neuroscience, Center for Contextual Psychiatry,

KU Leuven, Leuven, Belgium; Department of Psychiatry and Psychology, School for Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands; Health and Population Research Department, Institute of Psychiatry, King's College, London, UK

10.55-11.20 **COFFEE BREAK**

11.20-13.05 **SYMPOSIUM 6: NEURONUTRITIOLOGY**
Chair: SA Apryatin (Russia)

11.20-11.45 **A COMPARATIVE ANALYSIS OF ANXIETY LEVELS FOR DBCB TETRAHYBRID, DBA/2J INBREED AND CD-1 OUTBREED MICE STRAINS: CLASSIC AND ALTERNATIVE METABOLIC SYNDROME IN VIVO MODELS.** SA Apryatin, NA Petrov, KV Mzhelskaya, AS Balakina and NV Trusov, Federal Research Center of Nutrition, Biotechnology and Food Safety, Moscow, Russia

11.45-12.10 **CHANGES OF BEHAVIORAL CHARACTERISTICS IN THE RAT *IN-VIVO* MODELS OF METABOLIC SYNDROME.** KV Mzhelskaya, YS Sidorova, NA Petrov, SA Apryatin, NV Trusov, AS Balakina, VK Mazo and IV Gmoshinsky, Federal Research Centre of Nutrition, Biotechnology and Food Safety, Moscow, Russia

12.10-12.35 **EVALUATION OF INFLUENCE OF LIPID MODULE, ENRICHED WITH ASTAXANTHIN AND/OR PLASMALOGENS, ON BEHAVIORAL ACTIVITY OF ANIMALS UNDER STRESS.** Y Sidorova, V Sarkisyan, N Petrov, A Kochetkova and V Mazo, Federal Research Centre of Nutrition, Biotechnology and Food Safety, Moscow, Russia

12.35-12.50 **PROBIOTIC ENTEROCOCCUS FAECIUM L-3 CAN IMPROVE PSYCHO-EMOTIONAL STATE IN MULTIPLE SCLEROSIS PATIENTS.** AV Matsulevich, IN Abdurasulova, EI Ermolenko, GN Bisaga, GG Alekhina, DI Skulyabin, AN Suvorov and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg State Pediatric Medical University, St. Petersburg State University, Kirov Military Medical Academy, Saint-Petersburg, Russia

12.50-13.05 **CLINICAL AND EXPERIMENTAL EVIDENCE FOR THE ROLE OF GUT MICROBIOTA IN THE PATHOGENESIS OF AUTOIMMUNE DEMYELINATING DISEASE OF THE BRAIN.** IN Abdurasulova, AV Matsulevich, EA Tarasova, GG Alekhina, EI Ermolenko, GN Bisaga and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg State Pediatric Medical University, St. Petersburg State University, Kirov Military Medical Academy, St. Petersburg, Russia

13.05-13.35 **CONFERENCE PRESENTATION 5: CELLVIZIO LAB – A TOTALLY NEW DIMENSION OF IN VIVO STUDIES.** K Grohmann, Biogen-Analytica LLC, Moscow, Russia

13.35-14.30 **LUNCH BREAK**

14.30-16.45 **SYMPOSIUM 7: LAPIN BIOLOGICAL PSYCHIATRY SYMPOSIUM**
Chairs: IV Ekimova, PD Shabanov (Russia)

14.30-14.40 **INTRODUCTION**

14.40-15.00 **ISBS SPECIAL TALK: PEPTIDE DRUGS IN INCREASING THE REPRODUCTIIVE FUNCTIONS AND COPING TO STRESS IN RATS.** TN Sollertinskaja, ISBS Fellow, MV Shorokhov and AS Kourguzova**,** Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

15.00-15.20 **AGE-RELATED DIFFERENCES IN STRESS RESPONSIVENESS OF THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS IN NONHUMAN PRIMATES WITH VARIOUS TYPES OF ADAPTIVE BEHAVIOR.** ND Goncharova and OA Chigarova**,** Laboratory of Endocrinology, Research Institute of Medical Primatology, Sochi, Russia

15.20-15.35 **CRISPR/CAS9 KNOCK OUT OF SCHIZOPHRENIA RISK FACTOR MIR-137 GENE PRODUCT**. A Marakhovskaia, J Khlghatyan and JM Beaulieu, University of Toronto, Toronto, Canada

15.35-15.50 **EFFECTS OF NEONATAL LIPOPOLYSACCHARIDE TREATMENT ON *MMP9* AND *TIMP1* MRNA EXPRESSION IN THE RAT BRAIN.** AN Trofimov, AP Schwarz, K Fomalont, VA Schukina, EA Veniaminova, NA Markova, OE Zubareva and VM Klimenko, Institute of Experimental Medicine, St. Petersburg, Russia; University Hospital of Wurzburg, Wurzburg, Germany; National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD, USA; Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Institute of General Pathology and Pathophysiology, Moscow, Russia

15.50-16.10 **EMOTIONAL AND COGNITIVE ALTERATIONS IN THE RAT LACTACYSTIN MODEL OF THE EARLY STAGE OF PARKINSON'S DISEASE.** MV Chernyshev, IN Abdurasulova, AV Matsulevich, OA Sapach, AR Gazizova, IV Ekimova, ISBS Fellow, VM Klimenko, ISBS Fellow, and YuF Pastukhov, ISBS Fellow, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Experimental Medicine, St. Petersburg, Russia

16.10-16.30 **COFFEE BREAK**

16.30-16.45 **PHARMACOLOGICAL STUDY OF GHRELIN RESPONSE TO STRESS IN THE RAT BRAIN STRUCTURES.** PP Khokhlov, IYu Tissen, DN Zaporozchenko, AA Lebedev, ER Bychkov, YuN Bessolova, LK Khnychenko, GV Beznin, SG Tsikunov, ISBS Fellow, and PD Shabanov, ISBS Fellow, Anichkov Department of Neuropharmacology, Pavlov Physiological Department, Institute of Experimental Medicine, St. Petersburg, Russia

16.45-18.00 **SYMPOSIUM 8: CLINICAL NEUROSCIENCE**
Chairs: VM Klimenko, YuF Pastuhov (Russia)

16.45-17.00 **PARADIGM SHIFT IN MENTAL HEALTH CARE: PHARMACEUTIC AND PSYCHOTHERAPEUTIC TREATMENT OF MENTAL ILLNESSES.** D Petružytė, L Murauskienė, E Šumskienė, A Germanavičius, JM Diržienė and V Klimaitė, Vilnius University, Vilnius, Lithuania

17.00-17.15 **NEUROPSYCHOLOGICAL DISORDERS IN PATIENTS AT EARLY AND MID-STAGES OF PARKINSON`S DISEASE.** EV Gracheva, IV Miliukhina, PV Lebedev, TV Sergeev, SG Tsikunov, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg, Russia

17.15-17.30 **CORRELATION OF MULTIVOXEL MAGNETIC-RESONANCE SPECTROSCOPY OF THE BRAIN AND NEUROPSYCHOLOGICAL TESTING IN NON-DEMENTED HIV+ PATIENTS.** J Boban, D Kozic, ISBS Fellow, D Lendak, M Bjelan, A Ragaji, K Ivoševic, V Bugarski-Ignjatovic, V Turkulov and S Brkic, University of Novi Sad, Faculty of Medicine, Novi Sad, Vojvodina, Serbia

17.30-17.45 **SERUM ANTIOXIDATIVE ENZYMES LEVELS, OXIDATIVE STRESS PRODUCTS AND CYTOKINES OF ET PATIENT.** ZM Muruzheva, EA Skomorohova, IS Oblamskaya, MN Karpenko and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg, Russia

17.45-18.00 **GENERAL DISCUSSION**

20.00-22.00 **SOCIAL EVENT 4: CONFERENCE DINNER (admissions)**

Day 4. Fri, May 19, 2017

Venue: Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

09.00-11.00 **REGISTRATION**

09.30-10.00 **ROUND TABLE ON BIOETHICS**

10.00-12.40 **SYMPOSIUM 9: ZNRC ZEBRAFISH NEUROSCIENCE SYMPOSIUM**

Chairs: AV Kalueff, Russia, S Winberg, Sweden

10.00-10.05 **INTRODUCTION: THE INTERNATIONAL ZEBRAFISH NEUROSCIENCE CONSORTIUM (ZNRC)**

10.05-10.40 **STRESS COPING STYLES IN FISH - BEHAVIORAL CORRELATES, NEUROENDOCRINE AND MOLECULAR MECHANISMS.** S Winberg, A Mustafa, G André and P-O Thörnqvist, Uppsala University, Uppsala, Sweden; University of Western Australia, Australia

10.40-11.05 **ZEBRAFISH MODELS OF NEURODEVELOPMENTAL BRAIN DISORDERS: FOCUS ON AUTISM, ADHD AND COGNITIVE DISABILITY.** AV Kalueff, ISBS Fellow, and DA Meshalkina, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; School of Pharmaceutical Sciences, Southwest University, Chongqing, China

11.05-11.25 **ZEBRAFISH SELECTIVE BREEDING FOR BOLDNESS RESULTS IN DIVERGENT BEHAVIORAL PROFILES OF LARVAE FROM THE F1 GENERATION.** A Mustafa and S Winberg, Uppsala University, Uppsala, Sweden

11.25-11.45 **ACUTE ALPHA-NETA EFFECTS ON ZEBRAFISH BEHAVIOR AND SEROTONIN METABOLISM.** DA Meshalkina, EV Kysil, KA Antonova, MN Kislyk, EV Efimova and AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

11.45-12.00 **POPULAR ANTIFUNGAL DRUGS WITH ANTIGLUCOCORTICOID PROPERTIES, CLOTRIMAZOLE AND KETOCONAZOLE, CAUSE ANXIOLYTIC-LIKE BEHAVIOR AND MOTOR DISRUPTION IN ZEBRAFISH – A PILOT STUDY.** KA Demin, TO Kolesnikova, SL Khatsko and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

12.00-12.15 **EFFECTS OF U-47700, A μ-OPIOID RECEPTOR AGONIST, ON ADULT ZEBRAFISH BEHAVIOR TESTED IN THE NOVEL TANK TEST.** TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

12.15-12.30 **MODELING ANTIDEPRESSANT DISCONTINUATION SYNDROME (ADS) – PILOT STUDIES OF THE EFFECTS OF CHRONIC AMITRIPTYLINE DISCONTINUATION ON ZEBRAFISH.** TO Kolesnikova, SL Khatsko, KA Demin, DA Meshalkina and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia

12.30-12.40 **WHEN FISH TAKE A BATH: EXAMINING THE EFFECTS OF ALPHA-PYRROLIDINOPENTIOPHENONE (ALPHA-PVP), A BATH SALT "FLAKKA", IN ZEBRAFISH – PILOT STUDIES.** TO Kolesnikova, SL Khatsko, OS Eltsov, VA Shevyrin, YuYu Morzherin and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA

12.40-12.50 **CONFERENCE CLOSING**

12.50-13.15 **COFFEE BREAK**

19.00-22.00 **SOCIAL EVENT 5: THEATRE (admissions)**

POST-CONFERENCE SOCIAL EVENTS: MAY 20, 2017

10.15-15.00 **SOCIAL EVENT 6: VISIT TO PAVLOV LABORATORY AND MUSEUM**

10.00-16.00 **SOCIAL EVENT 7: TOUR TO PETERHOF (admissions)**

ABSTRACTS

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 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.

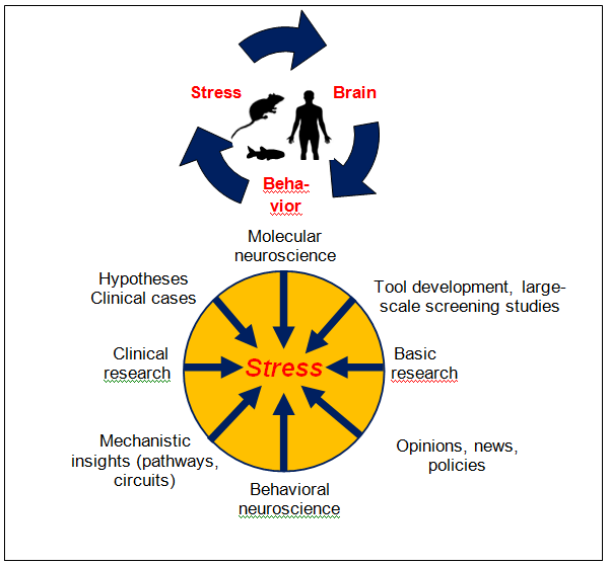

Figure 1. The proposed link between stress, brain and behavior: an ISBS perspective

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 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).

Do we need such meetings in this field? The growing number of biomedical conferences tends to pace with the increasing amount of generated knowledge. However, earlier this year, we attended a neuroscience conference, where a post-doc (very well presenting his poster) dove into deep molecular mechanisms, noting proudly "Behavior is nothing in neuroscience". We challenged this view then, and will reiterate again here – because brain is the body's most delicate and complex organ, and our behavior is the most important and sophisticated outcome of brain activity.

Thus, as we celebrate 20 years to STRESS AND BEHAVIOR conferences, our meetings will ensure that critical *behavioral* aspects of normal and pathological brain functions are always well represented and discussed in detail (Fig. 1). Lastly, this brings us to the importance of understanding behavior and using its correct quantification, to understand

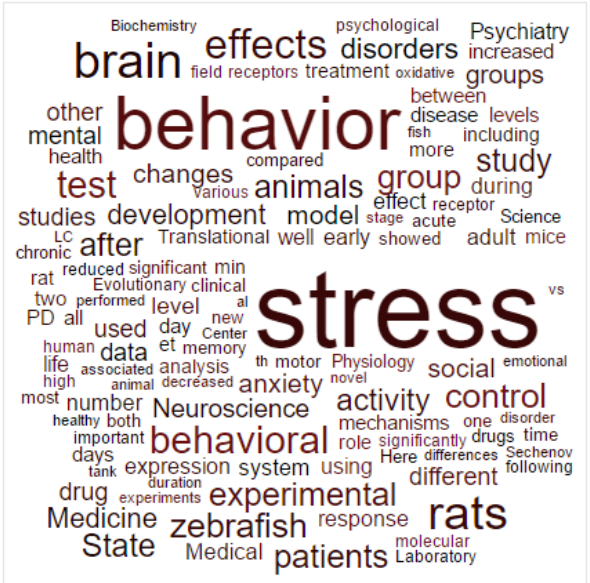

Figure 2. Word cloud generated from the text of the Conference abstracts, based on the word occurrence (>35 times)

complex human brain disorders. After all, this is what our meetings have been about in their first 20 years - and, hopefully, will continue to promote in the years to come.

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Day 1. Tue, May 16, 2017

OPENING PLENARY LECTURE – THE IRVING I. GOTTESMAN 2017 LECTURE: ETHOLOGICAL AND EVOLUTIONARY ASPECTS OF SUICIDE – IMPLICATIONS FOR UNDERSTANDING STRESS IN ANIMALS AND HUMANS. VA Rozanov, ISBS Fellow, Odessa National Mechnikov University, Odessa, Ukraine

INTRODUCTION: Social stress bridges animals and humans in their self-destructive behavior. On the other hand, suicide per se is a purely human phenomenon. It may, therefore, be productive to discuss an evolution of stress in human beings as compared to the animal world with regards to evolving suicide. **METHOD:** A search of published sources on evolutionary suicidology and ethological constructs associated with self-destructive behaviors in animals and suicides in humans. Integrating knowledge on evolutionary origins of social stress and mental disorders and discussing the changing nature of stress in humans. **RESULTS AND DISCUSSION:** There are many folkloric stories and some naturalistic anecdotal observations of animal behaviors, which may be perceived as equivalents of suicidal acts. Among behaviors resembling suicide in animals there are such as 1) self-mutilation and self-harming behavior, anxiety, impulsive and obsessive actions usually associated with social stress; 2) self-endangering behavior, possibly aimed at population size reduction in cases of overcrowding; 3) death by starvation most often associated with confinements, especially in the unnatural environment. As to the ethological constructs relevant for suicidal behavior, the most often mentioned are: 1) learned helplessness and entrapment; 2) fixed action pattern; 3) innate release mechanism; 4) care-eliciting behavior and social attraction holding power; 5) displacement activity and yielding behavior. Most of the above-mentioned behaviors seem to be more relevant for suicide attempts that for completed suicides. Moreover, all “suicidal” manifestations in animals lack fundamental component – the will and intention to die, which is often associated with such feature of stress in humans as mental pain (“psychache”). If we speak in terms of evolution, suicide is an evolutionary paradox so far as “suicidal genes” should be eliminated in generations. One of the models that try to explain this controversy is that suicide is a result of a breakdown of adaptive mechanisms in extremely stressful novel environments, social stress being the most relevant one. On the other hand, suicide remains a purely human phenomenon, and this may be due to the fundamental change in the nature of stress. In humans, due to learning and cultural transmission of moral and ethical norms, social and micro-social problems are leading to perceived stress based on the cognitive reappraisal of the situation. Besides, most of the completed suicides are committed in the context of psychiatric disorder, and feeling of stress may be seriously exacerbated by the subject’s impaired mental state. Thus, the mental (psychic) nature of human stress emerging together with conscious self-perception in the social environment may be the main distinctive feature of stress in humans.

ISBS PRESIDENTIAL LECTURE: THE FUTURE OF HALLICINOGENIC BIOMEDICINE. AV Kalueff, ISBS Fellow, St Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; ZENEREI Research Center, New Orleans, LA, USA

Psychedelic drugs, such as lysergic acid diethylamide (LSD), mescaline and psilocybin, exert profound effects on brain and behavior in both animals and humans, acting mostly of serotonergic 5HT2A receptors. After decades of stagnation in studying these compounds (due to unjust overregulation) globally, psychedelic drugs are now again being tested as potential treatments for human intractable disorders. Preclinical research of psychedelics complements human neuroimaging studies and pilot clinical trials, suggesting these compounds as promising treatments for addiction, depression, anxiety and other conditions. However, many questions regarding the mechanisms of action, safety and efficacy of psychedelics remain. Here, I will summarize recent preclinical and clinical data in this field of studying psychedelic drugs. I will further discuss their pharmacological mechanisms of action, and outline critical areas for future studies of psychedelic drugs, with the goal of maximizing the potential benefits of translational psychedelic biomedicine to patients.

ISBS SPECIAL TALK 1: AGEING AND INTRUSIVE THOUGHTS. JAK Erskine and GJ Georgiou, St George’s University of London, London, University of Hertfordshire, UK

INTRODUCTION: A study investigated the ability to suppress thoughts in the laboratory and how this was affected by the type of thought suppressed (positive, negative, neutral), participants’ age and working memory capacity

(WMC). Other linked variables (use of thought suppression, social desirability, and mindfulness) were measured to observe whether they modified susceptibility to thought intrusion. **METHODS:** Younger, middle aged and older adults were invited to the laboratory. Next all participants were asked to suppressed three different valenced thoughts in a counterbalanced order for 5-min per thought. Participants next completed a WMC task and finally questionnaire measures of the linked variables. **RESEARCH AND DISCUSSION:** Thought valence had no effect on intrusions during suppression. However, intrusive thoughts significantly reduced with age. Independent of age, higher WMC related to more intrusions. Only age and WMC independently and significantly predicted intrusions for all thought valences. There was no interaction between Age and WMC, and WMC reductions with age did not moderate the effect of age on intrusions.

SYMPOSIUM 1. ADVANCES IN GPCR BIOLOGY AND PHARMACOLOGY

Chair: RR Gainetdinov (Russia)

HIGH-THROUGHPUT SCREENING AND VALIDATION OF NOVEL LIGANDS OF THE HUMAN SEROTONIN RECEPTOR 5-HT$_{2C}$. YM Xu, iHuman Institute, Shanghai Tech University, Shanghai, China

G protein-coupled receptors (GPCRs), also known as seven transmembrane domain receptors, are the largest and most diverse family of membrane receptors in eukaryotes. Over 40% approved drugs on market target GPCRs, and therefore finding novel ligands for GPCRs remains a hot therapeutic topic. The serotonin receptor 5-HT2C influence various physical response including appetite, mood, nausea and sleep. Although market drugs have been developed to treat depression, schizophrenia and drug addiction, non-selective activation of 5-HT2A/2B is believed to lead to severe side effects. In the process of perusing new selective ligands, many cell-based functional assays, as well as ligand-binding assays are applied in high-throughput screening format, but false positive/negative often happens due to assay limitations. In this case, we adopted a comprehensive flow of various assays based on different principle to improve the hit rate. An in-house natural compound library was chosen here due to the diversity of molecular architectures and extensive bioactivities. Since the endogenous ligand 5-HT is a monoamine molecule, we focused on natural products with alkaloids that contain nitrogen. We firstly screened 5-HT2A/2B/2C receptor by fluorescence-based thermostability assay with over 300 plant-isolated compounds. The potential hits were then validated by mass spectrometry and calcium influx assay for binding affinity and function evaluation. When 5-HT2A/2B/2C receptors were activated by 3nM of 5-HT, (-)-crebanine showed higher antagonism potency in 5-HT2C receptor compared to 5-HT2A and 5-HT2B receptors.

GSK3B/FXR1P PATHWAY REGULATES HOMEOSTATIC SYNAPTIC SCALING. JM Beaulieu, A Evstratova, Departments of Psychiatry and Neuroscience, Faculty of Medicine, Université Laval-CRULRG, Québec, Québec, University of Toronto, Toronto, Canada

Gsk3β/Fxr1P pathway is implicated in emotional regulation, and is affected by various psychoactive drugs, including antipsychotics, antidepressants, and mood stabilizers in part via GPCRs. Fx1P also negatively controls long-term memory, synaptic LTP and GluA2 translation. Therefore, we applied the CRISPR/Cas9 technology to mimic pharmacological interventions and investigate functional consequences of Gsk3β/Fxr1P modulations directly in the brain of adult mice. Mice were injected into mPFC with AAV viruses expressing GFP-Fxr1, Gsk3 sKO or Ctrl (AAV SpCas9 + AAV GFP). Impact of viral vectors was tested three weeks after injections. Mice were either used for behavioral experiments including the open field exploration, the elevated plus maze and the dark light emergence tests, or for electrophysiological recordings. Acute cortical slices were prepared during specific day times, in some cases after 6 h of sleep deprivation. Primary cortical cultures were prepared from P2-3 mouse pups and used for experiments at DIV14. Overexpression of Fxr1P and sKO of Gsk3b in mPFC resulted in an anxiolytic-like behavioral responses as compared to controls in all behavioral tests. Furthermore, whole cell patch-clamp recordings of mPFC layer III-V pyramidal neurons revealed that it also significantly decreases frequency and amplitude of sEPSCs mediated mainly by AMPA receptors. Interestingly, I-V relationships of evoked EPSCs showed significant increase of rectification, indicating that change in the AMPA subunit composition may be involved. Additional experiments confirmed that inhibition of mPFC neurons by KORD was sufficient to induce anxiolytic behaviors in mice. We next investigated involvement of Gsk3β/Fxr1P pathway in the homeostatic plasticity First we used an established ex vivo model of synaptic up scaling in primary neuronal cultures (48 h TTX treatment). Fxr1P overexpression and Gsk3 KO did not affect EPSC amplitude in control, but prevented synaptic upscaling. Second, we used sleep deprivation which allows to induce homeostatic plasticity in vivo. In control conditions, the 6-h sleep deprivation evokes increase of sEPSC amplitude, this increase was abolished by Fxr1P overexpression and Gsk3b knockdown. Our observations uncover a role for the Gsk3β/Fxr1P pathway in the regulation of homeostatic synaptic plasticity, as well as its role in the anxiolytic behavior. Therefore, targeting this pathway may be efficient for the treatment not only of mood disorders but also CNS deceases with destabilized homeostatic plasticity, such as autism, epilepsy and chronic pain.

UNDERSTANDING OF NEURONAL FUNCTIONS OF TRACE AMINE-ASSOCIATED RECEPTORS: FOCUS ON TAAR5. S Espinoza, I Sukhanov, A Gerasimov, TD Sotnikova, D Leo and RR Gainetdinov, ISBS Fellow, Fondazione Istituto Italiano di Tecnologia, Genoa, Italy; Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Skolkovo Institute of Science and Technology, Skolkovo, Russia

Trace amine-associated receptors (TAARs) are a class of G protein-coupled receptors (GPCRs) found in mammals. TAARs family consists of 9 genes in human (including 3 pseudogenes) while 19 and 16 genes (including 2 and 1 pseudogenes) are present in the rat and mouse genome, respectively. While TAAR1 is expressed in several brain regions and its CNS function is well characterized, all the other TAARs have been

described in the olfactory epithelium and believed to serve as a new class of olfactory receptors. However, there is evidence that other TAARs, such as TAAR5, could play a role also in the central nervous system. In our study, we report that TAAR5 is expressed in distinct brain regions. By using a mouse line expressing beta-galactosidase under TAAR5 promoter, we noted TAAR5 expression in amygdala, enthorinal cortex and olfactory bulb. These data were confirmed by the quantification of TAAR5 mRNA using RT-PCR. Interestingly, we also found TAAR5 mRNA in human amygdala, suggesting a conservation of the expression between mouse and human. We then studied the in vitro pharmacology of the receptor and confirmed that 3-methylamine is a full agonist of the receptor. Similar to TAAR1, TAAR5 is poorly desensitized upon agonist stimulation and shows an almost complete lack of beta-arrestin2 recruitment. TAAR5-KO mice are viable and do not show gross abnormalities in several tests. The lack of TAAR5 does not seem to affect the dopaminergic system, as evaluated by the challenge with dopaminergic drugs in behavioral assays. Interestingly, 5-HT1A receptor activity was altered, as demonstrated by 8-OH-DPAT-induced hypothermia. Since serotonin and 5-HT1A receptor are involved in mood disorders we evaluated TAAR5-KO mice in depression and anxiety-related tasks. In certain behavioral paradigms, we noted that TAAR5-KO mice displayed anti-depressant-like phenotype and showed less anxiety in comparison to controls. In conclusion, TAAR5 is expressed in the mouse and human brain in regions involved in mood and cognition, and TAAR5-KO mice show altered depression and anxiety-related behaviors. This work was supported by the Russian Science Foundation grant 14-25-00065.

THE ROLE OF TAAR1 IN MECHANISMS OF DRUG ADDICTION. I Sukhanov, A Dorotenko, A Dolgorukova, M Dorofeikova, L Mus and RR Gainetdinov, ISBS Fellow, First St. Petersburg State Medical University, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Skolkovo Institute of Science and Technology (Skoltech), Skolkovo, Russia

BACKGROUND: Drug addiction remains challenging clinical problem, since no effective therapy has been discovered so far. Numerous studies indicate that the ability of drugs of abuse to increase dopamine release in certain brain areas may be the key characteristic of development, maintenance and reinstatement of drug addiction. Trace Amine-Associated Receptor 1 (TAAR1) is widely expressed in mesocorticolimbic and nigrostriatal dopamine pathways and plays a modulatory role in dopaminergic activity. The present study aimed to characterize the role of TAAR1 in different paradigms related to drug addiction. **METHODS:** The experimental procedures were adapted from previous studies. Sensitization to locomotor stimulant effect of nicotine was used to evaluate the TAAR1 impact to the development and the maintenance of reward sensitization to addictive drugs. Anti-compulsive effects of TAAR1 activation was investigate in schedule-induced polydipsia (fixed time 60 sec and fixed interval 60 sec schedules). Anti-impulsive effects of TAAR1 agonists was tested in Pavlovian auto-shaping procedure. Additionally, the locomotor effects of partial TAAR1 agonist, RO5263397, were assessed to exclude the role of locomotor side effects here. **RESULT:** Partial TAAR1 agonist RO5263397 prevented the development of nicotine sensitization and also blocked an induced nicotine sensitization in additional test. Pretreatment with RO5263397 decreased volume of consumed water in a dose dependent manner in schedule-induced polydipsia test. RO5263397 demonstrated also anti-impulsive action in Pavlovian auto-shaping procedure, blocking auto-shaping conditioned lever presses in rats. The results of these experiments indicate that activation of TAAR1 modulates several mechanisms related to drug addiction. These results further support previously proposed view that TAAR1 is a promising target for prevention and treatment of drug addiction. **RESEARCH SUPPORT:** The Russian Science Foundation for Basic Research RFBR grant 17-04-01714 and the Russian Science Foundation RSF grant 4–50–00069.

ISBS FELLOW TALK: SOCIAL CONFORMITY AS AN INFLUENCE FACTOR ON THE ETHANOL PREFERENCE IN RATS. EV Filatova, AA Orlov, AY Egorov, ISBS Fellow, and SV Afanas'ev, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: According to Cooper's classes of alcohol drinking motives (1994), the social conformity is one of the key factors of alcohol abuse in humans. Here, we study the influence of negative reinforcement motives (e.g., drinking to avoid social rejection) on alcohol consumption in animal model experiments. **METHODS:** Experiments were performed in individual rats housed in groups of three. Special social conditions allowed male rats to have the alternative drink in comparison to their cage mates. In some groups only one of the three rats consumed alcohol, while the other two drank water; in others groups only one of the three rats consumed water, while the other two get the alcohol. In control groups, all rats received alcohol or water. **RESULTS AND DISCUSSION:** We found the difference in the level of alcohol preference in individual and group intake. Collective alcohol consumption leaded to the formation of alcohol preference, in comparison to individual ethanol use, which does not differ from the control rats. We also found the uptrend of alcohol consumption compared to the control animals among individual 'water intake' rats housed with 'drinking' cage mates. Our data confirm the influence of "social conformity" or "desire to be like everyone else" on the formation of preference for alcohol. **RESEARCH SUPPORT:** State Registration N 01201351570.

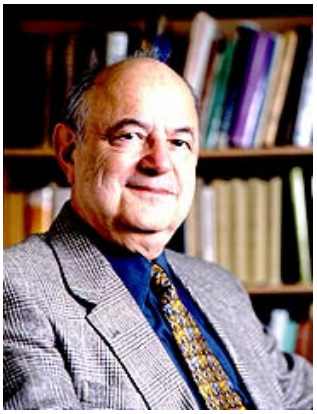
CONFERENCE PRESENTATION 1: INVESTIGATING RODENT BEHAVIOR IN AN AUTOMATED HOMECAGE SYSTEM INCREASES DATA REPRODUCIBILITY. J Fehmer, TSE Systems GmbH, Bad Homburg, Germany; LLC Alfa Mobili (the official representative of TSE Systems in Russia), St. Petersburg, Russia

Animal models for neuropsychiatric diseases are widely used in clinical research to develop new therapeutic strategies. Amongst others, scientists focus on the discovery of clinically effective drugs, which is typically done by using standardized behavioral tests to establish behavioral phenotypes of gene-targeted or transgenic animals. However, insufficient data reproducibility is becoming a major issue since recent publications report on many

findings from landmark studies being hard to replicate at pharmaceutical companies (e.g., Prinz et al. 2011). Apart from obvious scientific concerns, this creates serious financial, legal and ethical consequences, such as investigational costs for cases of misconduct, delayed drug development and potential risks to human volunteers and patients in subsequent preclinical studies (Steckler 2015). A large part of data variability observed within or across labs is caused by unpredictable changes in lab environment, experimenter interference or differential conditions in testing- and housing (Wahlsten et al. 2006). To combat such problems, TSE Systems introduced a standardized home cage testing system (IntelliCage) to automatically test group-housed animals within their social environment. The system requires no experimenter interference and allows high-throughput behavioral phenotyping over several days or weeks. IntelliCage allows a transfer of validated behavioral paradigms into automated setups as comparative studies revealed effects on learning and memory processes being similar to findings from e.g. Morris Water Maze or Vogel Conflict Test (e.g., Knapska et al. 2006). Studies using behavioral flexibility- and response-inhibition tasks proved IntelliCage to reliably assess executive functions (Gapp et al. 2014). Finally, transferring established behavioral paradigms to IntelliCage was shown to significantly reduce inter- and intra-lab-variability (e.g., Puscian et al 2005).

SYMPOSIUM 2: IRVING GOTTESMAN TRANSLATIONAL NEUROSCIENCE SYMPOSIUM

Chairs: MI Aghajanov (Armenia), D Kozic (Serbia)



INTRODUCTION: 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 ISBS publications. Recognizing his critical impact on the field, ISBS has set up a regular Gottesman Symposium in his honor. During these sessions, we continue to 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.

ISBS SPECIAL TALK 2: NEUROCHEMICAL SHIFTS IN NONSPECIFIC ULCERATIVE COLITIS, INDUCED BY DEXTRAN SODIUM SULFATE. MI Aghajanov, ISBS Fellow, AG Guevorkian, NCh Alchujyan, AA Aghababova and MR Hovhanniasyan, Heratsi Yerevan State Medical University, Buniatyan Institute of Biochemistry NAS, Yerevan, Armenia

INTRODUCTION: The nonspecific ulcerative colitis (NUC) is often comorbid with mental disorders. The chronic inflammation of the colon mucosa takes place against the background of the microbiota changes and increase of load bacterial antigens. This causes activation of the immune response of colon mucosa, initiates pro-inflammatory reactions. L-Arginine is a sufficient immune nutrient, it affects the activity of T-cells, natural killers, and some cytokine levels. New studies show a decrease in bioavailability of L-arginine in colon tissue and blood plasma in NUC patients. L-Arginine is an equal substrate for nitric oxide synthase (NOS) and arginase. The above-mentioned enzymes are reciprocally connected and are considered a new therapeutic target. Here, we explore metabolizing in the system intestine-blood-brain against the background of changes in the microbiota and behavior of animals at NUC. **METHODS:** Modeling of nonspecific ulcerative colitis in mice was performed by induction of dextran sodium sulfate (DSS). Clinical-pathological status of animals, as well as Morphological research, Microbiological analysis and Behavioral activity of mice were evaluated. **RESULTS AND DISCUSSION:** DSS-induced NUC is accompanied by disrupted indigenous microflora with the stimulation of growth of opportunistic microorganism Candida and manifestation of pathogenic Staphylococcus aureus, as well as signs of bacterial translocation. In contrast, in large intestine and blood leukocytes there was increase of arginase activity with simultaneous inhibition of iNOS/NO production, which partly provides milder course of NUC and speedy recovery of damages of intestinal and microbiotal mucosa after discontinuation of DSS. Meanwhile, we observed pathomorphological changes in the cerebral cortex and a region-specific activation of arginase in corticolimbic system, PFC, striatum, hippocampus and hypothalamus, with iNOS stimulating the release of proinflammatory mediators in the limbic system, which affected the behavioral reactions, manifested in the increase of anxiety and

suppression of the orienting-exploratory activity in some animals. Our data suggest the role of iNOS and arginase in central systemic mechanisms of NUC, linking emotional and cognitive CNS centers with bowel function at the periphery. Thus, further studies can help develop effective methods for preventing and treating NUC with comorbid mental disorders. **RESEARCH SUPPORT:** State Committee on Science, Ministry of Education and Science of Armenia Project 15T-3D174.

ISBS SPECIAL TALK 3: MODERN IMAGING MODALITIES IN DETECTION OF ALZHEIMER DISEASE AND OTHER TYPES OF DEMENTIA. D Kozic, ISBS Fellow, R Semnic, M Semnic, B Srdic-Galic, V Turkulov, S Stojanovic, O Nikolic, A Spasic, A Todorovic and N Boskov, University of Novi Sad Faculty of Medicine, Novi Sad, General Hospital Djordje Joanovic, Zrenjanin, Serbia

INTRODUCTION: With an increased prevalence of the population older than 65 years old (Alzheimer's Association, 2013), Alzheimer's disease became definitely severe and global public health problem and the most common cause of dementia. A neurodegenerative process in Alzheimer disease is characterized by the accumulation of insoluble protein aggregates within specific areas of the brain parenchima, such as amyloid-β (Aβ) plaques and neurofibrillary tangles, resulting in brain volume loss and progressive cognitive dysfunction. **METHODS:** Structural magnetic resonance imaging (MRI) and position emission tomography (PET) are powerful but conventional diagnostic modalities for the detection of Alzheimer disease. The atrophy of specific brain areas can be quantified via the segmentation of the brain parenchyma in BrainMagix's SurferMagix module (Hermoye et al, 2014). Multi-voxel magnetic resonance spectroscopy is able to detect subtle neurometabolic changes, while MR perfusion may detect brain regions of decreased blood supply. Diffusion tensor imaging is able to reveal disturbance of neuronal connectivity network. Amyloid imaging represents a major advance in neuroscience, enabling the detection and quantification of pathologic protein aggregations in the brain, focusing on PET with (11)carbon-labelled Pittsburgh Compound-B ((11)C-PIB), the most extensively studied and best validated tracer. **RESULTS AND DISCUSSION:** Structural and molecular imaging reveal medial-temporal atrophy, reduced uptake of 18F-FDG PET, increased retention of Aβ amyloid protein by amyloid-PET and reduced N-acetyl aspartate on magnetic resonance spectroscopy in different brain regions. These techniques are promising diagnostic tools that allow assessing in vivo Alzheimer disease pathology. However, Alzheimer's disease is not the unique cause of dementia. Significant white matter changes in vascular dementia, focal frontal or temporal atrophy in Pick's disease, brain stem neurodegeneration in multiple system atrophy can help to discriminate Alzheimer's disease from other causes of dementia from neuroradiologic perspective. **RESEARCH SUPPORT:** Provincial Secretariat for Science and Technological Development of the Autonomous Province of Vojvodina, project 114-451-2730/2016-01.

DECREASE IN PERCENTAGE OF GREY MATTER DURING PREGNANCY IN HEALTHY CONTROLS. J-M Le Melledo, A Ghuman, AM McEwen, DTA Burgess, CC Hanstock, P Seres, P Khalili, C Newman, GB Baker, ND Mitchell, J Khudabux-Der and PS Allen, University of Alberta, Alberta, Canada

INTRODUCTION: Little is known about the cerebral changes associated with pregnancy. Without information on the normal brain alterations associated with pregnancy, it is difficult to investigate the brain mechanisms responsible for the impact of pregnancy on mood, either directly during pregnancy or indirectly during the postpartum period. We were interested in measuring Glutamate (Glu) levels in the Medial Prefrontal Cortex (MPFC) in healthy control women using Proton Magnetic Resonance Spectroscopy (1H-MRS). **METHODS:** A total of 21 healthy pregnant women without current or past psychiatric disorder (pregnant HC: pHC) and fourteen non-pregnant healthy controls in the follicular phase of their menstrual cycle (Follicular Phase HC: FPHC) underwent 1H-MRS scans 2-3 weeks prior to delivery for pHCs and during the follicular phase of the menstrual cycle for FPHCs. Metabolites and Tissue composition were measured in the MPFC of pHC and FPHC (in a 2x3x3 cm3 voxel). **RESULTS AND DISCUSSION:** Glu levels and % in Grey Matter (%GM) were decreased in pHC vs FPHC (6.74 + 1.55, $p=0.001$ and 46.53 + 10.66 vs 60.43 + 6.98, $p<0.0001$ respectively). However, after correction for %GM (ANOVA), the difference in Glu level lost it statistical significance ($p=0.11$). There have been no previous investigations of changes in tissue composition in the brain of pregnant women. Glu is mainly found in GM which explains the loss of significance when changes in % GM was taken into consideration The drastic increase in female sex hormones as well as neuroactive steroids seen during pregnancy may be responsible for the observed changes in % in GM. This decreased % of GM may relate to the transitory self-report of decreased cognitive ability by pregnant women during pregnancy (pregnesia). **RESEARCH SUPPORT:** Canadian Institute of Health Research and the Cranston family.

ASSOCIATION OF THE GALANIN GENE POLYMORPHISM WITH THE PSYCHOLOGICAL CORRELATES OF STRESS RESISTANCE. VI Lioudyno, OE Zubareva, SG Tsikunov, ISBS Fellow, and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia

INTRODUCTION: The predictive value of genetic factors in vulnerability to stress is actively discussed. Galanin is a neuropeptide implicated in modulation of stress reaction and emotion-related behaviors. The aim of present study was to analyze the impact of rs948854 polymorphism of the galanin gene promoter on psychological markers of stress resistance. **METHODS:** 72 healthy young adult volunteers were included in the study. All participants were students recruited during their course in psychology. Total nuclear DNA was extracted from the buccal epithelium samples. To discriminate A and G alleles of rs948854 polymorphism, the polymerase chain reaction followed by the restriction fragment length polymorphism assay (PCR-RFLP) were used. To assess psychotic indicators associated with the stress resistance, several tests were performed. The strength of neural

processes (the type of nervous system) was measured using tapping-test. The Eysenck Personality Questionnaire (EPQ) and Cloninger's Temperament and Character Inventory (TCI) evaluated personality traits. Self-report questionnaires were used to assess the impulsivity and self-control behavior. The examined parameters were compared in minor allele carriers (AG and GG genotypes) and homozygous carriers of A-allele (AA genotype). The first group consisted of 33 people, and the second - from 39. **RESULTS AND DISCUSSION:** The analysis revealed that G-allele carriers have reduced ability to exert self-control and more expressed signs of impulsive behavior that can be maladaptive in stress conditions. When the neuroticism level (measured by EPQ test) was analyzed the significant interactions of rs948854 genotype, sex and strength of nervous processes was demonstrated ($F=5.89$; $p=0.005$). Female carriers of G-allele with the high level of neuroticism were individuals with weak type of the nervous system. The opposite association was found in males, where high level of neuroticism was observed in the G-allele carriers with strong and average types of the nervous system. In addition, significant negative correlation between neuroticism level and self-control behavior was demonstrated ($r=-0.34$; $p=0.003$). Thus, the influence of rs948854 polymorphism of the galanin gene promoter on neuroticism level and impulsive behavior demonstrated here strongly supports the role of galanin in determining the type of behavioral responses to stress. The carriage of minor allele influences in different ways neuroticism levels in male and female, suggesting an additional gender-specific mechanism of vulnerability to stress-induced emotional disturbances.

CONFERENCE PRESENTATION 2: MULTI-FUNCTIONAL MEASUREMENT SYSTEMS APPLICATION IN PRECLINICAL DRUG RESEARCH (LABORAS, SONOTRACK, DSI-TELEMETRY). GA Piavchenko, L Bachdasarian, R Bulthuis and VI Nozdrin, J-SC Retinoids, Preclinical Research Center, Moscow, Medical Institute, Histology, Cytology and Embryology Department, Orel State University, Orel, Russia; Metris B.V., Hoofddorp, The Netherlands

Modern trends in pharmaceutical science development require a sufficiently high level of preclinical research quality. To achieve this goal in laboratory animal experiments, it is necessary to implement a complex evaluation of the drug effect. In particular, it is important to assess the morphological and physiological organism condition, and the animals themselves should be contained in a controlled environment. Russian pharmaceutical science embarked on the principles of good laboratory practice following. Morphological estimation of the drug effect is to examine the changes in the organs and tissues structure. Such methods of drug effect evaluation reflect only structural changes, and do not allow establishing functional responses to the drug use in vivo. To assess the physiological effect of substance on animals, one needs to take into account the functional response of the organism. One of the most accessible for this purpose is the open field test. However, its use is associated with the presence of a number of drawbacks, such as subjective data and low reliability. These deficiencies are lacking in hardware and software systems that can automatically collect the studied parameters (behavioral reactions, physiological parameters and ultrasonic vocalizations of laboratory animals), and carry out its analysis, storage and protection. In research laboratory practice, Laboras (behavioral reactions evaluation – motor activity, eating and drinking, sleeping, grooming, immobility, rearing, etc.), Sonotrack (ultrasonic vocalizations evaluation – the type of vocalizations, their duration and frequency) and DSI systems (telemetric physiological parameters evaluation) are used. When all parameters are simultaneously recorded in multiple devices connected to a single computer, it is possible to assess the same act that was registered by these systems, which enables the functional assessment of the drug influence and to operate a large number of data from various independent evaluation methods. This ensures high reliability and conclusiveness/validity of the results.

ISBS BOOK CLUB: PRESENTING "HEALTH OF MAN (FROM THE POINT OF VIEW OF MODERN STRESSOLOGY)". AS Tadevosian and AA Muradyan, Heratsi Yerevan Medical State University, Yerevan, Armenia

In the last decades, the questions about man's health caused heightened interest in the area of the public healthcare all over the world. The concern is raised by data on life expectancy of men in developing and industrialized countries, which is 4-6 (in other countries 8-10) years shorter than life expectancy of women. Previously, this was explained it by biological laws of sexual selection and specific functions of the man and woman. In contrast to this generally accepted approach, the authors, Drs Tadevosian (psychiatrist and stressologist) and Muradyan (urologist and sexopathologist) put emphasis on the psychosocial essence of a man, the characteristics of his mental world and his sensitivity. The authors have large clinical experience, which they share with readers using common 'understandable' language. Their chosen approach is based on the fact that man is always on the "crest of the wave" in the stressful ocean of the life: HE first accepted strokes of a bad luck and looked for islands of hope and stability, but finding them, once again came back in the whirlpool of the life events. Because only in search of "new", the man finds sensation of full value of the life. Therefore, the study of the internal mental function of a man is the most reliable path to the exploration of the underlying mental processes affecting the health, life and healthy longevity. The book consists of 3 parts. Each part covers one side of a common problem, however, the single methodology in the form of the adaptable psychosomatic approach is preserved through the book. The first describes unconscious "secrets of the soul" of a man, which create unrealized chronic pressure that may play a role as the etiologic factor for the development of psychosomatic disorder. The second part of the book focuses on problems of the libido, logos and love. It emphasizes that these three components coexist together, only each of them has a different age for its peak. The third part - "Threshold medicine" - is based on stressology - the field of medicine studying maladaptation states "it are not health already, but are not yet the illness". There is a big layer of functional disorders with equal probability of either returning to the healthy state, or deepening transition into pathology. Based on the mechanism of general adaptation syndrome (GAS) and its axes (anxiety, worry and asthenia), each of them has become independent, and can be switched by autonomous regulation not only by the external factors, but also in response to internal conflicts,

thoughts and memories. The book's clinical section describes threshold syndromes, homosexuality and suicide, and discuss the biological and psychological factors influencing GAS, and provide psychoanalytic explanations of psychologic maladaptations. The conclusion is written in a unique style (in the form of a myth) discussing the knowledge of the individual, the problem of the brain and consciousness, and understanding of a soul. The book is rich in clinical examples from the authors' own long-term medical practice.

Day 2. Wed, May 17, 2017

SYMPOSIUM 3: ZOFIA ZUKOWSKA STRESS NEUROSCIENCE SYMPOSIUM
Chairs: VM Klimenko (Russia), S Salim (USA)

INTRODUCTION: Prof. ZOFIA M. ZUKOWSKA (1948-2017) 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.

ISBS SPECIAL TALK 4. PSYCHOLOGICAL STRESS AND OXIDATIVE STRESS: CAUSE OR CONSEQUENCE? S Salim**,** Department of Pharmacological and Pharmaceutical Sciences, College of Pharmacy, University of Houston, Texas, USA

INTRODUCTION: Biochemical integrity of the brain is vital for normal functioning of the central nervous system (CNS). One of the contributing factors of cerebral biochemical impairment is a chemical process called oxidative stress. Oxidative stress occurs upon excessive free radical production due to insufficiency of counteracting antioxidant response system. The brain with its high oxygen consumption and lipid-rich content is highly susceptible to oxidative stress. Therefore, oxidative stress-induced damage to the brain has a strong potential to negatively impact normal CNS functions. The brain is a target of stressful and often traumatic experiences. Therefore, recovering from stressful experiences is crucial for normal brain function. In fact, persistent psychological stress often disrupts recovery or adaptive mechanisms causing cognitive and emotional disturbances. It is well-recognized that stress adaptation is an integration of a highly complex multi-systemic response mechanism yet, the biochemical determinants of stress response are not known. **METHODS:** We have employed numerous behavioral and pharmacological approaches to examine role of oxidative stress in stress-recovery processes. Defective oxidative-antioxidative balance seems to be a critical component of maladaptive stress responsiveness in rodents. Induction of various forms of psychological stress including social defeat, sleep deprivation, single-prolonged stress and traumatic stress procedures were utilized. **RESULTS AND DISCUSSION:** Our work has suggested that induction of various forms of psychological stress including social defeat, sleep deprivation, single-prolonged stress, traumatic events, all lead to behavioral and cognitive deficits in rats, along with an increase in oxidative stress markers in the periphery as well as in selected regions of the brain including the hippocampus, amygdala and the prefrontal cortex. Heightened oxidative stress is associated with decreased levels of antioxidant enzymes including Cu/Zn superoxide dismutase (SOD), Mn-SOD, glutathione reductase-1 and glyoxalase-1. Additionally, pharmacological strategies to limit oxidative stress replenished antioxidant pool and rescued or prevented some of the behavioral and cognitive deficits observed in a rat social defeat model. These data suggest that critical examination of oxidative stress pathways in animal models of psychological stress may reveal molecular targets critical for development of therapeutic interventions. **RESEARCH SUPPORT:** The National Institutes of Health NIH/NIMH grant 2R15MH093918-02.

PSYCHOLOGICAL IMPACT OF TRAFFIC-RELATED AIR POLLUTION: INSIGHTS FROM AN ANIMAL MODEL. A Salvi, G Patki, H Liu and S Salim, University of Houston College of Pharmacy, Houston, Texas, USA

INTRODUCTION: Air pollution from vehicle exhaust is a leading cause of mortality due to lung and heart disease; however, effect of exhaust emissions on brain and its psychological impact has been largely ignored. Here, vehicle exhaust-induced psychological alterations in rats were examined in a laboratory setting using a

simulated vehicle exhaust exposure (SVEE) model. Prolonged exposures to the gaseous constituents of vehicle exhaust, namely, carbon dioxide (CO2), carbon monoxide (CO) and nitrogen dioxide (NO2) are known to increase oxidative stress. Recent studies from our laboratory have established a causal link between oxidative stress and behavioral as well as cognitive deficits. Therefore, we hypothesized that prolonged exposures to pro-oxidants from vehicle exhaust elevate oxidative stress leading to behavioral and cognitive deficits. And, interventions that limit/prevent oxidative stress such as a mitochondria-permeable antioxidant, MitoQ, can protect SVEE-induced impairments. **METHODS:** Four groups of adult male Sprague Dawley rats were included: Control+Vehicle (C+V), Control+MitoQ (C+M), Exposure+Vehicle (E+V) and Exposure+MitoQ (E+M). The MitoQ groups received 250µM of MitoQ for 4 weeks via drinking water. Vehicle groups received normal drinking water during this period. Following the treatment, exposure rats were exposed to a simulated mixture of vehicle exhaust containing 0.04% CO2, 0.9 ppm NO2 and 3 ppm CO. Exposures were performed in whole body exposure chambers 6h daily for 2 weeks. Duration of exposures was comparable to daily exposure of exhaust levels in areas of high traffic. Control rats were exposed to normal air for the same duration. Following SVEE, comprehensive behavioral and cognitive analysis was performed to assess anxiety-like, depression-like behavior as well cognitive function and intelligence quotient (IQ) levels in the rats. **RESULTS AND DISCUSSION:** An increase in anxiety-like and depression-like behavior as well as impaired memory and low IQ was observed in E+V rats as compared to C+V and C+M rats. This indicates that rats exposed to simulated vehicle exhaust suffered from behavioral and cognitive deficits. However, these deficits were not seen in E+M rats suggesting that pre-treatment with MitoQ protected the rats from vehicle exhaust-induced alterations. Thus this study identified behavioral and cognitive impairments associated with exposure to pro-oxidants in vehicle exhaust in rats. It also identified potential role of the antioxidant MitoQ in preventing these impairments. Further experiments in this study may help reveal involvement of oxidative stress in SVEE-induced behavioral and cognitive impairments. **RESEARCH SUPPORT:** The National Institutes of Health NIH/NIMH grant 2R15MH093918-02

LOSS OF ALPHA2 SUBUNIT OF GLYCINE RECEPTORS AFFECTS MATURATION OF CORTICO-STRIATAL CIRCUITRY. SM Molchanova, J Comhair, D Karadurmus, SN Schiffmann, J-M Rigo, D Gall and B Brone, Laboratory of Neurophysiology, Université Libre de Bruxelles, BIOMED Research Institute, University of Hasselt, Belgium; Neuroscience Center, University of Helsinki, Finland

INTRODUCTION: Glycine receptors are ligand-gated chloride channels, expressed in the brain and spinal cord. Glycine receptors containing the alpha2 subunit are highly expressed in the developing brain, where they regulate migration and maturation of the cortical neurons and promote neonatal spontaneous neuronal network activity, needed for the development of synaptic connections. Several mutations in the X-linked gene GLRA2, encoding the alpha2 subunit, have been found in boys with autism spectrum disorder, pointing at possible involvement of glycinergic transmission in development of cognitive abilities. We have shown previously that medium spiny projection neurons (MSNs) in the dorsal striatum express tonically active alpha2-containing GlyRs, which stabilize the resting membrane potential and set the offset of action potential firing. However, the function of glycine receptors in developing striatum has not been studied yet. The aim of this work was to describe the role of glycine receptors in development of cortico-striatal connections. **METHODS:** Experiments have been done on neonatal and adult mice of Glra2 knockout strain. Expression of glycine receptor subunits was evaluated by RT-PCR done on tissue dissected from dorsal striatum. Electrophysiological properties of developing and adult MSNs were studied ex vivo in cortical and striatal slices. Morphological characterization of MSNs was done by imaging of biocytin-filled cells. Behavioral analysis was performed using Glra2 knockout and wildtype four-month old males. **RESULTS AND DISCUSSION:** Here, we show that the expression of alpha2 subunit is upregulated in the dorsal striatum of neonatal mice. In MSNs, evoked glycinergic currents have higher density in one-week-old mice, compared to adults. A fraction of neonatal MSNs was spontaneously active, and in Glra2 knockouts, the frequency of spontaneous action potentials in these active cells was reduced. Deletion of Glra2 also affected functional maturation of glutamatergic synapses on MSNs. Frequency of miniature glutamatergic postsynaptic currents was reduced in MSNs of knockout animals, starting from P7 and into adulthood, without changes in spine density or morphology of the dendritic tree. In the adult Glra2 knockouts, basic locomotion and the anxiety level were not affected, but memory consolidation during striatum-specific motor learning tasks was impaired. Taken together, these results demonstrate the involvement of glycine receptors in maturation of cortico-striatal circuitry. **RESEARCH SUPPORT:** Interuniversity Attraction Pole (IAP – P7/10) from the Belgian Science Policy Office (Belspo), FRS-FNRS and FMRE.

THE EXPRESSION FORECAST OF POST-TRAUMATIC STRESS DISORDER IN FEMALE RATS. NK Apraksina, TV Avaliani and SG Tsikunov, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg, Russia

Understanding the pathobiology of the post-traumatic stress disorder (PTSD) is an important biomedical problem. Our aim was to assess PTSD-like states caused by strong psychogenic trauma (survival stress) in rats depending on their baseline behavioral characteristics. Behavioral indicators (locomotor and exploratory activity, anxiety, reaction to an aversive stimulus) were evaluated in Wistar female rats (n=30). The "mink reflex" (exploratory behavior) and general locomotor activity were record in the open field test (OP). The level of anxiety was assessed in the plus maze test (PM). Conditioned response of active avoiding (AACR) in the rats was modeled in shuttle chamber. The psychogenic trauma in female rats was modeled by placing them with a predator (a tiger python) who killed and ate one of the exposed rats. Behavioral parameters were evaluated 7 days after traumatic experience. Severity of depressive component behavior in stressed rats was verified in a test for 1% sucrose preference (reduction of >50% of sucrose consumption was considered as anhedonia). Two groups of animals (Group A and B) were isolated in the analysis of the initial behavioral parameters in female rats. The group A demonstrated lower locomotion activity than group B ($p < 0.01$), low research activity- indicator mink reflex was lower than the other animals ($p < 0.05$), low anxiety compared with individuals in group B ($p < 0.01$). The group A

was characterized by a low response rate (average reaction time of disposal was higher compared to the group B ($p < 0.05$) in developing AACR. Female rats recorded suppression of motor and exploratory activity, increase the level of anxiety after psychogenic trauma, indicated the development of PTSD. Analysis of sucrose consumption of stressed rats revealed two groups of rats among experimental animals. There were rats with anhedonia and without anhedonia. It could also indicate the presence of different types of PTSD. Severity of depressive component behavior in PTSD correlated with baseline behavioral performance in rats, and was characteristic of the female rats of group A. The form of PTSD without anhedonia correlated with initial high motor activity, increased anxiety, active avoidance reaction to the aversive stimulus, and characterized the B group of rats. Thus, the baseline type of behavior of female rats can influence the severity of the developing PTSD-like state. Analyses of initial individual performance with the development of anhedonia in female rats after psychogenic trauma can serve as a method to predict and identify possible distinct sub-types of PTSD.

MECHANISMS AND CONSEQUENCES OF THE DELAY IN BRAIN DEVELOPMENT IN RATS SUBJECTED TO THE PRENATAL HYPOXIC STRESS. DS Vasilev, NL Tumanova, NM Dubrovskaya and IA Zhuravin, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg State Pediatric Medical University, St. Petersburg, Russia

INTRODUCTION: The delay in brain development is common in animal models utilizing various stressors during embryogenesis. Such a delay affects motor skills during early postnatal ontogenesis. Since mechanisms of unspecific delay in brain development remain unclear, we investigated the consequences of the prenatal hypoxic stress and their possible mechanisms. **METHODS:** On the 14th day of pregnancy, female rats were exposed to hypoxic stress (7%O2, 3 h), and the cortical tissue structure and behaviors were analyzed in their pups. The formation of the motor skills of the pups (P0-P20) was analyzed with the set of the standard tests: forelimb placing, suspending on rotating grid and horizontal wire etc. On P10, the ultrastructure of the parietal cortex was analyzed using FEI Tecnai V2 (FEI, USA) transmission electron microscope. The amount of the protein transthyretin (TTR) in the whole placenta of pregnant female rats, exposed to hypoxia on 14th day of pregnancy, were compared with naïve controls with a Western blot technique. **RESULTS AND DISCUSSION:** On P0-P20, we found the delay in development of the motor skills in pups exposed to prenatal hypoxic stress. We also found some features of the delay in development of the cortical tissue in P10 pups exposed to prenatal stress, including increased volume of intercellular spaces as well as the number of the growth cones. The number of developed synapses, especially the axon-spine ones, was sufficiently decreased compared control pups. Our data show the delay in the development of cortical neuropile and in the differentiation of cortical neurons of the pups exposed to prenatal hypoxic stress. On Day 15 of pregnancy, the amount of TTR protein in the placenta of the animals exposed to hypoxic stress significantly decreased vs. naïve control. TTR is the main transporter of the thyroid hormones in the blood. Reduced TTR level in the placental tissue may indicate a failure in the thyroid transport from a mother to an embryo. The thyroid hormones are essential for the early brain development. The deficit of their transport very often causes CNS developmental delays, leading to the temporary delay in the development of the motor skills during early postnatal ontogenesis. **RESEARCH SUPPORT:** RFBR 16-04-00694 and 17-04-01536.

DISTURBED VOCAL COMMUNICATION IN COMMON MARMOSET FAMILY WITH AN AUTISM-MODEL CHILD. K Mimura, K Nakagaki and N Ichinohe, Department of Ultrastructural Research, National Institute of Neuroscience, National Center of Neurology and Psychiatry (NCNP), Tokyo, Japan

INTRODUCTION: Autism spectrum disorder (ASD) is one of the most common developmental disorders. Most children with ASD demonstrate delays in language development. Parents of these children may also feel frustration and stress because they cannot communicate with their children (Hastings, 2002). Here we examine vocalization abnormality of common marmoset (*Callithrix jacchus*) families consisting normal parents with a juvenile of ASD model. **METHODS:** The marmoset autistic model were made by injecting in-utero the valproic acid (VPA), which increase autism occurrence in human being and also rodents. In the families with VPA exposed children, the dams received seven oral administrations of sodium valproate at 200 mg/kg/day from day 60 to 66 after conception. The experiment utilized 16 children of marmosets - 9 VPA-exposed and 7 unexposed (UE) - consisting of one or two juveniles 1-5 month old, and their respective parents. To compare social communication of family including autistic dum, vocalizations of family consisting either VPA or UE one juvenile were recorded for 30 min in their homecage. Vocal spectrogram was used to define and count 9 call types. **RESULTS AND DISCUSSION:** There were significant differences of call-uses between VPA and UE families. In VPA families, social isolation call “phee” frequency and agitation call “twitter” was increased, on the other hand, “trill” call frequency, supposed ‘felling affinity’, was decreased. These two groups were significantly discriminated by outlier analysis based on Mahalanobis’ distance. Thus, quantitative analysis of verbal communication in family with ASD children could be useful and noninvasive criterion of patient himself and his family in common marmoset. **RESEARCH SUPPORT:** JSPS Research Fellowship PD (26-10961).

THE IMPACT OF EARLY LIFE STRESS ON DISTRIBUTION OF H3K4ME3 HISTONE MODIFICATION IN MURINE PREFRONTAL CORTEX: THE ROLE IN GENE EXPRESSION. VV Reshetnikov, AA Lepeshko, NI Ershov, YuA Ryabushkina, AA Studenikina, NP Bondar and TI Merkulova, Institute of Cytology and Genetics SB RAS, Novosibirsk State University, Novosibirsk State Medical University, Novosibirsk, Russia

INTRODUCTION: The early life is an important period for the development of the nervous system and for the programming behavioral phenotype in later life. The different events as a stress or an abuse and a neglect can result in behavioral and metabolic disturbances, cognitive disorders and other negative outcomes that could

persist throughout life. Molecular mechanisms of the delayed impact of these effects are likely mediated by epigenetic changes, in particular, by histone modifications. The aim of this work is studying the effects of stress in early life on the genome-wide distribution of H3K4me3 histone modification in prefrontal cortex of male C57BL/6 mice and its correlation with gene expression. H3K4me3 histone modifications are localized in active promoter regions. **METHODS:** We explored the effects of two types of early life stress: prolonged separation of pups from their mothers (3 h per day, maternal separation, MS) and short separation (15 min per day, handling, HD) during the first 2 weeks of life vs. nonhandled control group (NH). We evaluated the behavioral phenotype of the adult mice (3 months) using plus maze and social interaction test then the prefrontal cortex was taken for further analyses. Chromatin immunoprecipitation was performed using antibody H3K4me3 and followed by sequencing (ChIP-seq). **RESULTS AND DISCUSSION:** MS group showed a reduced moved distance while HD group revealed a reduced anxiety and an increased communicative behavior to compare with control. However, we have not found any significant changes in H3K4me3 profiles in HD group to comparison with control NH group. Contrariwise, we have revealed significant differences in H3K4me3 modification levels between MS and NH groups in 10 chromatin loci (q-value <0.05).The changes of only a few loci were affected by early life stress and this apparently indicates the stability of the distribution of H3K4me3 modification in mice prefrontal cortex. The revealed loci are located in the promoters of 16 genes, from which 11 are functionally annotated. The corresponding protein products of 8 genes are associated with the nervous system development. Using the real-time PCR we assessed the expression of these genes on extended groups of animals. Two of the 11 genes (Pip4k2a, Ddias) showed significantly increased expression in MS group compared to NH group. Pip4k2a encodes an enzyme that catalyzes the phosphorylation of phosphatidylinositol 5-phosphate to 4,5-biphosphate, that is the second messenger for many cell processes. Reducing activity of the PIP4K2A enzyme in humans is associated with mental illnesses, including schizophrenia and bipolar disorder. Recent studies have also shown the role of this enzyme in the regulation of gene expression in the glutamate system. Ddias encodes the protein Noxin that acts as an anti-apoptotic agent involved in DNA repair and cell survival. Noxin may be involved in the cell defense system, as it is activated by various stress stimuli, helps cells to withdraw from cycling, and opposes apoptosis. We also evaluated the expression of methyltransferase Kmt2a (Mll1) and Kmt2d (Mll4) and demethylase Kdm5a (Jarida1), which play the key roles in the formation and removal of H3K4me3 modifications, but we did not reveal significant differences between the groups. Thus, our results indicate that maternal deprivation alters behavioral phenotype and activates the promotors of 16 genes that represent potential targets of early postnatal stress. Nevertheless, the active state of the promoter regions was associated with altered basal expression in only two cases. Further investigation will clarify the role of candidate genes in the long-lasting effects of early life stress. **RESEARCH SUPPORT:** The Russian Science Foundation project 16-15-10131.

CHANGES IN ADULT NEUROGENESIS IN TWO PARADIGMS OF STRESS IN RATS. VA Aniol, NA Lazareva, AA Yakovlev, AO Manolova and NV Gulyaeva**,** Institute of Higher Nervous Activity and Neurophysiology, Moscow, Russia

INTRODUCTION: Chronic stress is a widespread condition leading to various brain pathologies, including depression and post-traumatic disorder. The exact way of long-term action of stressful impacts remains not completely understood. A possible mechanism may involve changes in adult neurogenesis, caused by stress condition and leading to formation of abnormal neuronal circuits. **METHODS:** We applied two paradigms of the chronic stress: chronic unpredictable mild stress (CUS) and early-life inflammatory stress (ELIS). In the CUS paradigm, rats were subjected to a series of stressful events including food and/or water restriction, cage tilt, crowded housing, isolation, and inversion of the light-dark schedule. Stressors were changed twice a day and presented randomly during two months. After completion of CUS protocol, animals were assessed in behavioral tests and sacrificed for analysis of neurogenesis. In ELIS paradigm, rat pups were injected with bacterial lipopolysaccharide on postnatal days 3 and 5, and behavior and neurogenesis were assessed later in adulthood, at the age of 3 months. **RESULTS AND DISCUSSION:** Two stress paradigms have led to opposing effects on neurogenesis. The proliferation of precursor cells after completion of stress, assessed by PCNA staining, was unaffected in both paradigms. However, the neuronal differentiation assessed by doublecortin staining was suppressed by ELIS and enhanced by CUS. On the other hand, the number of new neurons and astrocytes generated from the cells which were born during early-life inflammation was increased in the dentate gyrus of rats subjected to ELIS. Collectively, our results suggest the difference between the ways in which these two stress paradigms influence the process of postnatal neurogenesis in the hippocampus of rats. **RESEARCH SUPPORT:** RFBR grant 16-04-01513 and RSF grant 14-25-00136.

THE IMPORTIN OF ANXIETY-RELATED BEHAVIORS. N Panayotis, A Sheinin, SY Dagan, F Rother, G Volpert, MM Tsoory, E Hartmann, M Bader, AH Futerman, I Michaelevski and M Fainzilber, Departments of Biomolecular Sciences, and Veterinary Resources, Weizmann Institute of Science, Rehovot, Sagol School of Neuroscience, Department of Biochemistry and Molecular Biology, Tel Aviv University, Tel Aviv, Israel; Max-Delbrück-Center for Molecular Medicine, Berlin, Center for Structural and Cellular Biology in Medicine, Institute of Biology, University of Lubeck, Lubeck, Germany

INTRODUCTION: The mechanisms of synaptonuclear transport and the transcriptional pathways at the core of neuronal disorders, are poorly understood. The importin family of nuclear import factors has pivotal roles in such pathways, due to their involvement in intracellular transport from both synapse to soma and cytoplasm to nucleus. Mammals express six different isoforms of importin α, which bind an Importin β to form transport complexes for specific cargoes. **METHODS:** We addressed the role of importin α isoforms in mammalian CNS by evaluation of a systematic series of importin α knockout mice. A comprehensive battery of behavioral tests was used to investigate spontaneous and novelty-induced locomotion, basal ganglia function, motor coordination, neuromuscular integration, anxiety-related behaviors and memory. Subsequent analyses using acute-brain slice

electrophysiology, RNA-seq, bioinformatics, imaging and pharmacology was used in order to delineate the contribution of genes and signaling pathways involved in the identified phenotype and screen for new therapeutic approaches. **RESULTS AND DISCUSSION:** During the course of comprehensive behavioral profiling of importin α mouse mutants, we identified an importin α knockout (KO) mouse with significantly reduced anxiety levels. Electrophysiological recordings in acute hippocampal slices showed a reduced short-term and presynaptic plasticity (paired-pulse facilitation deficit, lower PTP), while LTP was not affected in these mutants. We then performed transcriptional profiling (RNA-seq) from hippocampal extracts of wild type versus mutant animals after exposure to an anxiogenic drug. Interrogation of the Connectivity Map® (CMap) database with lists of the deregulated genes enabled the identification of drugs that may mimic importin-dependent transcriptional signatures. The anxiolytic properties of the top candidates were confirmed in behavioral assays. Our current efforts are focused on the delineation of pathways common to both importin α and drug-dependent reduction of anxiety. **RESEARCH SUPPORT:** European Research Council (Grant 339495), the Chaya Professorial Chair in Molecular Neuroscience (MF), and the French Ministry of Foreign Affairs International Volunteers Program (NP).

PREFRONTAL MRNA EXPRESSION OF SHORT AND LONG D2 DOPAMINE RECEPTOR ISOFORMS AND COGNITIVE IMPAIRMENTS IN RATS FOLLOWING CHRONIC, EARLY-LIFE INTERLEUKIN-1β TREATMENT. AP Schwarz, AN Trofimov, VI Lioudyno, DS Antonov, OE Zubareva and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry, Peter the Great St. Petersburg Polytechnic University, St. Petersburg, Russia

INTRODUCTION: D2 dopamine receptors are involved in various CNS pathologies including attention deficit hyperactivity disorder, schizophrenia, Parkinson disease and affective disorders. Long (D2L) and short (D2S) alternative splice isoforms of the D2 dopamine receptor gene appear to play different roles in behavioral regulation. However, their contribution to neurodevelopmental disorders remains unclear. The aim of the present study was to investigate mRNA expression of D2L and D2S dopamine receptors in the rat medial prefrontal cortex (mPFC), a brain region associated with the development of cognitive malfunctions caused by early life immune activation. **METHODS:** All experiments were performed on Wistar male rats. Pups were injected with 1 μg/kg hrIL-1β or saline at P15-21 (i.p., daily), or left intact. Working memory in the Y-maze spontaneous alternations paradigm and learning ability in passive avoidance (PA) test have been evaluated in juvenile (P25-30), adolescent (P42-50) and adult (P75-90) animals. A part of adult animals was also trained in active avoidance (AA) paradigm. Prefrontal D2S and D2L mRNA expression was measured by qRT-PCR at P27, P45-50 and P75-90 (24 h after Y-maze test; 1 h after AA-training). Statistical analysis was performed using parametric (ANOVA, t-test) or non-parametric (Kruskall-Wallis, Friedman) tests based on normality of data distribution (assessed by Shapiro-Wilk's test) in SPSS-19. **RESULTS AND DISCUSSION:** Early life IL-1β treatment impairs working memory in juvenile, adolescent and adult rats, however long term memory in PA test was affected only in adult animals. D2S mRNA expression was decreased in adolescent and adult animals compared to juveniles in all experimental groups. Although no developmental changes in the D2L mRNA expression were found, this measure was increased in juvenile rats treated with IL-1β at P15-21 compared to intact group. In the mPFC of both adult controls (intact and saline treated), D2L mRNA was downregulated after AA training, while D2S mRNA level remained unchanged but negatively correlated with learning ability. These effects were absent in rats treated with IL-1β during early life. Thus, D2S and D2L mRNA isoforms in the mPFC are differentially regulated during postnatal development and active avoidance training, and dysregulation of their expression may be one of the mechanisms of cognitive malfunction caused by early-life immune challenge**.** **RESEARCH SUPPORT:** RFBR project 16-34-00873 mol_a.

CONFERENCE PRESENTATION 3: STATE OF THE ART IN BEHAVIORAL NEUROSCIENCE – ADVANCES IN VIDEO TRACKING, GAIT ANALYSIS AND OTHER TECHNIQUES. A Willemsen and A Biarslanova, Noldus Information Technology, Wageningen, The Netherlands

Advances in behavioral neuroscience have been driven by technology for the past decades. Automation offers big advantages in terms of productivity, standardization and reproducibility. Video tracking is a platform technology in many paradigms Other techniques are used for different purposes, such as specialized gait analysis and motor performance / motor learning. Technology has accelerated in recent years, using advances in video standards and image analysis. There have also been strides forward in integration of in vivo technologies like telemetry, optogenetics and calcium imaging. This talk gives an overview of tools and technologies for rodents and zebrafish, and discusses the boundaries of current technologies. It is suitable for those who have an interest in measuring behavior in rodents, fish and other species.

CONFERENCE PRESENTATION 4: BREAKING BOTTLENECKS: AUTOMATED AND AFFORDABLE SYSTEMS FOR BEHAVIORAL MONITORING AND COGNITIVE EXPERIMENTS. JM Daggett, Zantiks Ltd, Cambridge, UK

Zantiks automated behavioral units are complete, networked systems. Our small, simple to use, affordable units standardise locomotor activity monitoring (circadian, toxicological, genetic), simple learning experiments (startle, habituation), and operant conditioning experiments (5CSRTT). Results are processed in real-time: data are immediately available for statistical analysis. Units use InfraRed video tracking, provide an isolated, consistent environment, and are equipped with visual and vibratory stimuli. The larger units can deliver solids and liquids (food rewards and chemical stimuli), aversive stimuli (electric shocks) and are delivered with appropriate cages, tanks and inserts. Control is from any networked device capable of web browsing (e.g., phone, tablet, laptop, chromebook, desktop). Zantiks units are currently available in three sizes and are designed for use with model

organisms including rats (LT), mice, adult zebrafish (AD), larval zebrafish, Drosophila and Daphnia (MWP), but may be used with many other species. We enable animal behavior to be measured simply.

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

Our projects are centered around people who currently suffer from or have dealt with addictions and other mental problems. 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 art pieces.

SYMPOSIUM 4: MODERATED POSTER SESSION

DIFFERENTIAL EFFECT OF BERBERINE AND MINOCYCLINE, THE INHIBITORS OF TRYPTOPHAN–KYNURENINE METABOLISM, ON NEGATIVE GEOTAXIS OF DROSOPHILA MELANOGASTER. VV Navrotskaya and G Oxenkrug, Karazin Kharkiv National University, Kharkiv, Ukraine; Tufts University, Tufts Medical Center, Boston, USA

The up-regulation of kynurenine (KYN) pathway of tryptophan (TRP) metabolism has been suggested as one of the mechanisms of aging and aging-associated disorders. We have found that *Drosophila melanogaster* mutants with deficient formation of KYN had longer life span than wild type flies; and that inhibitors of TRP–KYN metabolism (including those available for human use – berberine and minocycline) prolonged life span of wild-type flies. Literature data suggest that prolongation of life span does not necessarily associated with the improvement of health span. Therefore, in addition to the candidate drug effect on life span, it is important to assess its effect on health span as well. One of the biomarkers of health span is locomotor activity. Flies exhibit several forms of locomotor behavior, and the robustness of each behavior declines with age. The vertical climbing (or negative geotaxis) assay measures the ability of the organism to climb the walls of a vial when startled, and is an assessment of the animal's ability to complete a strenuous activity (climbing against gravity, which provides insight into the fly's level of fitness). Present study assessed the effect of berberine and minocycline on climbing activity of wild type flies. Flies were maintained on a standard Drosophila medium; 1mM of berberine (Sigma Aldrich Chemical Co, USA) or 0.87 mM of minocycline (Sigma Aldrich Chemical Co, USA) were added to nutrition medium. The climbing index was expressed as percentage of the number of flies that climbed to the top of vial relative to the total number of flies tested. Berberine stimulated vertical climbing of flies by 39%. Life span of flies from this variant, as already noted, also increased – mean by 27%, maximum by 78%. Minocycline, as berberine did, also stimulated vertical climbing of flies (by 46%) and increased mean and maximal life span. However, the effect of these two TRP–KYN metabolism inhibitors on flies viability was different: minocycline decreased quantity and survivorship of pupae filial generation while berberine did not affect the number of pupae of filial generation and decreased their lethality. The results of the study suggest that berberine prolongs life- and improves health-span (increasing viability and locomotor activity) of *Drosophila melanogaster*. Berberine may be a candidate drug for prevention and treatment of aging and aging-associated medical and psychiatric disorders. As for minocycline, further experiments may clarify whether lower doses of it would not affect viability of pupae but prolong life span of flies and stimulate locomotor activity.

FEAR CONDITIONING ACTIVATES BASOLATERAL AMYGDALA COMPLEX IN INDUCIBLE TPH2 KNOCKOUT (ICKO) MICE. B Aboagye, K-P Lesch, S Popp and W Jonas, Division of Molecular Psychiatry, ZEP, University of Wurzburg, Wurzburg, Germany; Department of Psychiatry and Psychology, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands

INTRODUCTION: Amygdalar nuclei are involved in the acquisition and expression of fear responses. Malfunctioning of these nuclear complexes is due in part to dysregulation in dorsal raphe serotonin (5HT) neurotransmission, however the neural mechanisms involved are yet to be fully deciphered. Inducible Cre-mediated recombination of Tryptophan hydroxylase 2 (Tph2), which leads to depletion of 5HT in raphe nuclei provides spatiotemporal evidence for 5HT function in contextual fear responses. This study characterizes a mouse model for acute inducible brain serotonin depletion on fear expression. **METHODS:** Mice (10-12weeks old) expressing Cre-recombinase under the Tph2 specific promoter with Exon V of Tph2 flanked by lox P site were injected with tamoxifen (2mg, daily for 5 consecutive days) to induce conditional Tph2 deletion (Tph2 icko). Six weeks after injection, the mice were subjected to contextual fear conditioning in an automated fear conditioning chamber. Brains were fixed through transcardial perfusion with 4% PFA and stained for neuronal activation marker, *c-fos*, in the amygdala. **RESULTS AND DISCUSSION**: On day 1, as indicated by freezing duration, fear acquisition was equal in all mice. After fear acquisition a significant ($p<0.001$) increase in *c-fos* expression in the basolateral nucleus of the amygdala in all conditioned mice compared to home cage control mice was detected. Interestingly, during retrieval of contextual (fear) memory on day 2, an interaction between genotype and time ($p=0.0208$) was detected for freezing. Tph2 icko mice (Tph2fl/fl) significantly froze more than Tph2+/+ ($p<0.01$) controls especially within the first 20sec in the original conditioned context, providing evidence that time dependent 5-HT depletion increases aversive contextual memories. This indicates that the basolateral amygdala complex may be involved in fear acquisition and serve as a critical site for therapeutic targeting in managing fear-related conditions. **RESEARCH SUPPORT:** German Research Foundation (DFG: SFB TRR58-A05); German

academic exchange services (DAAD) and German Excellence Initiative to the Graduate School of Life Sciences (GSLS), University of Würzburg.

COMPARING EARLY- AND LATE-ONSET ANOREXIA NERVOSA: A PEEK INTO THE STRESS-BEHAVIOR CORRELATE. SM Tan, V Kwok, A Loh, KA Zainal and HY Lee, Singapore General Hospital, Singapore

INTRODUCTION: There has been evidence of an increased incidence of older onset AN, with the illness arising in adulthood. Conflicting findings highlight a lack of understanding of late onset AN. This is particularly disconcerting, given that such cases are harder to diagnose and, therefore, have a poor outcome. Hence, we conducted this study with the following aims: To describe the clinical features of patients with late onset AN; to evaluate differences between early- and late-onset AN. **METHODS:** This is a database analysis, conducted within the Eating Disorders Service in Singapore General Hospital, an urban tertiary referral Centre. The Eating Disorders Service is the largest specialist centre dedicated to the treatment of eating disorders in Singapore. On average, 8-9 new cases are seen monthly. Cases with age of onset at 25 years or older were categorized as late onset AN. **RESULTS AND DISCUSSION:** A total of 577 patients were diagnosed with AN between 2003-2014. Early and late onset AN cases were similar in most aspects. There was a greater proportion of patients with late-onset AN who identified relationship problems as a trigger for their eating disorder, while these patients reported less teasing/comments from others. This suggests important etiological differences between these two groups of patients. As one ages, one's body image appreciation, social roles and social environment undergo changes. Relationships formed during adulthood take on a different dimension, involving meaning-making and undertaking new responsibilities. Existential well-being (i.e., beliefs and feelings of meaningfulness, purpose and satisfaction with life progress) correlates with the successful negotiation of these relationships, the failure of which may engender existential anxiety in the individual. Yalom had noted no alternative way of dealing with these existential issues other than by confronting them, and some individuals develop convoluted ways of avoiding them. It is possible that AN may serve as a maladaptive attempt to deal with negative states regarding control and meaning in life, whereby the symptoms serve to provide an exaggerated sense of control and inflated sense of uniqueness. In addition, there has been some evidence suggesting that existential considerations become more relevant in life as individuals get older. The relevance of this was subsequently established, where eating disorder symptoms were found to correlate with existential well-being in late onset AN, but not in early onset AN. In this context, the existential anxiety arising from relationship issues could well be an etiological factor unique to late onset AN. In conclusion, existential anxiety is associated with late onset AN. Our findings reinforce the notion that stress and illness behavior are highly correlated.

SEX DIFFERENCES IN ACUTE STRESS EFFECTS ON SPATIAL MEMORY AND HIPPOCAMPAL FUNCTION. VN Luine, RE Bowman, JL Gomez and PA Serrano, Hunter College of CUNY, New York, NY, Sacred Heart University, Fairfield, CT, USA

INTRODUCTION: Chronic stress elicits sexually dimorphic effects on spatial memory: males are impaired on several tasks following stress while females often show resilience to the same stressors, with either no changes or enhanced performance, in the same spatial memory tasks. However, few studies have examined the effects of acute stress on spatial memory in both sexes. Here, we investigated effects of an acute stress, 6 h in a plastic restrainer, on spatial memory. Spatial memory was assessed using the object placement task. We measured levels of protein kinase M zeta (PKMz) and GluA2 (AMPAr subunit), in the hippocampus to determine whether changes in these proteins may underlie effects of stress. PKMz is important for synaptic plasticity and maintenance of memory, and GLuR2 is an important mediator of synaptic activity. **METHODS:** Young adult, male (n=24) and female (n=24) Sprague Dawley rats were randomly assigned to control or restraint, 6hr. Two cohorts were utilized: cohort 1 was sacrificed immediately following the stress session and trunk blood was collected for corticosterone measurement and brains for analysis. Cohort 2 was allowed 30 min recovery from restraint stress and then tested on object placement. Brains and sera were collected immediately following the memory test. Corticosterone was measured by ELISA after extraction with diethylether. Hippocampal tissue was homogenized and centrifuged to obtain the cytosol and post-synaptic density (PSD) fractions. Western blot analysis measured protein levels. The Object Placement task assessed spatial memory. In the training trial (T1), rats explored two objects for 3 min. Following a 2 h inter-trial delay, one object was moved to a new location, and rats explored for 3 min, retention trial (T2). The exploration time in sec is reported for T1, and the exploration ratio, time at new location/total exploration time is reported for T2. Data analyzed by two-way ANOVA and appropriate post hoc tests. **RESULTS AND DISCUSSION:** Stress did not alter exploration in the training trial for object placement (OP), and consistent with previous studies, control males performed the retention trial better than females. Stress decreased male, but not female, exploration ratios, indicating female resilience to stress (FCON were different from MCON and MSTR but not FSTR, $p < 0.004$). Corticosterone (CORT) returned to control at 6 h post stress, and no sex differences in levels were present. If subjects performed an OP test, CORT was also at control levels, but females, control and stressed, had higher levels than males. Stress increased PKM zeta in hippocampal cytosol fraction of females, but no changes were seen in the post-synaptic density (PSD) fraction. Levels of PKM zeta in hippocampus significantly correlated with OP only in the stressed male group. More PKM zeta was associated with higher ratios. Stress did not alter GLuR2 in the hippocampus in either sex. Thus, consistent with effects of chronic stress, spatial memory in females is resilient to acute stress. Current data suggest that increases in hippocampal PKMzeta may underlie sex differences in cognitive responses to acute stress and contribute to the preservation of spatial memory in both sexes. **RESEARCH SUPPORT:** NIH grants GM 60665 and RR03037.

NEUREXAN® INFLUENCES STRESS-INDUCED ACTIVITY OF THE ANTERIOR CINGULATE CORTEX AND ASSOCIATED BRAIN REGIONS. A Kühnel, Y Fan, L Fensky, V Teckentrup, M Schultz and M Walter, Clinical Affective Neuroscience Laboratory, Magdeburg, Department of Psychiatry, CBF, Charité, Berlin, Department of Psychiatry and Psychotherapy, University of Tübingen, Tübingen, Leibniz Institute for Neurobiology, Magdeburg, Biologische Heilmittel Heel GmbH, Baden-Baden, Germany

BACKGROUND: Neurexan®, a medicinal product sold over the counter (OTC), is composed of four ingredients, *Passiflora incarnata* (passionflower), *Avena sativa* (oats), *Coffea arabica* (coffee) and *Zincum isovalerianicum* (zinc valerianate). Neurexan® has been investigated in patients with symptoms related to acute stress, nervousness/restlessness, and insomnia. The underlying neuronal mechanisms that lead to the reduction of those symptoms are less clear. Two areas of importance in stress reaction are the anterior cingulated cortex (ACC) as well as the Amygdala. Previous studies showed that especially the dorsal ACC (dACC) influences the generation of autonomic arousal. Similarly, electrical stimulation of the ACC leads to changed physiological processes like heart rate and blood pressure. Additionally, the dACC is activated under cognitive stress. Thus, the dACC seems to be an important area controlling stress reactivity. We hypothesize Neurexan to induce changes in the activation of dACC and associated areas during a stress task. **METHOD:** The drug effect of a single dose was investigated using a randomized, placebo-controlled, double-blind, two-period-crossover design. A total of 36 male subjects (aged 31-59) took part in the experiment and completed various fMRI tasks. The stress response was induced using the ScanSTRESS (Streit et al, 2014), which uses arithmetic tasks as well as mental rotation tasks. Additionally the stress response was measured by saliva cortisol concentration and visual analogue scales (VAS) for nervousness and anxiety. **RESULTS:** Paired-t-test analysis showed a significant cluster in the region of interest right dACC in the contrast placebo > verum in rotation stress > rotation control after correcting for multiple testing in the ROI. Additionally correlations with relevant psychological and endocrine measures will be presented. **CONCLUSION:** The intake of single dose of Neurexan® significantly reduces right dACC activation during psychosocial stress compared to the intake of placebo. **RESEARCH SUPPORT:** Biologische Heilmittel Heel GmbH, Baden-Baden, Germany.

EFFECTS OF NEUREXAN® ON EMOTIONAL BRAIN RESPONSE. L Fensky, V Teckentrup, A Kühnel, M Schultz, Y Fan and M Walter, Department of Psychiatry and Psychotherapy, University of Tübingen, Leibniz Institute for Neurobiology, Magdeburg, Clinical Affective Neuroimaging Laboratory, Magdeburg, Biologische Heilmittel Heel GmbH, Baden-Baden, Department of Psychiatry, Charité, CBF, Berlin, Germany

INTRODUCTION: Neurexan®, a medicinal product sold over the counter (OTC), is composed of four ingredients, *Passiflora incarnata* (passionflower), *Avena sativa* (oats), *Coffea arabica* (coffee) and *Zincum isovalerianicum* (zinc valerianate). Neurexan® has been tested in patients with acute stress, nervousness/restlessness, and insomnia. Induced stress sensitizes the amygdala, which increases vigilance/anxiety and drives in turn the stress response. The amygdala is involved in the emergence of fear and emotional behavior. Amygdala reactivity to negative stimuli is a reliable phenotype that closely associates with stress regulation and can be assessed in the Hariri paradigm. Furthermore, a linkage between an increased level of a stress hormone and increased emotional response to angry faces exists in patients with social phobia. As previous research suggested an attenuated neuroendocrine stress response in healthy volunteers induced by Neurexan®, we wanted to further explore its effects on emotional brain response. **METHODS:** In a randomized, placebo-controlled, double-blind, two-period crossover trial brain response to the Hariri task, an emotional paradigm, of 39 healthy, moderate stressed males was measured after intake of a single dose of Neurexan® and placebo control via 3 Tesla functional magnetic resonance imaging. **RESULTS AND DISCUSSION:** Paired t-test analysis showed a significant drug effect ($p<0.05$, corrected for multiple comparisons), in the left amygdala. Plotted β values showed stronger amygdala activations in placebo vs. verum condition. We found a significant reduction of BOLD response to negative faces in the left amygdala during the Neurexan® vs. the placebo session. Neurexan® reduced the emotional brain response to negative stimuli. **RESEARCH SUPPORT:** Biologische Heilmittel Heel GmbH, Baden-Baden, Germany.

THE EFFECTS OF 2-[4-(TRIFLUOROMETHYL)PHENYL]-5,6-DIHYDRO-4H-PYRROL-[1,2-C] TRIAZOLO-7-IUM-3-OLATE IN ADULT ZEBRAFISH IN THE NOVEL TANK TEST. TO Kolesnikova, SL Khatsko, AV Zhdanov, TV Gluhareva, Yul Nein and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: Mesoionic 1,2,3-triazolium-5-olate, and especially their fused analogues are poorly known class of heterocyclic compounds, so preclinical screening to identify their potential pharmacological properties is one of the important task in chemistry and pharmacology. Zebrafish (*Danio rerio*) is a very popular animal model for toxicology and neurobiology research and CNS drug discovery. Here we characterized behavior effects of a 2-[4-(trifluoromethyl)phenyl]-5,6-dihydro-4H-pyrrol-[1,2-c]triazolo-7-ium-3-olate in adult zebrafish. **METHODS:** 96 adult wild type short- fin zebrafish were used. Zebrafish were housed in 40-L tank, according to the standards of zebrafish care. All fish were experimentally naïve before testing. The novel lank test was utilized to assess zebrafish behavior for 5 min following their 20-min exposure to 1, 5, 10, 25 and 50 mg/L of the drug. We analyzed the latency (s) and number of top entries, time spent in the upper half, duration and frequency of freezing and the number of anxiety-like erratic movements. **RESULTS AND DISCUSSION:** While the tested compound does not alter behavioral parameters at 1, 5, 10 and 25 mg/L, its higher dose of 50 mg/L significantly increased freezing frequency ($p=0.0024$) and duration ($p=0.0022$). Also, the drug reduced the number of top entries ($p=0.0009$) and time in the upper part of the tank ($p=0.0010$), and prolonged the top latency ($p=0.0006$), compared with control group. Taken together, our results suggest that this new chemical substance is likely to have psychoactive anxiogenic-like, sedative or intoxicating properties. **RESEARCH SUPPORT:** Ural Federal University, Ekaterinburg, Russia.

SOCIODEMOGRAPHIC CHARACTERISTICS OF BOSNIAN WAR VETERANS WITH ENDURING PERSONALITY CHANGE AFTER CATASTROPHIC EXPERIENCE DIAGNOSIS. S Sarkic-Bedak, A Hrnjica, I Lokmic-Pekic, S Bise, B Kurtovic and M Ahmic, Cantonal Psychiatric Hospital Sarajevo, Sarajevo, Bosnia and Herzegovina

INTRODUCTION: Although the war in Bosnia and Herzegovina has ended 20 years ago, war veterans with the ICD-10 diagnosis F62.0 (enduring personality change after catastrophic experience) are on the margins of the society, unemployed and at the verge of existence. These patients have sno adequate family or social support, no possibility of occupational retraining, and therefore, lack proper integration into the society. Consequences of such situation can be seen through family relationships dysfunction, feelings of rejection, comorbidities and in particular, abuse of alcohol. Psychological destabilizations are often, which are causing new re-hospitalizations. **OBJECTIVE:** To examine the sociodemographic characteristics of the B-H war veterans hospitalized in our hospital in 2014-2016. **MATERIALS AND METHODS:** Twenty patients fulfilling the ICD-10 criteria for F62.0 diagnosis were analyzed for their sociodemographic characteristics (age, education, employment status, marital status) as well as most frequent disease symptoms and comorbidities. **RESULTS:** Patients were male (100%), with average age of 51; 12 (60%) patients had completed secondary education, 1 patient (5%) had completed college education, and 7 patients (35%) had completed primary school education. 12 (60%) patients were married, 6 (30%) were divorced, while 2 patients (10%) were single. Only 2 patients (10%) were employed, 5 patients (25%) retired, and 13 (65%) patients remained unemployed without income. All patients were participants of war (100%), out of which 17 patients (85%) were soldiers, and 3 patients (15%) were civil victims of war. The most frequent symptoms in all examinees were insomnia, nightmares, depressive mood and social isolation. Alcohol abuse, as the most frequent comorbid state was present in 11 patients (55%), while 9 of them (45%) do not consume alcohol. **CONCLUSION:** All analyzed patients were socially endangered and lacked an adequate social or family support. This represents an important social problem, and, in addition to the medical treatment *per se*, requires a multidisciplinary approach with an active engagement of the wider social community.

DIFFERENTIAL FOREBRAIN c-FOS EXPRESSION INDUCED BY NOVELTY AFTER CHRONIC STRESS. AI Bulava, OE Svarnik and YI Alexandrov, Laboratory of Psychophysiology, Institute of Psychology RAS, Moscow, Russia

INTRODUCTION: Induction of immediate early genes (IEG), such as *c-fos*, may be important and necessary for the establishment of prolonged functional changes in neurons for learning and memory. Effects of the novelty on *c-fos* expression in rat brain are extensively studied. However, less is known about the cellular and molecular changes that are induced in the brain by novelty after chronic stress. **METHODS:** Adult male rats were subdivided into two experimental groups. “Stressed group” rats received a single 5-min of inescapable electric footshock (15×10s, 1 mA) exposure for 14 consecutive days. A group of rats not exposed to the footshock served as “unstressed control group”. Both groups were placed in a novelty context for 5-min. Intact control animals were kept in individual cages in a dark/light cycle-controlled vivarium. Novelty-induced *c-fos* expression was assessed in localized regions of the basal forebrain, including the frontal cortex (Fr3), prelimbic cortex (PrL), rostral cingulate cortex (Cg1), primary and secondary motor cortex (M1, M2). For detection of c-Fos protein, the well-established immunohistochemical diaminobenzidine technique was applied. **RESULTS AND DISCUSSION:** All investigated areas of the forebrain showed differential activation by novelty vs. intact animals. c-Fos induction was different between the two groups of rats: unstressed and stressed. We also observed specific pattern of novelty-induced *c-fos* expression after chronic stress as compared to unstressed rats. These results indicate that the brain sub-systems differ under chronic stress, likely preparing the body to future environmental changes. **RESEARCH SUPPORT:** RSF grant 14-28-00229.

THE INFLUENCE OF INTRA-UTERINE HALOPERIDOL INTRODUCTION ON THE POSTNATAL SLEEP–WAKEFULNESS CYCLE (SWC) FORMATION IN RATS. EA Aristakesyan, VV Kuzik, IY Morina and EP Stankova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

Dopamine and its receptors are present in the developing rat brain since 13-15 day of embryonal period. During this period, embryonal dopamine affects neurogenesis, neuronal migration and differentiation of brain structures. Formation of the dopamine synaptic contacts usually occurs at the end of embryonic development and in the early postnatal development period (ending at 1.0-1.5 months, when there is a final formation of the sleep-wakefulness cycle, SWC). This study aimed to assess the effects of intrauterine drug induced dopamine imbalance on postnatal development of SWC. **METHODS:** We performed laparotomy surgery in pregnant Wistar rats (n=15) on the 19th day of pregnancy. Fallopian tubes with the fetuses were extracted, and each fetus was injected by 0.1-0.2 ml aqueous solution of haloperidol, the blocker of dopamine D2 receptors, into amnion at 50 mkg/kg. Fetuses of control rats (n=6) were injected with saline. Fetuses were then returned to the abdominal cavity, and midline abdominal incision was sutured in layers. To register the SWC electrodes were implanted in the motor cortex and hippocampus to all surviving after intrauterine haloperidol introduction pups E19 (n=7) and control pup groups (P30) (n=14), aged 27-30 days. The duration of the SWC registration was 3 h. The registration of SWC in P30 group rats before and after injection of haloperidol (50 mkg/kg) was 3+3 h. **RESULTS AND DISCUSSION:** Surgery and haloperidol injection in fetus amnion at 19 days of gestation does not impair the course of pregnancy in general. However, unlike control females, the duration of pregnancy in E19 female rat group increased by week. Newborn rats were weaker and number of offspring was the less (4-5 instead of 8-12 animals in control group). E19 pups gained weight slowly and often died 1-2 days after birth. They started gaining weight on third week of life, and their weight was the same as their peers rats to the 4th week. In intact rats (P30) aged 30-37 days, the

WSC was presented by wakefulness (W) 47.2±4.4%, cataleptic stage (CS) 6.4±2.3%, slow-wave sleep phase (SWS or NREM sleep 29.1±3.3% and sleep with rapid eye movements (REM sleep) 10.4±3.3%. At monthly E19 rats pups W share was 25.3±2.3%, CS representation increased by 31.3% and reached 12.82±2.23%, significantly increased the share of NREM (54.9±2.21%) due to the greater representation of deep sleep stage. REM representation was reduced to 6.9±0.73%. EEG pattern was characterized by the dominance slow delta-waves, whose amplitude reached 160-220 mkV, also changing the character of the REM sleep EEG pattern. In intact rats, for the REM phase of sleep dominated theta wave range, but in E19 rat pups are dominated alpha and beta oscillations ranges band activity. Haloperidol injection to P30 rats caused similar changes in the SWC timing, however, they developed only at the second hour after injection, but disappeared by the 3rd hour. **CONCLUSION:** Our findings suggest that prenatal haloperidol introduction in rat fetus has teratogenic effects in general. The introduction of the D2 receptor blocker is especially dangerous at the early gestation periods of 13-14 days of embriogenesis - the time when the formation and differentiation of CNS structures, particularly hippothalamic-hippocampal system of SWC integration, only begins. Also, the dopamine receptor system in that period has no embryogenesis neurotransmitter function, but affects neurogenesis, afferentation and neuronal migration. Blocking D2 receptors at later gestation stages (E19) has less damaging effects on the CNS sleep regulating centers. The thalamo-cortical system of SWC integration in rats is usually formed during this embryonal period. Nevertheless, the damaging effect of haloperidol on SWC persisted long enough until the puberty in the E19 rat pups.

INVESTIGATION OF DEPRESSIVE SYMTOMS AND NEURODEGENERATION IN MESOLYMBIC SYSTEM IN A RAT MODEL OF A PRECLINICAL STAGE OF PARKINSON'S DISEASE. AR Gazizova, DV Plaksina and IV Ekimova, ISBS Fellow, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Parkinson's disease (PD) is a chronic disorder characterized by core motor symptoms and a wide range of non-motor symptoms. Depression negatively affects the quality of life of PD patients and can antedate the development of motor phenomena by several years [Ossowska et al. 2013]. Pathomechanisms underlying depressive symptoms in PD are unknown. There are no data on whether the emotional disturbances could be diagnostic markers of a preclinical stage of PD. Studies on PD patients with depression show destructive changes in mesolimbic dopamine (DA)-ergic pathway (ventral tegmental area (VTA) and ventral striatum, VS). The aim of this study was to assess whether the pathomorphological alterations in mesolimbic DA-ergic system are linked to appearance of depressive-like behavior in a rat model of a preclinical stage of PD. **METHODS:** The work was carried out in male Wistar rats (250-300 g). Intranasal injections of specific proteasome inhibitor lactacystin (LC) were used to mimic a preclinical stage of PD. To quantify the number of DA-ergic neurons in the VTA and their axons in the VS immunohistochemical methods with antibodies against tyrosine hydroxylase were applied. To detect anhedonia (a core symptom of depression), the sucrose preference test was used. **RESULTS AND DISCUSSION:** Earlier, we showed that a model of a preclinical stage of PD induced by intranasal LC injections is characterized by the absence of motor phenomena and subthreshold degeneration level in DA-ergic nigrostriatal and olfactory systems [Ekimova et al. 2016]. The present study demonstrates the loss of 27% of DA neurons in the VTA and 23% of their axons in the VS 21 days after the initial LC injection. That corresponds to subthreshold degeneration level compared to level in a clinical stage (50-70%). Destructive changes in mesolimbic system were accompanied by hedonistic deficits, reflected by reduced sucrose preference. **CONCLUSION:** Our results suggest that the development of depressive-like state occurs at subthreshold neurodegeneration level in the VTA and the VS in a rat model of a preclinical stage of PD. Depression symptoms with other non-motor markers can be used for early PD diagnosis. **RESEARCH SUPPORT:** Russian Science Foundation Grant 16-15-00278. Morphological studies were conducted at the Center for Collective Use of IEPB RAS.

NEUROPROTECTIVE EFFECTS OF CHAPERONE GRP78 IN A RAT MODEL OF PARKINSON'S DISEASE. MB Pazi, DV Plaksina, LE Nitsinskaya and IV Ekimova, ISBS Fellow, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Parkinson's Disease (PD) is a progressive neurodegenerative disorder characterized by disturbances in motor behavior and other forms of behavior (e.g., anxiety and depression). One of the reasons for neuronal death in the brain during PD is formation of toxic aggregates of α-synuclein in cytosol and endoplasmic reticulum (ER). Members of a heat shock proteins family HSP70, especially cytosol inducible Hsp70 and glucose regulated heat shock protein (Grp78) of ER, prevent formation of toxic protein aggregates through controlling folding and refolding. Grp78 exerts neuroprotective effects in animal models of senile retina degeneration, cerebral ischemia and α-synuclein pathology [Gorbatyuk et al. 2012]. The aim of this study was to establish and evaluate the neuroprotective activity of Grp78 in a rat model of neurodegeneration in the nigrostriatal system mimicking a preclinical stage of PD. **METHODS:** Experiments were carried out on male Wistar rats (230-250 g). To develop a model of the nigrostriatal system degeneration mimicking a preclinical stage of PD, we used proteasome inhibitor lactacystin (LC) bilaterally injected into the Substantia Nigra pars compacta (SNpc) twice, with a 7-day interval. Recombinant human protein Grp78 BiP was delivered intranasally 4 and 24 h after each LC injection, and 7 days after the last injection. Twenty-one days after the first LC microinjection, behavior tests were performed and the animals were sacrificed for further immunohistochemical and biochemical analyses. **RESULTS AND DISCUSSION:** Microinjections of LC in the SNpc resulted in the loss of 17% of dopaminergic nigral neurons and their axons in dorsal striatum, and an increase in the number of microglial cells in the SNpc by 43%; it also elevated TH levels in dorsal striatum. No motor impairments were observed. Such changes are peculiar for the preclinical stage of PD. Treatment with Grp78 increased the number of survived DA-ergic neurons in the SNpc and their axons in the dorsal striatum 1.3 times compared with untreated animals. Number of microglial cells in the SNpc and TH content in the dorsal striatum returned to control values. The obtained results indicate

neuroprotective potential of Grp78 and may be used for developing the strategy for preventive treatment of PD. **RESEARCH SUPPORT:** State budget assignment for 2013-2017 (State reg. 01201351570). Morphological studies were conducted at the Center for Collective Use of IEPB RAS.

AMPHETAMINE AFFECTS BEHAVIORAL PATTERNS OF OBSESSIVE-COMPULSIVE AND ADDICTIVE GAMBLING IN THE RAT MARBLE BURYING TEST. ND Yakushina, AG Pshenichnaya, VA Lebedev, ER Bychkov, KE Gramota, YuN Bessolova, KA Privalov, AM Potapkin and PD Shabanov, ISBS Fellow, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: The rodent marble burying test is a useful test for modeling the obsessive-compulsive disorder as a neurobiological component of pathological gambling. Several behavioral components of obsession (obsessive and anxious ideas) and compulsions (obsessive actions) directed to anxiety reduction are modeled in this test. Animal models of gambling behavior could make a significant contribution to improving our understanding of the neural and neurochemical basis of gambling. Serotonin and dopamine play important roles in impulsivity and addiction, and also contribute to gambling behavior (Zeeb et al. 2009). **METHODS:** The effect of psychostimulant amphetamine on rat behavior was studied in the marble burying test, anxiety-phobic model (scale), open field (evaluation of motor and emotional activity) and resident-intruder test (intra-species behavior). **RESULTS:** Amphetamine at 0.5 and 1.5 mg/kg increased the number of buried marbles and elevated anxiety levels in dose-dependent manner, accompanied with reduction of explorative activity, elevation of motor activity and the number of individual behavioral patterns. **CONCLUSIONS:** The dopaminergic system of the brain activated with amphetamine is involved in obsessive-compulsive behavior and pathological gambling. Pathological gambling as a type of addictive human pathological conditions includes motivational sphere that manifests as the obsessive-compulsive disorder due to altered brain dopaminergic system. Since pathological gambling is often viewed as an addiction/dependence disorder, modeling its dopaminergic mechanisms will help identify and clarify common brain mechanisms of gambling addiction and obsessive-compulsive behavior.

DOPAMINE REINFORCING AND OREXIGENIC EFFECTS DURING ELECTRICAL STIMULATION OF THE LATERAL HYPOTHALAMUS IN RATS. YuN Bessolova, OA Yakovlev, AA Lebedev, ER Bychkov, VA Lebedev and PD Shabanov, ISBS Fellow, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: The present study focuses on the involvement of several neurochemical systems in the regulation of neural populations in the lateral hypothalamus in feeding behavior and emotional reinforcement of the brain. Human and animal eating disorders occur due to an imbalance in the mechanisms of coupling appetitive, i.e., the emotional-motivational component of appetite, and consummator stages of goal-directed behavior. The resultant hyperphagia or hypophagia further lead to serious endocrine and metabolic changes. Medial forebrain bundle passes through the lateral hypothalamus having predominantly dopamine nature and plays a key role in the reinforcing properties of psychotropic drugs. It is therefore important to investigate the effects of dopamine reinforcement mechanisms that evaluate pragmatic importance and possibility of food and emotional behavior. An extrahypothalamic CRF system, the extended amygdala, triggers brain activation of the central stress-dependent mechanisms, thereby contributing to pathogenetic mechanisms of neurochemical imbalance of appetitive and consummatory stages, and the formation of a food addiction. **METHODS:** We investigated the structural and functional organization of the center of hunger and center of the reward of the lateral hypothalamus using stereotaxic methods, implanting chronic electrodes into the lateral hypothalamus and utilizing electrical stimulation of subcortical brain structures. **RESULTS:** Electrical stimulation of the same electrode in the lateral hypothalamus induced both self-stimulation in Skinner box and orexigenic effects of well-fed rats in the chamber to test food behavior. Current thresholds were lower by 7-9% during testing the orexigenic effects in the chamber to test food behavior. Sulpiride (20 mg/kg i.p.), an antagonist of D2 dopamine receptors, abolished both self-stimulation in Skinner box and orexigenic effects (intake of food pallets). Sulpiride 5 mg/kg i.p. had smaller effect on both self-stimulation and orexigenic effects in the chamber to test food behavior. At the same time sulpiride 5 mg/kg i.p. decreased number of pedal pressing in Skinner box by 18% and increased current thresholds by 13%. Sulpiride at 5 mg/kg i.p. increased number of electrical primings to food intake by 66% and decreased number of food pellets by 28%. **CONCLUSIONS:** Overall, our data support that lateral hypothalamic electrode stimulation may enhance a hedonic taste signal, to effectively make food taste better. This effect can be mediated by direct lateral hypothalamic projections to the dopamine system. Hedonic enhancement may be a psychological mechanism for producing increases in food intake, and can also contribute to electrode self-stimulation effects. Lateral hypothalamic stimulation is similar to palatable food in inducing both appetite and reward (Hoebel, 1988).

TAUREPAR PROTECTS THE ISCHEMIC RAT BRAIN AGAINST OXIDATIVE STRESS AND BEHAVIOR DISORDERS. VV Bulion, EN Selina and IB Krylova, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Oxidative stress plays a significant role in the pathogenesis of ischemic cerebrovascular disorders. The basic mechanisms of neuronal damage and disruption of brain integrative activity include depletion of energy resources, violation of ionic homeostasis, excess accumulation of excitatory amino acids, and overproduction of reactive oxygen species. Brain tissue is particularly sensitive to oxidative stress. Therefore, the search for effective substances that can prevent the development of oxidative stress and reduce the ischemic brain damage is of current interest. In our department of neuropharmacology, the N-phenylalkyl derivative of neuroactive sulfoaminoacid taurine, taurepar, was synthesized. The antioxidant effect of this compound is shown

in CCl4 toxic liver injury model. The aim of this work was to study the antioxidant properties of taurepar in the brain ischemia and its effect on memory, learning and behavioral responses in rats. **METHODS:** Experiments were performed on male Wistar rats. The influence of taurepar (25 mg/kg) on energy metabolism, lipid peroxidation and antioxidant system in the brain during acute ischemia caused by complete bilateral occlusion of the common carotid arteries (90-min and 24-h occlusion) was studied. Taurepar effect on the cognitive functions was tested in the brain chronic ischemia model (21 days) with complete occlusion of the left common carotid artery and restricted up to 50% from baseline blood flow in the right common carotid artery. **RESULTS AND CONCLUSIONS:** Acute cerebral ischemia resulted in decrease of ATP and increase of lactate. The maximum changes were observed after 90-min occlusion. The 24-h ischemia led to intensified lipid peroxidation and inhibited antioxidant system. Taurepar normalized energy metabolism, reduced intensity of lipid peroxidation and restored enzyme activity of antioxidant system. Chronic cerebral ischemia resulted in emotional behavior changes, research and motor activity. Animals demonstrated amnesia of passive avoidance conditioned reflex (PACR). Taurepar limited or eliminated cognitive impairment of brain. It enhanced locomotor and research activity, improved emotional behavior and prevented amnesia of PACR. Thus, taurepar can contribute to maintaining long-term memory engrams and consolidating of the information received. Antiamnestic effect of taurepar can be due to its metabolic (antioxidant) and membrane-stabilizing properties.

DERIVATIVE OF FLUORENCARBONIC ACID PREVENTS DEPLETION OF MONOAMINES LEVELS IN THE BRAIN OF DEPRESSED RATS. LK Khnychenko, EE Yakovleva and ER Bychkov, Anichkov Department of Neuropharmacology, Institute of Experimental Medicine, St. Petersburg, Russia

Pharmacotherapy of anxiety-depressive disorders has attracted particular attention of researchers and clinicians due to intense pace of modern lifestyle, physical/emotional stress, and increased prevalence of mental disorders. Modern treatment strategy of anxiety-depressive disorders does not fully meet the practical needs of medicine, and numerous antidepressants and anxiolytics used in clinic are not without drawbacks. Therefore, the development of a new approach to pharmacological correction of anxiety and depressive disorders remains relevant. In our Department of Neuropharmacology at IEM, the structural analogues of benactizine (amizil), a derivatives of fluorencarbonic acid, providing central muscarinic anticholinergic action has been synthesized. Compounds of this series, showing pronounced psychotropic effect, do not have side peripheral anticholinergic effects. Depression develops due to deficits of activity of different brain regions, and is accompanied by aberrant monoamine metabolism. Here, we study the influence of hydrochloride 2-(diethylamino)-ethylic ether of 9-hydroxy-9-H fluorencarbonic acid on the content changes of monoamines and their metabolites in the brain structures in a rodent model of depression, modeled in rats with a single injection of reserpine (4 mg/kg). The contents of monoamines in the hypothalamus and striatum were determined by HPLC. Preliminary injections of the original derivative hydrochloride 2-(diethylamino)-ethylic ether of 9-hydroxy-9-H fluorencarbonic acid (9 mg/kg) prevent depletion of monoamines levels caused by the injection of reserpine in the hypothalamus (NE, 5-HT 5-HIAA) and striatum (DA, 5-HT, 5-HIAA). Importantly, the observed neurochemical changes (removal of serotonin deficiency, stabilization of the content of norepinephrine and dopamine) correlate with high antidepressant activity of this substance the detected in the forced swimming test (Porsolt test). It is possible that the structural analogue of amizil takes part in the processes of normalization of 5-HT and NE in rats with depression-like states, and this may exert an antidepressant effect. These data substantiate the prospect of development (based on derivative of fluorencarbonic acid) of a novel domestic antidepressant.

BEHAVIORAL EFFECTS OF TILETAMINE, A NON-COMPETITIVE N-METHYL-D-ASPARTATE (NMDA) RECEPTOR ANTAGONIST, IN ADULT RATS IN THE OPEN FIELD TEST. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov, YuYu Morzherin and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: With the wide spread of drug abuse globally, studies of biological effects of ketamine and its chemical analogs, such as tiletamine, become necessary. Like ketamine and phencyclidine, tiletamine is a non-competitive N-methyl-d-aspartate (NMDA) receptor antagonist commonly used in veterinary medicine for anesthesia of dogs and cats. The aim of this study was to characterize acute behavioral effects of tiletamine in adult rats. **METHODS:** A total of 60 white 6-month-old female rats were used for this study. The open field test was utilized here to assess rat behavior for 5-min following a 10-min or 30-min pre-treatment with tiletamine given by intraperitoneal injection. All rats were experimentally naïve prior to their acute exposure to 1 and 10 mg/kg of tiletamine (N=10 per group), and were housed in groups of 5 per cage at Ural Federal University Animal Facility, according to the standards of laboratory rat care. Here, we assessed the latency, duration and frequency of locomotor activity, freezing, rearing, and wall-leaning behavior. **RESULTS AND DISCUSSION:** Overall, tiletamine at the dose of 1 mg/kg did not change any parameters 10 or 30 min past injection. However, 10 mg/kg tiletamine significantly reduced the duration and frequency of freezing ($p < 0.001$), as well as wall-leaning ($p < 0.01$) and rearing ($p < 0.01$) behavior, but increased number of horizontal locomotion measure - squares crossed ($p < 0.001$) in the open field test 10 and 30 min after the administration, compared with control. In addition, tiletamine also caused overt disorientation and aberrant locomotion (e.g., ataxia and/or posture instability). Thus, tiletamine is likely to have psychoactive sedative-like properties in rodent models, suggesting that novel CNS drugs can be developed based on targeting central NMDA receptors. **RESEARCH SUPPORT:** Ural Federal University, Russia.

EFFECTS OF U-47700, A μ-OPIOID RECEPTOR AGONIST, IN ADULT MICE IN THE OPEN FIELD AND THE TAIL-FLICK TEST. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: Developed in 1978, 3,4-dichloro-N-[(1R,2R)-2-dimethylamino)cyclohexyl]-N-methylbenzamide (U-47700), is a μ-opioid receptor agonist acting as an analgetic ~7.5 times more potent than morphine. The global use and abuse of U-47700 are currently on the rise, necessitating a better understanding of tiletamine effects in-vivo. Here, we characterize acute behavioral and analgesic effects of U-47700 in adult mice. **METHODS:** 50 white outbred 6-month old male mice were used for this study, exposed to the open field test 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 examined the latency, duration and frequency of locomotor activity, freezing and vertical rearing behavior. The tail-flick test was used to assess analgesic properties of the drug in response to the 54-56 ºC water immersion. **RESULTS AND DISCUSSION:** Overall, U-47700 at 1 mg/kg does not change behavioral parameters following the 60-min exposure. At 5 and 10 mg/kg doses, U-47700 significantly increased duration and frequency of mouse freezing and rearing behavior, compared to controls. At the 25 mg/kg dose, the drug caused prominent catalepsy-like responses of the hindlimbs and Straub tail (paralleling well-known morphine catalepsy), inhibited exploratory and locomotor activity, and caused overt disorientation, ataxia and abnormal breathing. In the tail-flick nociception test, reduced pain sensitivity to high temperature was observed at 10 and 25 mg/kg. Taken together, these findings suggest U-47700 as potent psychoactive drug with sedative-like properties and robust analgesic effects.

ANTISTRESS PROPERTIES OF "A" AND "B" COMPOSITIONS. AF Safonova, Institute of Experimental Medicine, St. Petersburg, Russia

Extraordinary challenges of the body cause noticeable changes in organs and tissues. The purpose of the present study was to determine the possible preventive and medical action of "A" and "B" products on macro- and the microscopic changes in organs arising in water-immersion stress. These products are highly concentrated cellular fraction obtained from special culture of S-yeast. "A" and "B" compositions differed on protein, polysaccharides content, in particular, glucans. The water-immersion stress in rats was caused by 6-h immersions up to the xiphoidal process of the immobilized animals into a pool with water of room temperature. "A" and "B" drugs in the doses of 50 and 250 mg/kg (aqueous solution) were introduced via the probe into the stomach 30 min before stress influence with the preventive purpose and within 7 days after stress influence - with the medical purpose. The control group of animals received normal saline solution in equivocal volume. The effect of the studied compositions was estimated on weight indexes of body weight, internal organs and internal gland secretion. Their histomorphological structure was studied in collaboration with Prof. AS Gordeladze. The water-immersion stress without use of the studied compositions caused a complex of morphological changes which expressiveness varied in different animals and different organs of one animal. Morphological expressions of microcirculation with organ and intra-organ redistribution of blood in the lungs, liver, adrenal glands were constant that correlated with their weight indexes. In all animals, multiple erosions in the stomach, disturbances of spermatogenesis, expressed marrow hyperplasia in adrenal glands, decreased thickness of cortex layer and medulla delymphatization in thymus were found in all animals. At preventive introduction of "A" and "B" compositions, no differences from control were registered. At medical introduction of the compositions within 7 days after stress, modeling distinct dynamics of recovery processes was observed. The main manifestations of pathological processes normalization were in the stomach, lungs and ovary. They were expressed by erosion healing with full regeneration; increase of compensatory-adaptive processes in adrenal glands, thymus, liver; restoration of spermatogenesis; lack of blood flow disorders and pathology of respiratory compartments of lungs; increase of body weight. When comparing morphological data for two drugs, no differences were found. However, at medical introduction of "B" composition in the dose of 250 mg/kg, there were morphological signs of more complete recovery in the stomach, liver and ovary.

ACUTE EFFECT OF MANUAL LYMPHATIC DRAINAGE IN MEN AND WOMEN ON STRESS BIOMARKERS. MSM Pires-de-Campos, EAM Camargo, AL Souza, PC Silva, DM Marcorin, LL Rodrigues, and DM Grassi-Kassisse, Methodist University of Piracicaba, State University of Campinas, Campinas, Brazil

INTRODUCTION: Manual lymphatic drainage (MLD) restores and maintains the hydroelectrolytic balance, as well as, steroid hormones also interfere in this balance, such as the cortisol. Its secretion follows the circadian rhythm (RCC), with higher concentration in the morning and lower in the night. Changes in concentration or rhythmicity indicate stress, interfering in the sympathoadrenal axis. The heart rate variability (HRV) is an indirect non-invasive technique widely used to analyze the activity of the autonomic nervous system on cardiac rhythmicity. In addition, it is not yet fully understood how MLD interferes with these biomarkers of stress. We aimed to compare the acute effect of MLD in men and women on stress markers through the concentration (CC) and rhythmicity of cortisol (RCC) and HRV. **METHODS:** 40 healthy and sedentary volunteers, 7 men (22.6±1.1 years; BMI 23.2±1.2 kg/m2), 33 women (21.5 ± 0.5 years old, BMI 21.5 ± 0.4) were assessed. The experiments were carried out in an environment with temperature and relative humidity controlled, (22-24 °C, 40-60%), always in the morning, in two 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. The HRV was collected for 15 min at the baseline, 0 (before) and 105 min (after) of the MLD and evaluated the 5 min more stable. **RESULTS:** The groups did not present differences in CC upon waking or in daily production. RCC was preserved on the control day. However, with MLD there was no daytime fall in CC for men, whereas in women there was a decrease in CC at noon in relation to the control day. The MLD did not change the daily cortisol production of the groups, nor was there any difference between the groups. The study of the HRV, in the time domain analysis using the geometric method (SD1, SD2 and SD1 / SD2 ratio), as well as the frequency domain analysis (LF, HF and LF / HF ratio) demonstrated that in both groups were predominantly vagal on the control day. The MLD promoted greater sympathetic activity in men, and in women vagal activity was observed after the technique. MLD alters the rhythmicity of cortisol and promotes sympathetic predominance in men, but lowers CC in women. **RESEARCH SUPPORT:** Fapesp – São Paulo

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EFEECTS OF AGRP ON NOREPINEFRINERGIC BRAIN NEURONS. LO Saveleva, AL Mihrina and IV Romanova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

INTRODUCTION: Norepinephrinergic (NE) brain neurons are involved in regulation of various functions in human and animals, including stress responses. The investigation of mechanisms of regulation of NE-neurons functional activity is an important problem of stress physiology. In the brain, the agouti-related peptide (AgRP) is expressed in hypothalamic arcuate nucleus neurons, which project to various brain regions, including NE-areas locus coeruleus (LC) and the nucleus tractus solitaries. The aim of the investigation is to study the effect of AgRP on NE neurons of LC. **METHODS:** C57BL/6J mice after anesthesia were injected with 0.6 nmol of AgRP25-51, or AgRP83-132 or 0,9% NaCl (control) in the LC (AP=5.5mm; L=1mm, DP=3.5mm) bilaterally. Three hours after the injections brains were fixed for immunohistochemical (ABC), real-time PCR and HPLH analyses. **RESULTS AND DISCUSSION:** The analysis of LC coronal brain sections shows the reduction of the optical density of phosphorylated form of tyrosine hydroxylase (TH-serine31; 47 %, $p<0.05$) and reduction of dopamine-β-hydroxylase (DBH; 62 %, $p<0.05$) in the NE-neurons after AgRP25-51 injections. Injections of AgRP83-132 led to reduction of optical density of TH-serine31 (33 %, $p<0.05$), TH-serine40 (47%, $p<0.05$) and DBH (44%, $p<0.05$). The expression of the NE transporter gene significantly decreased after injection of AgRP83-132 and AgRP25-51 (75% and 93%, correspondingly). The HPLH analysis showed lower NE levels in the striatum (54 %, $p<0.05$) and cerebral cortex (22 %, $p>0.05$) after injection of AgRP25-51. TH and DBH are key enzymes of NE biosynthesis. Phosphorylation of serine residues leads to the transition of TH to the active form. These enzymes optical density reduction and the decrease of NE level in striatum and cortex indicate the inhibition of the NE neurons functional activity by AgRP fragments. Thus, changes of NE level after AgRP treatment may affect stress response. Collectively, our data demonstrate a suppressive effect of AgRP fragments on NE neurons via different intracellular pathways.

Day 3. Thur, May 18, 2017

SYMPOSIUM 5: WORK STRESS
Chair: Ph Fauquet-Alekhine (France)

INTRODUCTION: UNDERSTANDING WORK STRESS

MODELING HEART RATE VS SHORT-TERM MENTAL STRESS INDICATORS. Ph Fauquet-Alekhine, L Rouillac, J Berton and JC Granry, Department of Psychological and Behavioral Sciences, London School of Economics and Political Science, London, UK; Laboratory for Research in Science of Energy, France and Germany, Nuclear Power Plant of Chinon, Avoine, University Hospital of Angers, France

INTRODUCTION: Many research domains have identified and studied mental stress as a crucial factor of influence or consequence: for example, mental stress may affect performance or social interaction, may cause or be a consequence of pathologies; it is also studied when combined with tiredness or related to sleepiness. Different kinds of mental stress were identified, mainly chronic stress and short- term (acute) stress. Two ways have mainly been developed for stress state assessment: subjective through questionnaire or objective through physiological measurements. Considering studies available in the literature, we found that healthy subjects' response in terms of average heart rate could present a typical shape when varying with stress increasing, stress being objectified by an indicator such as the difficulty of the context or an indicator like the workload or the assessment of a perceived stress; the shape of the curve between the average heart rate HR (Heart Rate) and the stressor indicator S could be seen as $HR \propto Sa$ where a was a positive number smaller than 1 in case of healthy subjects under short term mental stress. This finding let us thought that, in case of healthy adult subjects submitted to short term mental stress, there may be a generalized relationship between the average heart rate considered as a physiological response to the stress, relationship independent from the kind of stressor but depending on its intensity. Such a correlation noted by Levy et al. (1998) but did not give rise to a model. **METHODS:** The method consisted in working the hypothesis of pattern by gathering data providing HR and ratio of frequency power of HRV (Heart Rate Variability) for different conditions of stress. The resulting correlation was then used to formulate a mathematical expression of the hypothesis of pattern shaping the model. The model was then assessed by testing its reliability when applied to HR variation versus different types of stress indicators. **RESULTS AND DISCUSSION:** To shape the model, 10 studies were used, involving 202 subjects and providing N=32 points. Among these studies, only those regarding healthy subjects were considered, implying sometimes to select only data of the control group of the study. The correlation obtained gave $r(N=32)=0.88$ ($p<0.0001$) for $a=0.2$. Mathematical developments led to the model: $HR = kS^a + c$ with: $k = \alpha / a S_1^{(a-1)}$ and: α is the slope of the linear approximation when S tends to zero, a=0.2 is the coefficient obtained through the shaping correlation. S1 is a constant to be adjusted regarding the range of experimental data covered by the linear approximation when S tends to zero. Further tests with experimental data led to consider that S1 was to be adjusted to 15% of the range of experimental data covered by the linear approximation when S tends to zero. To assess the model, 8 studies providing HR vs different types of stress indicators (EMG, GSR, Work Load, questionnaires such as STAI-S, ALES) with data respecting the conditions for applying the model (healthy subjects, short term mental stress) providing 24 points spread into 8 samples of subjects (one per study) and gathering altogether 295 healthy adult

subjects. When studies considered two cohorts of subjects, one made up of healthy subjects and the other made up of subjects with pathologies or psychological problems, only healthy cohort was considered. The correlation obtained between the model and the data provided by the literature gave $r=0.95$ ($p<0.0001$) which allowed us to validate the model. Limits are that the model applies for healthy adults only, does not apply when the stress process is disturbed (instant feedback of stress state to subjects for example or second stress following a post-stress relaxation phase), was tested with values of HR not exceeding 101 bpm; however, we may assume that the model follows an asymptotic trend for higher values. As a perspective, we may assume that a modified model (with another value of the power a for example) could fit data of patients concerned by a given disease or a family of diseases. Similarly, we may assume the same for patients experiencing two consecutive episodes of short-term mental stress.

EXPERIMENTAL METHOD FOR THE ASSESSMENT OF HUMAN REACTIONS IN MICROSTRESS. V Ababkov, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: The theoretical and methodological base of the experimental method was build on R. Lazarus (1981) cognitive-phenomenological approach and understanding of stress as transaction process. The stress includes psychological and physiological reactions. Everyday life events are considered as stressors which could be systematized by the level of negative effect and time for post adaptation. The taxonomy includes everyday stressors or daily hassles, critical or traumatic stressors and chronic stressors (Perrez et al, 1998). Here, daily hassles have been modeled by two types of experimental situations similar to everyday stressors. **OBJECTIVE AND AIMS:** The study objective was to identify some psychological and endocrine human reactions in response to different everyday stressors in healthy young males and females. The following study aims were defined: to identify emotional, cognitive and behavioral reactions and gender specific in response to experimental stressors; to investigate stress reactivity of hypothalamic-pituitary-adrenal axis in two modeled stress situations assessing the cortisol level in saliva; to evaluate the psychophysiological reactions in response to experimental stresses; to evaluate the feasibility and the ability of the proposed method. **METHODS:** Two experimental stress-inducing situations were developed to address study objective and aims. 1. Public speaking stress. To model this type of stress situation we have used the version of classic Trier Social Stress Test in Halpern's (2002) modification (Kirschbaum et al, 1993, Haplern, 2002). 2. Stress in response to the communication with opposite sex unknown interviewer (sexual behavior). To model this type of stress we have used modified experimental situation based on dating interview (Halpern, 2002). The modification and tailoring of Halpern's experimental procedures were important to address cultural, ethical and economical specific of the population. The inclusion criteria included the willingness to participate in 2-day experiments, age 18-34, no medical condition required hormonal therapy, no psychiatric or psychological conditions identified as the barriers for understanding informed consent. The total sample size was 151 participants, male and females, aged 19-34. The recruitment was conducted using two approaches: face-to-face recruiting at the educational settings and recruiting through internet social networks. Each of participants participated in two experimental procedures in two different days with no longer than 1-week interval. The scheduled time for the experiments were the same to avoid the influence of daily cortisol level variations. The saliva collection for cortisol level detection for all study participants was conducted using the following algorithm: a) the saliva samples collection happened during time period between 2 PM – 8 PM; b) 1 h prior to the saliva collection time (scheduled experiment time) the participants were not allowed to eat, smoke and drink other beverages except water; c) three samples of saliva were collected for each of participant at each of 2 days experiments – pre-test before experimental procedure, 1 post-test right after experiment and 2 post-test in 10 - 20 min after the experimental procedure. The 10 psychometric and 4 physiological measures and instruments were used for pre- and post-experiment and evaluating stress reactivity. For the analysis of the data the following statistical procedures and methods were used: descriptive statistics, dispersion and regression analysis (SPSS, version 18). **RESULTS AND DISCUSSION:** General results and conclusion. Research data supports the consideration that stress reactivity is stable individual's characteristic which is manifested constantly in different stressful situations. The complex correlations between the types of stress reactivity and self-assessment of mental state and used coping-strategies were detected. The important data was discovered about the correlation between adverse childhood experience, health risk behaviors and level of stress reactivity. The main result of the conducted study are developed experimental model of human's micro stress and piloted methods for its assessment. The proposed model of experimental stress is based on complex investigation of cortisol, psychophysiological and mental parameters. While cortisol level is an objective parameter of stress, psychomental parameters are much more subjective and mediated comprehensively. The choice of psychometric tests and methods should be based on the specific of evaluation related to experimental situation. The most informative method among psychophysiological measures was tensometry which provided the most accurate and objective data. **RESEARCH SUPPORT:** St-Petersburg State University grant «Endocrine and psychological determinants of human's behavior in stress» FN01201174042.

STRESS ASSESSMENT USING EXPERIENCE SAMPLING: CONVERGENT VALIDITY AND CLINICAL RELEVANCE. T Vaessen, M van Nierop, U Reininghaus and I Myin-Germeys, Department of Neuroscience, Center for Contextual Psychiatry, KU Leuven, Leuven, Belgium; Department of Psychiatry and Psychology, School for Mental Health and Neuroscience, Maastricht University, Maastricht, The Netherlands; Health and Population Research Department, Institute of Psychiatry, King's College, London, UK

INTRODUCTION: Subjective appraisal and experience are key aspects of stress, but most questionnaires fail to assess these measures within the transitory time-window of the acute stress response. The experience sampling method (ESM) overcomes this issue and allows for in-the-moment assessment of subjective appraisal of a situation and the stress response reflected in current subjective distress or increases in negative affect and symptomatology. **METHODS:** Here, we discuss these measures and assess their validity and clinical relevance

based on previous literature. **RESULTS AND DISCUSSION:** Several established physiological markers of the stress response relate to ESM measures of subjective distress and affective and psychotic reactivity to daily life stressors. Across the psychopathology spectrum, ESM measures indicated increased stress sensitivity and a pathology-specific physiology. Childhood trauma and stressful life events are likewise associated with a sensitized affective response to daily stressors as measured with ESM, and in these groups psychotic stress reactivity specifically increased in psychotic individuals. Thus, although there remains room for improvement, the evidence suggests that ESM measures of subjective distress and affective and psychotic reactivity are indeed valid and meaningful. **RESEARCH SUPPORT:** European Research Council Consolidator Grant.

SYMPOSIUM 6: NEURONUTRITIOLOGY

Chair: SA Apryatin (Russia)

A COMPARATIVE ANALYSIS OF ANXIETY LEVELS FOR DBCB TETRAHYBRID, DBA/2J INBREED AND CD-1 OUTBREED MICE STRAINS: CLASSIC AND ALTERNATIVE METABOLIC SYNDROME IN VIVO MODELS. SA Apryatin, NA Petrov, KV Mzhelskaya, AS Balakina and NV Trusov, Federal Research Center of Nutrition, Biotechnology and Food Safety, Moscow, Russia

INTRODUCTION: Using experimental classical and alternative in vivo mouse models of metabolic syndrome allows for the development of the main signs of this disease within 8 weeks. One of the most informative indicators sensitive to diet-induced metabolic syndrome are behavioral responses, an important component of which is anxiety level in experimental animals. The aim of our research work was a comparative analysis of the anxiety levels in the classical and alternative metabolic syndrome in vivo mouse models of induced by diet consumption with an increased quota of sucrose. **METHODS:** Studies carried out female mice (8-10 weeks) CD-1 (ICR-1) outbreed strain, DBA/2J inbreed strain and DBCB tetrahybrid (F2 obtained by cross of four inbreed strains C57Bl/6J, CBA/lac, DBA/2J and BALB/c). The animals were divided into 6 groups of equal number (N=8). During the 55 and days the animals of the 1st (DBCB tetrahybrid), 3rd (DBA/2J) and 5th (CD-1) group received a control balanced diet corresponding AIN93, and 2nd (DBCB tetrahybrid), 4th (DBA/2J) and 6th (CD-1) groups - 30% sucrose solution instead of water. Anxiety level was evaluated in the "elevated plus maze" test. **RESULTS AND DISCUSSION:** Comparative analysis of the time spent by the animal in the open and closed arms showed clear differences in anxiety levels between outbreed (CD-1), inbreed (DBA/ 2J) mice strains and DBCB tetrahybrid. Testing for 55 days revealed significant differences of slots held by animals in open and closed arms between groups 1 and 2 (control and experimental groups DBCB tetrahybrid, respectively) and groups 3 and 4 (control and experimental group DBA/2J strain, respectively). The highest level of anxiety was observed in group 1 (control, DBCB tetrahybrid). The anxiety level of DBCB tetrahybrid on 30% sucrose diet was significantly decreased in comparison with the control group, while DBA/2J inbreed strain with increased sucrose quota had the opposite effect. Levels of anxiety CD-1 outbreed line in groups 5 and 6 did not differ statistically. The same trend was observed for the activity index. Our results suggest possible role of an excessive amount of high sucrose diet as a stress factor (anxiety level rise) for the more sensitive DBA/2J inbreed strain, and no impact on the level of anxiety for CD-1 outbreed strain. Using of DBCB tetrahybrid as an alternative in vivo models of metabolic syndrome showed a significant decrease of anxiety level on the high carbohydrate diet compared with the control group, which, in turn, demonstrated the highest anxiety. Thus, the DBCB tetrahybrid showed the highest level of anxiety and can be a good model for the study of anxiety level changes. The genetic characteristics of different outbreed/inbreed strains and hybrids of mice have a significant impact on the anxiety level and activity index. **RESEARCH SUPPORT:** Federal Agency of Scientific Organizations program 0529-2015-0006 «The search for new molecular markers of nutrition-related diseases: genomic and post-genomic analysis" for 2015-2017.

CHANGES OF BEHAVIORAL CHARACTERISTICS IN THE RAT *IN-VIVO* MODELS OF METABOLIC SYNDROME. KV Mzhelskaya, YS Sidorova, NA Petrov, SA Apryatin, NV Trusov, AS Balakina, VK Mazo and IV Gmoshinsky, Federal Research Centre of Nutrition, Biotechnology and Food Safety, Moscow, Russia

INTRODUCTION: Metabolic syndrome, diabetes, obesity and other nutrition-related diseases have one of the leading places in the morbidity's structure of the population of Russia. One of the main causes of alimentary disease prevalence worldwide is eating disorders and dietary imbalance, in particular, an increased content of saturated fats in the diet and simple sugars (with vitamins' and trace elements' deficiency). In addition, a significant role in the development of such diseases is played by sedentary lifestyle and high stress pressure, which affect neuromotor functions and anxiety. Here, we examine changes in various behavioral parameters of laboratory animals in in-vivo models of metabolic syndrome, caused by feeding different diets with a high content of various carbohydrates. **METHODS:** Studies were carried out on female of Wistar rats line average weight 146 ± 3 g. For 120 days, the animals received: 1st group – control balanced diet corresponding AIN93; 2nd – control diet supplemented with 30% glucose solution instead of water; 3rd – control diet supplemented with 30% fructose solution instead of water; 4th – control diet supplemented with 15% glucose and 15% fructose solution instead of water; 5th – control diet supplemented with 30% sucrose solution instead of water. The level of systolic and diastolic blood pressure of the rats was measured by the tail cuff using Non Invasive Blood Pressure devise (ADinstruments, Australia) on the 52nd and 112th days of the experiment. Muscle tone in rats was assessed by the strength of the grip of the front paws of rats prior to feeding the experimental diets (day 0) and then to days 34, 65, 97 and 118. Level animals evaluated in the Elevated plus maze test (Panlab, Spain) at days 36 and 57 of the experiment. Evaluation of animal behavior and memory were carried out using a test "passive avoidance" (CRPA). **RESULTS AND DISCUSSION:** On 34th day, muscle strength compression rate was significantly higher in animals of experimental groups compared to control animals. Significant increasing in grip strength index was observed in all treatment groups compared to Day 0. The maximum increase in grip strength was on 65th day, the difference between groups was leveled. At 118th day, grip strength decreased in all groups of animals, a group of

Control and Test 2 to the benchmark of Day 0. In groups 3, 4, 5 rate of muscle strength and grip even declined, but remained significantly above baseline Day 0, and (unlike the control group) was significant. Analyses of anxiety showed no between-group differences in all three tests. Testing the cognitive functions of animals by the method of CRPA showed that the differences between the groups of animals in terms of both short and long-term memory were non-significant ($p > 0.1$) by $\chi 2$. Thus, the relative decline of muscle tone can represent one of the indicators of metabolic disorders that accompany the development of the metabolic syndrome in the later stages of the experiment. We also found decreased anxiety levels in groups with higher quota of simple carbohydrates. **RESEARCH SUPPORT:** Federal Agency of Scientific Organizations program 0529-2015-0006 «The search for new molecular markers of nutrition-related diseases: genomic and post-genomic analysis" for 2015-2017.

EVALUATION OF INFLUENCE OF LIPID MODULE, ENRICHED WITH ASTAXANTHIN AND/OR PLASMALOGENS, ON BEHAVIORAL ACTIVITY OF ANIMALS UNDER STRESS. Y Sidorova, V Sarkisyan, N Petrov, A Kochetkova and V Mazo, Federal Research Centre of Nutrition, Biotechnology and Food Safety, Moscow, Russia

The main nutrients that are important in stress condition are lipids and antioxidants as a source of labile components in nervous tissue. Here, we studied the usage of the lipid module, containing docosahexaenoic acid (DHA) – omega-3 PUFA, necessary for normal brain activity. Effect of DHA, when consumed as a part of phospholipids is of special interest due to the specific distribution in nervous tissue. The main representatives of DHA-rich phospholipids are plasmalogen phospholipids (a special class of ether lipids), which play the role of DHA depot in nervous tissue. Astaxanthin is a natural antioxidant, well known for its polyfunctionality of biological activity, as the functional food ingredient is has a high potential for increasing of work capability and the ability of an organism to restore after intensive physical or mental activities. Lipid module is a mixture of high oleic sunflower oil (88,8%), coconut oil (6,3%) and *Schizochytrium* sp. microalgae oil (5% of DSM, life'sDHATM C53-O100). Fifty adult male Wistar rats of 125–130 g body weight purchased from Stolbovaya Center (Russia). The experimental design was approved by the Animal Ethics Committee of the Federal Research Centre of Nutrition and Biotechnology. A 32 day experiment was conducted to study the effect of enriching the diet of rats with lipid module (5% instead of sunflower oil) enriched by astaxanthin or plasmalogens (0.05 and 0.1%, respectively), or their combination, on the level of anxiety in elevated plus maze, cognitive functions in Morris water maze and rats` physical fatigue after exhaustive exercise in forced swimming test using the Smart video tracking system (Panlab Harvard Apparatus, Spain). The concentration of corticosterone in the serum during the general adaptation syndrome was evaluated by Corticosterone EIA kit (UK). The enrichment of lipid module by astaxanthin exerts an adaptogenic effect by reducing the main biomarker of stress systems in the blood (corticosterone) after stress exposure by exhaustive exercise. Enrichment of lipid module by plasmalogens improves cognitive functions in Morris water maze test, however, the favorable effect was accompanied by lower resistance to stress and increased anxiety. The negative effects of plasmalogens presumably were mitigated by its combined action with astaxanthin in the composition of the lipid module. We demonstrated that combinations of lipid module, enriched only with ASTA or the mixture of ASTA and PG, for further inclusion in specialized food products composition can be promising. **RESEARCH SUPPORT:** Russian Scientific Foundation grant 14-36-00055.

PROBIOTIC ENTEROCOCCUS FAECIUM L-3 CAN IMPROVE PSYCHO-EMOTIONAL STATE IN MULTIPLE SCLEROSIS PATIENTS. AV Matsulevich, IN Abdurasulova, EI Ermolenko, GN Bisaga, GG Alekhina, DI Skulyabin, AN Suvorov and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg State Pediatric Medical University, St. Petersburg State University, Kirov Military Medical Academy, Saint-Petersburg, Russia

Multiple sclerosis (MS) belongs to the most acute socially significant issues of neurology as leads to an early invalidism of young adult. The disease has a number of features of a clinical picture, including psycho-emotional disorders and disturbances of functions of gastrointestinal tract which significantly influence quality of life of patients. Disturbances of intestinal microbiocenosis (dysbiosis) can influence both the MS as well as psycho-emotional state. Considering what at 90% of patients with MS comes to intestinal dysbiosis, there is a question of need of correction of this state. The aim of the study was to assess a possibility of improvement of a psycho-emotional state of MS patients during course of dysbiosis using probiotic of *Enterococcus faecium* L-3. 30 people with the diagnosis of MS and duration of disease between 1-19 years, took part in research. 15 people obtained *E. faecium* L-3 on 50 ml (9,0 lg CFU/ml) 2 times a day within 3 weeks (experimental group - EG). 15 people without probiotic treatment made the control group (CG). Psycho-emotional state was assessed using standard tests: “dominating state" and "current status” by Kulikov, a scale of situational (reactive) anxiety by Spilberger-Hanin, and methods of differential diagnosis of depression by Zung. All patients were tested twice. After using the probiotic, almost 70% of patients of EG showed significantly improved emotional status, strength, satisfaction with life quality, where 25% of patients remained unaffected. In CG, positive changes were noted only at 10% of patients and 80% had negative dynamics. It is possible that improvement of psycho-emotional status of EG patients is due to the known capability of probiotic bacteria to synthesize serotonin or other neuromediators, and to stimulate their production by cells of an organism or other microbiota. Our results show a possibility of using *E. faecium* L-3 for improving psycho-emotional state of MS patients without applying psychotropic drugs. **RESEARCH SUPPORT:** 16-15-10085 RSF grant.

CLINICAL AND EXPERIMENTAL EVIDENCE FOR THE ROLE OF GUT MICROBIOTA IN THE PATHOGENESIS OF AUTOIMMUNE DEMYELINATING DISEASE OF THE BRAIN. IN Abdurasulova, AV Matsulevich, EA Tarasova, GG Alekhina, EI Ermolenko, GN Bisaga and VM Klimenko, ISBS Fellow, Institute of

Experimental Medicine, St. Petersburg State Pediatric Medical University, St. Petersburg State University, Kirov Military Medical Academy, St. Petersburg, Russia

Modern omics technologies have enabled in-depth characterizing multiple of microorganisms that inhabit the human body. The highest occurrence of microorganisms is in the gut, especially its lower parts (>1,000 species). Studies on GF-animals have shown that intestinal microbiota affects the host, including the development and functioning of the immune and nervous systems. Currently, formed an idea of their axis intestinal microbiota-brain with bi-directional influence actively explores the role of intestinal microbiota in various diseases, as well as experimental and clinical data about its involvement in the pathogenesis of multiple sclerosis (MS) and other neurodegenerative diseases. Our research in the model of RS-experimental allergic encephalomyelitis (EAE) pointed out that the development of the CNS pathologies in animals is accompanied by the development of intestinal dysbiosis and for different phases of the disease is characterized by changes to certain kinds of microorganisms. Dysbiosis intestines also detected the majority (90%) patients with MS, and it has seen even in patients without gastrointestinal disorders and eventually observed his aggravation. Since the modified composition of microflora impairs the quality of life of patients and can affect the course of disease, there is a need to correct this condition. For this purpose, various probiotics based on strains of *Lactobacilli, Bifidobacteria, Enterococci*, are used. Previously, we showed that probiotic *Enterococcus faecium*-3 corrects animal experimental dysbiosis, reduces the severity of EAE similar to COPAXON (an immunomodulator used in MS treatment) and can also have a positive impact on the behavior of healthy rats intake E. faecium -3 (9.0 lg CFU/ml) “Avena”, p.o. 50 ml twice a day for 21 days in patients with MS showed improvement of gastrointestinal tract and normalization of the intestinal microflora composition. *E. faecium* L3 quite effectively ousted *Clostridia perfringens, Proteus mirabilis, Citrobacter spp.*, partially - *Staphylococcus aureus, Klebsiella spp.*, hemolytic *Escherichia coli*. After the correction, however, the number of enteropathogenic *E. coli* and *Enterobacter spp* remained unaltered, likely requiring a longer course for their elimination. To ascertain whether probiotic enterococci for these kinds of bacteria, as well as to determine the optimal duration and repetition correcting courses, further studies are needed, including with individual selection of most effective probiotic. **RESEARCH SUPPORT:** RSF grant 16-15-10085.

CONFERENCE PRESENTATION 5: CELLVIZIO LAB – A TOTALLY NEW DIMENSION OF IN VIVO STUDIES.
K Grohmann, Biogen-Analytica LLC, Moscow, Russia

Preclinical studies using laboratory animals are crucially important for scientific and practical medicine. They expand our knowledge about different diseases and help us to validate new drugs. The majority if data in preclinical studies is obtained through various in vivo visualization techniques. They are proven to be effective and reliable for many different applications, including neuroscience. Fluorescent confocal in vivo in situ microscope Cellvizio Lab covers the increasing need for cellular-level images in molecular imaging combined with none or minimal invasiveness for longitudinal studies. It offers a unique solution for the studies of peripheral and central nervous systems. Cellvizio is able to image along nerves at a cellular level resolution, monitor nerve regeneration over time and evaluate microvessel damage in diabetic neuropathies. It enables investigation of blood-brain barrier and even real-time monitoring of the neuron activity in the brain of a living animal. Cellvizio is truly universal visualization system that ensures high data reproducibility and quality in longitudinal studies.

SYMPOSIUM 7: LAPIN BIOLOGICAL PSYCHIATRY SYMPOSIUM
Chairs: IV Ekimova, PD Shabanov (Russia)

INTRODUCTION: 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 the most cited papers published in this journal in the last 50 years. Lapin’s studies have contributed greatly to the development of newest serotonergic antidepressants, such as SSRIs, currently representing the most prescribed group of psychotropic drugs in the world. Prof. Lapin was also the first to report the neuroactive effects of kynurenine and its derivatives – a discovery that opened another rapidly expanding area of glutamatergic psychopharmacology. A talented professional musician, prolific writer, painter, and an enthusiastic athlete, Prof. Lapin was a strong supporter of ISBS, and generously shared his knowledge with colleagues and students at our “Stress and Behavior” conferences and ISBS summer schools. His enthusiasm, friendship, generous support of junior colleagues, and the deep knowledge as both a clinical and experimental neuropharmacologist (‘humanists’ and ‘animalists’, as he called them), made a long-lasting impact on his colleagues and students. This regular ISBS symposium will continue Lapin’s scientific legacy in the field of biological psychiatry.

ISBS SPECIAL TALK: PEPTIDE DRUGS IN INCREASING THE REPRODUCTIIVE FUNCTIONS AND COPING TO STRESS IN RATS. TN Sollertinskaja, ISBS Fellow, MV Shorokhov and AS Kourguzova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Stress is the main cause of affective brain disorders. The study of prenatal stress in postnatal developing is a key problem of modern medicine. Stress of different genesis during pregnancy often leads to delayed embryo development, also causing cardiovascular, neurological and neuroendocrine diseases. At this point, the search of new therapeutic drugs without adverse effects to correct deficits of postnatal ontogenesis is the key problem of physiology and medicine. The important role in compensating brain functional disturbances is played by bioactive peptides and their synthetic analogs applied clinically (e.g., Semax). Although a new peptide drug, ACTH6-9, has been synthesized recently, the effects of Semax and ACTH6-9 on reproductive functions remain unclear. **THE AIM:** The comparative study of Semax and ACTH6-9 effects on reproductive activity and functional state of rat postnatal ontogenesis. **MATERIALS AND METHODS:** The experiments were performed in 40 rats. The first study utilized freely-moving animals, while the second study used animals placed into special equipment to register vegetative (ECG, pneumogram) parameters. Semax and ACTH6-9 were applied intranasally or i.m. at low doses (0.1-0.5 and 0.1-0/3 mkg/animal, accordingly). **RESULTS AND DISCUSSION:** Stress of pregnant rats induces psychoemotional and behavioral disturbances in offsprings. Multiple ACTH6-9 injections at the early stage of the pregnancy (15-20 days) led to increased reproduction functions (19-20 pups vs. normal 8-9). ACTH6-9 increases some innate behaviors in pups, including food motivation- and exploration, and reduces aggression and anxiety/fear. These effects of ACTH6-9 were long-lasting. The main simple forms of conditional reflexes originated quickly, on Day 2. ACTH6-9 increases the pup resilience to stress. Compared with ACTH6-9, Semax injection in pregnant rats did not increase reproductive functions, innate behavior and conditioning. In pups, anxiety state evoked by cold stress, was restored faster (in 20 min) vs. 3-4 days in controls. The pre-injection of Semax exerted similar effects, although ACTH6-9 effects were more robust. Overall, Semax and ACTH6-9 exerted distinct effects on rat vegetative parameters, with Semax action being more significant on heart endpoints, and ACTH6-9 – on pulmonary endpoints. The two drugs' effects on neocortex involved different limbic areas, with Semax targeting the hippocampus, and ACTH6-9 – the hypothalamic nuclei. **RESEARCH SUPPORT:** Russian Foundation for Basic Research grant 15-08-0635315.

AGE-RELATED DIFFERENCES IN STRESS RESPONSIVENESS OF THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS IN NONHUMAN PRIMATES WITH VARIOUS TYPES OF ADAPTIVE BEHAVIOR. ND Goncharova and OA Chigarova, Laboratory of Endocrinology, Research Institute of Medical Primatology, Sochi, Russia

INTRODUCTION: The hypothalamic-pituitary-adrenal (HPA) axis is a key adaptive neuroendocrine system essential for adequate stress responsiveness and health. Disruption of corticosteroid regulation due to severe stress is associated with pathological states, such as psychiatric disorders, metabolic syndrome, cardiovascular disorders, immunopathologies and diabetes. The probability of post-stress syndrome is sharply increased by the age. However, the same stressful event can cause various symptoms and severity of stress-related disorder in different individuals, including the elderly. Thus, the elucidation of individual characteristics of the HPA axis responsiveness to acute psycho-emotional stress at different ages, becomes necessary. Here, we study individual characteristics of the HPA axis responsiveness to acute stress exposure (ASE) at different age periods in young adult and in old physically healthy female rhesus monkeys that differ in their behavioral responses to stress. **METHODS:** Fourteen female rhesus monkeys with healthy standard adaptive behavior (control, SB, 7 young and 7 old) and 14 monkeys with depression-/anxiety-like behavior (DAB, 7 young and 7 old) was subjected to acute stress exposure (restraint for 2 h, ASE). We measured plasma levels of corticotrophin (ACTH), cortisol (F), dehydroepiandrosterone sulfate (DHEAS), and malondialdehyde (MDA) concentration in erythrocytes. **RESULTS AND DISCUSSION:** We found no intergroup differences in the HPA axis response to ASE in young animals. During aging, the monkeys with SB showed reduced ACTH response to ASE, whereas the monkeys with DAB demonstrated its increase. The old animals with DAB in response to ASE demonstrate the most pronounced HPA axis deficits, such as the highest levels of ACTH, the lowest levels of DHEAS, reduced F levels and the highest values of the F/DHEAS molar ratio. The F/DHEAS ratio positively correlates with MDA concentration in erythrocytes that is the biomarker of an intensity of the free radical processes and accelerated aging. Thus, our data suggest the old monkeys with DAB as individuals with higher vulnerability to adverse effects of ASE and accelerated aging. **RESEARCH SUPPORT:** Russian Foundation for Basic Research project 15-04-07896 A.

CRISPR/CAS9 KNOCK OUT OF SCHIZOPHRENIA RISK FACTOR MIR-137 GENE PRODUCT. A Marakhovskaia, J Khlghatyan and JM Beaulieu, University of Toronto, Toronto, Canada

INTRODUCTION: Schizophrenia (SZ) is a highly heritable mental disorder affecting around 1% of the general population. Among 108 genomic loci identified to be associated with SZ in a large-scale genome-wide association study (GWAS) was a single-nucleotide polymorphism (SNP) within an intron of MIR137HG. This gene encodes miR-137, a microRNA (miRNA), involved in the post-transcriptional regulation of mRNAs. Expression of miR-137 is enriched in the brain of mice and human where it plays an essential role in function and development. Moreover, miR-137 is downregulated in SZ patients carrying that SNP. Common ways to achieve miRNA loss-of-function involve utilizing antisense molecules or miRNA sponges. However, this approach appeared to be insufficiently robust and lacking sensitivity. The CRISPR/Cas9 system is a genome editing method allowing for multiple applications. Here we explore CRISPR/Cas9 as a tool to engineer miR-137 loss-of-function mutations. **METHODS:** sgRNAs against precursor molecule have been designed and two guides were selected (g1 and g3). These sgRNAs could induce indel mutation affecting miRNA maturation by Dicer and Drosha respectively. Both guides were cloned into a CRISPR-Cas9 expression vector, encoding Cas9 and a puromycin resistance gene.

Neuro2A cells were transfected with the different vectors and selected by puromycin for 48 h. After selection, cells were collected for RNA extraction and qPCR analyses of miR-137 expression. **RESULTS AND DISCUSSION**: The results of qPCR for CRISPR-Cas9 mutants revealed no difference in the expression level of mature miR-137-3p for g1, while for g3 we detected a molecule with higher melting temperature and no traces of mature mir-137-3p. Further characterization showed that the molecule with higher melting temperature corresponded to an incompletely processed miRNA precursor. These data indicate that we successfully created a knockout of miR-137 by Drosha processing site disruption. Afterwards, we evaluated mRNA expression changes with Mouse Gene 2.0 ST microarrays for knock-out condition vs. control and co-expression network analyses was performed to evaluate the impact of miR-137 knock out in Neuro2A cells. **RESEARCH SUPPORT:** CIHR project grant to JM Beaulieu.

EFFECTS OF NEONATAL LIPOPOLYSACCHARIDE TREATMENT ON *MMP9* AND *TIMP1* MRNA EXPRESSION IN THE RAT BRAIN. AN Trofimov, AP Schwarz, K Fomalont, VA Schukina, EA Veniaminova, NA Markova, OE Zubareva and VM Klimenko, Institute of Experimental Medicine, St. Petersburg, Russia; University Hospital of Wurzburg, Wurzburg, Germany; National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD, USA; Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Institute of General Pathology and Pathophysiology, Moscow, Russia

Perinatal brain pathologies impair the development of CNS functioning and cause chronic cognitive dysfunction. These conditions are associated with high production of pro-inflammatory cytokines by the cells of the immune and nervous systems. Neurons express receptors for pro-inflammatory cytokines, which provides evidence for the functioning of cytokines as neuromodulators. The exact molecular and cellular mechanisms of cytokines in the impairment of brain development have not been fully elucidated. Here, we studied the expression of neuroplasticity-regulating genes matrix metalloproteinase-9 (Mmp9) and tissue inhibitor of metalloproteinases-1 (Timp1) in the medial prefrontal cortex and hippocampus. Wistar rat pups were treated with lipopolysaccharide (LPS; 25 μg/kg i.p., P15, P18, P21), an inducer of pro-inflammatory cytokines. Adolescent and adult LPS-treated animals demonstrated increased anxiety-like, decreased exploratory behavior in the open field arena, and poorer learning in the active avoidance task and Morris water maze. The expression of *Mmp9* and *Timp1* differed in the cortex and hippocampus of pups vs. adult untrained rats, and remained unchanged in rats trained in either learning task, revealing that prolonged pro-inflammatory challenge during early postnatal development negatively affects the plasticity factors involved in memory acquisition in adulthood. Collectively, these results suggest that an increase in cognitive stimulation may be an effective approach to reduce the negative effects of neonatal immune challenges on brain functioning. **RESEARCH SUPPORT:** RFBR 16-34-00316.

EMOTIONAL AND COGNITIVE ALTERATIONS IN THE RAT LACTACYSTIN MODEL OF THE EARLY STAGE OF PARKINSON'S DISEASE. MV Chernyshev, IN Abdurasulova, AV Matsulevich, OA Sapach, AR Gazizova, IV Ekimova, ISBS Fellow, VM Klimenko, ISBS Fellow, and YuF Pastukhov, ISBS Fellow, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Identification and search for the early features of Parkinson's disease (PD) is one of the central points in preventing the development of this incurable neurodegenerative disorder. Emotional and cognitive impairments, long attributed to the latest stages of PD along with motor dysfunctions, are currently considered as potential candidates for early markers of PD. Here, we attempted to develop a preclinical model of PD using intranasal administration of proteasome inhibitor lactacystin (LC) to detect emotional or cognitive changes in rats. **METHODS:** Experimental group of rats were intranasally given twice (with 1-week interval) lactacystin per each nostril. The control group received phosphate-buffered saline in the same manner. The open field (OF) and the elevated plus maze (EPM) tests were separately performed in three sessions: I – background (before LC injections); II – on Days 9 and 13 following the first LC injections for the OF and EPM test, respectively; III – on Days 21 and 22 following the first LC, respectively. A sucrose preference test for anhedonia was conducted before and on the 23-rd day after the first LC injection. A new object recognition test was given on Days 10-11, and the Y-maze test was used on Day 12 after the first LC. **RESULTS AND DISCUSSION:** Behavioral testing revealed no significant differences during the background session (I). Repeated sessions (II) of the OF test detected higher anxiety in the LC group vs. control. Rats treated with LC significantly reduced the percentage of central zone ambulations, but not time spent there. The EPM test, which is more sensitive to anxiogenic/anxiolytic effects, showed no changes in anxiety-like behavior, although the LC group exhibited more locomotion, as measured by the number of closed arm entries. In the OF test, which is more informative for locomotor behavior, no difference between the groups was observed for locomotor activity measured by peripheral ambulations. However, 45 % of LC-treated rats exhibited locomotion similar to the background session, whereas other rats and controls decreased this activity, suggesting habituation. Also, 45 % of subjects in the LC group displayed impaired new object recognition, indicating memory deficits. The most sensitive assay to detect cognitive dysfunctions was the Y-maze test, eliciting negative effect of LC treatment in almost all subjects, thus showing the development of emotional and cognitive disorders in Session II. Another repeated session (III) of the OF test displayed a retention of enhanced locomotion in the LC group, suggesting impaired habituation. This group exhibited a higher level of peripheral and total ambulations as well as explored a larger number of holes compared to the control. An increase in the level of anxiety, found in the session II, was not observed in either the OF or the EPM test. However, the LC group reduced sucrose (20%) consumption, indicating anhedonia, a sensitive marker of depression. Overall, data from this experimental model of the preclinical stage of PD reveal interesting temporal dynamics of behavioral changes, with early consequences of LC administration including cognitive deficits (e.g., attenuation of habituation, impaired spatial working memory and non-spatial long-term memory) and anxiogenic-like behavior (which later turns into a depressive-like state). **RESEARCH SUPPORT:** Russian Science Foundation grant 16-15-00-278.

PHARMACOLOGICAL STUDY OF GHRELIN RESPONSE TO STRESS IN THE RAT BRAIN STRUCTURES. PP Khokhlov, IYu Tissen, DN Zaporozchenko, AA Lebedev, ER Bychkov, YuN Bessolova, LK Khnychenko, GV Beznin, SG Tsikunov, ISBS Fellow, and PD Shabanov, ISBS Fellow, Anichkov Department of Neuropharmacology, Pavlov Physiological Department, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Stress response is a complex integrated process, where the nervous, immune and endocrine systems interact. Ghrelin neuropeptides are signaling molecules with a wide range of diverse functions. Besides other functions, ghrelin takes part in the brain reinforcement phenomena. The relations of reinforcement and stress events are the points of great interest. Here, we evaluate the response of ghrelin system to psycho-emotional stress in rats. **METHODS:** Wistar rats were exposed to predator, a python snake. The rats underwent an acute stressor influence. The effect of stress influence had been evaluated with behavioral tests. Then certain brain structures (amygdala, hippocampus and hypothalamus) were separated, homogenized and studied on unacylated ghrelin content with the high sensitive ELISA method. Ghrelin (Tocris, UK) was used as a ghrelin receptor agonist, whereas D-Lys3-GHRP-6 (Tocris, UK) was used as a receptor antagonist. The intranasal administration of preparations were applied at 40 µg/kg for agonist, and 80 µg/kg for antagonist, respectively, for 7 days. **RESULTS:** DAG had been determined in every brain structures tested. In controls, the concentrations of DAG were 0.152±0.014, 0.105±0.023 and 0.347±0.017 ng/mg in the amygdala, hippocampus and hypothalamus respectively. After snake exposure, the concentrations were 0.020±0.001, 0.016±0.001 and 0.018±0.001 ng/mg in the amygdala, hippocampus and hypothalamus, respectively. After intranasal administration of ghrelin agonist, the values were 0.020±0.001, 0.016±0.001 and 0.016±0.001 ng/mg, respectively in these brain structures. After ghrelin antagonist administration, the respective concentrations were 0.020±0.002, 0.016±0.001 and 0.016±0.001 ng/mg. **CONCLUSION:** The ghrelin signaling system is suppressed after psycho-emotional stress, whereas desacyl-ghrelin plays an important part in complex circuits of post-stress pathways. The response of ghrelin signaling system to stress likely involves desacyl-ghrelin, but not ghrelin receptor GHSR1.

SYMPOSIUM 8: CLINICAL NEUROSCIENCE

Chairs: VM Klimenko, YuF Pastuhov (Russia)

PARADIGM SHIFT IN MENTAL HEALTH CARE: PHARMACEUTIC AND PSYCHOTHERAPEUTIC TREATMENT OF MENTAL ILLNESSES. D Petružytė, L Murauskienė, E Šumskienė, A Germanavičius, JM Diržienė and V Klimaitė, Vilnius University, Vilnius, Lithuania

INTRODUCTION: Here, we present an ongoing research project „Paradigm Change of Mental Health and Well-being in Lithuania: Towards Empirically Valid Model" (2015-2017) and its pilot findings. This project aimed to contribute to the paradigmatic change by scientific research and evaluation of efficacy of pharmaceutic and psychotherapeutic treatment to psychological and social functioning, and to estimate economic burden of treatment and mental diseases that society must pay. We aim to create a valid model that enables evaluation of efficacy of different patterns of treatment by various social, psychological and economical rates. **METHODS:** An interdisciplinary research project implemented by a diverse group of researchers (experts in psychology, psychiatry, sociology and economy) to achieve 6 goals each accomplished using different methods (quantitative, qualitative) and data sources (data bases of medical and social services providers, documents, mental health care experts and service users): 1) comparison of economic burden of mental illness and expenses of various treatment forms, 2) longitudinal research of economic effectiveness of various treatment forms of mental illnesses, 3) longitudinal research of changes in symptoms and social adaptation levels in groups of patients who received different mental health treatment forms, 4) research of subjective perception of patients, who received different forms of mental health treatment, of their condition and it's changes, 5) research of attitudes of mental health treatment practitioners and policy makers towards different forms of mental health treatment, 6) analysis of discourse on pharmaceutic and psychotherapeutic treatment forms in publicist, professional and scientific literature. **RESULTS AND DISCUSSION:** As data gathering and analysis are still ongoing, we will present very recent pilot results. Data obtained during the qualitative experts interviews show domination of biomedical approach and the lack of psychotherapeutic treatment, with patients being more satisfied with psycho- than pharmacotherapy. Initial analyses of quantitative data show that psychotherapeutic treatment has better outcomes in patients' health and socio-economic functioning. **RESEARCH SUPPORT:** Research Council of Lithuania.

NEUROPSYCHOLOGICAL DISORDERS IN PATIENTS AT EARLY AND MID-STAGES OF PARKINSON`S DISEASE. EV Gracheva, IV Miliukhina, PV Lebedev, TV Sergeev and SG Tsikunov, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: According to Braak staging non-motor symptoms of Parkinson`s disease (PD) manifest earlier than motor symptoms (MS). The most common neuropsychological disorders in PD are cognitive impairment (CI) - 90-95%, anxiety (A) and depression (D) - 60-90%. Two different mechanisms of pathogenesis of affective disorders (AD) include pathology of brain neurotransmitter systems and the psychological reaction to the diagnosis. Earlier it was thought that AD are more common at early and more advanced stages of PD, because proper dosage of dopaminergic medications improves patient`s quality of life and decreases reactive component of AD. **AIM:** Here, we conduct a comparative analysis of neuropsychological disorders at early and mid-stages of PD. **METHODS:** The study included 49 patients with PD (male – 21, female - 28): 32 patients at early stage (1,0-2,0 Hoehn and Yahr stage), 17 patients at mid-stage (2,5-3,0 Hoehn and Yahr stage), groups matched by age and sex, average age 68.7±6.9 years. Mini-mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Sheehan Patient-Rated Anxiety Scale (ShARS), Hospital Anxiety and Depression Scale (HADS) were

used to assess neuropsychological status. **RESULTS:** A direct correlation was found between the PD stage (1st group – early stage, 2nd – mid-stage) and the severity of neuropsychological disorder: ShARS r=0,34, HADS-D r=0,41 (p<0,05). 1st group showed A in 25%, D in 46,8%, 2nd group showed A in 43,8%, D in 68,8%. ShARS, HADS-A, HADS-D revealed a larger severity of AD in patients with PIGD subtype in comparison to tremor dominant subtype, although the differences did not reach the degree of reliability, there also was no difference in the CI severity between these 2 groups. A direct correlation was found between the PD stage and CI severity: MMSE r=0,40, MoCA r=0,42 (p<0,05). 1st group showed CI in 62,5%, 2nd group – in 81,2%. A direct correlation was found between the severity of CI and neuropsychological disorders: between MMSE and ShARS r=0,34, HADS-D r=0,39, between MoCA and ShARS r=0,35, HADS-D r=0,29 (p<0,05). **DISCUSSION:** Neuropsychological disorders in mid-stage patients were more severe than at early stage, thereby refuting the view that proper dosage of dopaminergic medications (which effectively compensates MS at mid-stage) also makes AD less intense than at early stage. Thus, the reactive component of affective disorders in PD appears to play less important role than supposed previously. Our study demonstrates the importance of neuropsychological status assessment at any stage of disease progression, and of timely antidepressant selection.

CORRELATION OF MULTIVOXEL MAGNETIC-RESONANCE SPECTROSCOPY OF THE BRAIN AND NEUROPSYCHOLOGICAL TESTING IN NON-DEMENTED HIV+ PATIENTS. J Boban, D Kozic, ISBS Fellow, D Lendak, M Bjelan, A Ragaji, K Ivoševic, V Bugarski-Ignjatovic, V Turkulov and S Brkic, University of Novi Sad, Faculty of Medicine, Novi Sad, Vojvodina, Serbia

INTRODUCTION: Early HIV invasion of the brain triggers a cascade of inflammation and neuronal damage that is attenuated only to a part after initiation of combined antiretroviral therapy (cART). There is persistent neuronal injury attributed to chronic immune activation and inflammation, a keystone of neurodegeneration in HIV-associated neurocognitive disorder (HAND). The aim of this study was to test correlations between neurobiochemical profile obtained on magnetic-resonance spectroscopy (MRS) and results of thorough neuropsychological testing in chronically infected non-demented HIV+ subjects. **METHODS:** We performed long echo time multivoxel MRS in grey matter of anterior and posterior cingulate gyrus in 27 HIV+ patients on 3T MR scanner, analyzing following metabolite ratios: NAA/Cr (neuronal loss and dysfunction) and Cho/Cr (inflammation/immune activation). In all subjects we performed synchronous neuropsychological testing consisting of: mini-mental state examination (MMSE), trial making test form A and B (tmA and B), Fonemic and categorial fluency, Rey auditory-verbal learning test (RAVLT), Rey-Osterrieth complex figure test (ROCF), Wisconsin sorting card test (WSCT), Wechsler memory scale-revised (WMS-R) and Beck depression inventory (BDI). **RESULTS AND DISCUSSION:** In ventral anterior cingulate (involved in emotional regulation) there was positive correlation of NAA/Cr and Cho/Cr with MMSE and tmA and B. Dorsal anterior cingulate (involved in cognition and motor control) showed positive correlation of NAA/Cr and Cho/Cr with fonemic and categorial fluency. These results speak for early deterioration of processing function, attention and concentration, as well as verbal material recall. In posterior cingulate (involved in cognition and attention) we showed positive correlation of NAA/Cr with MMSE, tmA and B, fonemic fluency, and positive correlation of Cho/Cr with fonemic fluency and RAVLT. These results confirm the multifunctionality of this region, as well as major negative effect of chronic HIV infection in this particular region. NAA/Cr correlated negatively with BDI throughout cingulate gyrus, concordant with previous studies presenting high prevalence of depression in chronically HIV-infected subjects. **RESEARCH SUPPORT:** Provincial Secreteriat for Science and Technological Development of Autonomous Province of Vojvodina.

SERUM ANTIOXIDATIVE ENZYMES LEVELS, OXIDATIVE STRESS PRODUCTS AND CYTOKINES OF ET PATIENT. ZM Muruzheva, EA Skomorohova, IS Oblamskaya, MN Karpenko and VM Klimenko, ISBS Fellow, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Essential tremor (ET) is the most common movement disorder, characterized by postural and kinetic tremor of the upper limbs and sometimes other body parts. Despite the long history of the study of this disease, its etiology and pathogenesis remains poorly understood. However, recently there has been a discussion of neurodegenerative nature of the changes observed in ET, such as cerebellar degeneration and the presence of Lewy bodies in the brain stem, which can serve as proof of affiliation the ET to group of neurodegenerative diseases. Since oxidative stress and neuroinflammation are both involved in neurodegeneration, here we assess the level of oxidative stress indicators (superoxide dismutase activity (SOD), malondialdehyde (MDA)) and inflammation (C-reactive protein (CRP), tumor necrosis factor alpha (TNF-alpha), interleukin-10 (IL-10), ceruloplasmin (CPU)) in the peripheral blood of patients with ET. **SUBJECTS AND METHODS:** The study population consisted of 32 ET patients, aged 18 to 81, diagnosed based on Tremor Investigation Group criteria (1995). 12 patients had predominant head tremor, and 20 patients - predominant arm tremor. Symptoms prevailed for the period of 5-40 years. The control group consisted of 23 healthy individuals. Patients with signs of the acute the inflammatory process were excluded from both the ET and control groups. All subjects signed informed consent for the study, approved by the Institute of Experimental Medicine. In the serum of patients with ET and control group measurement of the concentration of SOD, MDA and CPU usage measured by colorimetric method, and CRP, TNF-alpha and IL-10 by ELISA. **RESULTS AND DISCUSSION:** CPU level in patients with ET was 0.338±0.020 g/l, similar to controls (0.342±0.020 g/l, p=0.8690). CRP and TNF in ET group (4.0±0.5 mg/l and 61.0 ±3.0 pg/ml, respectively) also did not differ from the control group (5.7±0.9 mg/l and 69.4±3.6 pg/ml, respectively, p=0.07-0.09). Of the 32 patients with ET, IL-10 level was different from zero in 4, and averaged 4.5±1.5 pg/ml vs. different from zero at 5 out of 23 control patients, average 0.5±0.1 pg/ml. SOD activity in the control group was 19.7±1.7 CU, similar to ET (23.5±2.5 CU, p=0.2704). MDA levels in patients with ET were lower than in the control group (2.8±0.1 vs. 3.5±0.1 umol/l respectively, p=0.00011). Separating patients with ET based on the prevalence of jitter, revealed that those with the dominant hand tremor, CPU was 0.373±0.02 g /l, higher than in patients with

head tremor (0.303±0.02 g/l, p=0,046). Other indicators in the selected groups were unaltered, therefore necessitating further research of objective markers of inflammation and oxidative stress in patients with ET.

Day 4. Fri, May 19, 2017

SYMPOSIUM 9: ZNRC ZEBRAFISH NEUROSCIENCE SYMPOSIUM
Chairs: AV Kalueff, Russia, S Winberg, Sweden

INTRODUCTION: THE INTERNATIONAL ZEBRAFISH NEUROSCIENCE CONSORTIUM (ZNRC)

As more and more labs are establishing zebrafish (*Danio rerio*) projects, zebrafish are rapidly becoming a popular model organism for neuroscience research. Created in February 2010, ZNRC is an active community of over 40 zebrafish laboratories worldwide which offers excellent networking opportunities, research collaboration and peer support for zebrafish neuroscience research. This regular Day 4 Symposium is co-sponsored by ISBS and ZNRC, to promote translational biopsychiatry and stress research using novel model organisms, such as zebrafish.

STRESS COPING STYLES IN FISH - BEHAVIORAL CORRELATES, NEUROENDOCRINE AND MOLECULAR MECHANISMS. S Winberg, A Mustafa, G André and P-O Thörnqvist, Uppsala University, Uppsala, Sweden; University of Western Australia, Australia

In teleosts, as in other vertebrates, divergent stress coping styles usually referred to as proactive and reactive has been described. Proactive animals are bold, aggressive, make active attempts to escape or fight stressors whereas reactive individuals are shy, non-aggressive and respond to threats by a passive response. Physiologically, the reactive coping style is characterized by high sympathetic reactivity but a more modest elevation of plasma glucocorticoids in response to stressors. Again, reactive animals show the opposite pattern, responding to stressors with high plasma glucocorticoids and relatively low catecholamine levels. Differences in stress coping style are also reflected in how individuals perceive and react to their environment. Reactive animals are more responsive to environmental cues and show a more plastic behavior whereas proactive animals develop behavioral routines. Stress coping style is heritable but is also modified by environmental cues, especially social interaction. We use the zebrafish (*Danio rerio*) as a model to study mechanisms controlling stress coping styles. A selective breeding program is performed to generate two strains of zebrafish displaying divergent stress coping styles. Initial breeders were identified from a population of wild caught zebrafish by behavioral screening, and used to generate F1. Thereafter, the procedure was repeated in subsequent generations (F2 in progress). The F1 behavior of these strains was screened throughout development. In an attempt to study the effects of social stress, brain tissue was sampled from bold (proactive) and shy (reactive) fish with experience of being either socially dominant or subordinate in a pair. The results show that already in the F1 generation there is a clear divergence in behavioral profiles of fish selected for bold (proactive) and shy behavior (reactive). Bold and shy fish show differences in the brain expression of genes related to serotonergic, dopaminergic, histaminergic and the opioidergic systems. The serotonergic system is clearly affected by social stress whereas differences in dopaminergic, histaminergic and opioidergic neurotransmission between bold and shy fish appear less affected by social interaction. **RESEARCH SUPPORT:** The Swedish Research Council (VR), The Swedish Research Council Formas, the ERA and Era-net WinFish.

ZEBRAFISH MODELS OF NEURODEVELOPMENTAL BRAIN DISORDERS: FOCUS ON AUTISM, ADHD AND COGNITIVE DISABILITY. AV Kalueff, ISBS Fellow, and DA Meshalkina, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Ural Federal University, Ekaterinburg, Russia; School of Pharmaceutical Sciences, Southwest University, Chongqing, China

Neurodevelopmental disorders (NDDs) are highly prevalent and severely debilitating brain illnesses caused by aberrant brain growth and development (Homberg et al, 2016). Resulting in cognitive, social, motor, language and affective disabilities, common NDDs include autism spectrum disorder (ASD), intellectual disability (ID), communication/speech disorders, motor/tic disorders and attention deficit hyperactivity disorder (ADHD). Affecting neurogenesis, glia/neuronal proliferation and migration, synapse formation and myelination, aberrant neural development occurs over a long period of time. Genetic, epigenetic, and environmental factors play a key role in NDD pathogenesis. Animal models are an indispensable tool to study NDDs, and the zebrafish (*Danio rerio*) is rapidly emerging as a promising new model organism in this field. For example, as a highly social and genetically tractable organism, zebrafish have recently been applied to model a variety of deficits relevant to ASD (Stewart et al, 2014; Meshalkina et al, 2017). We also recognize the value of zebrafish in understanding cognitive phenotypes, relevant to ID and a wide range of other NDDs. There is also a growing potential of zebrafish models for high-throughput genetic mutant and small molecule screening (e.g., amnestics, cognitive enhancers, neurodevelopmental/neurodegenerative drugs), which becomes critical for identifying novel candidate genes and molecular drug targets to treat NDDs. Paralleling clinical findings, we will comprehensively evaluate various zebrafish-based tests and models which target key (social, cognitive, motor) neurobehavioral domains of ASD, ADHD, ID and other common NDDs in zebrafish. Bridging both traditional (rodent) and alternative (zebrafish) NDD models, we will outline the emerging areas of research in this field, and emphasize how preclinical zebrafish-based models may play a key role in gaining translational and mechanistic insights into NDDs and their therapy.

ZEBRAFISH SELECTIVE BREEDING FOR BOLDNESS RESULTS IN DIVERGENT BEHAVIORAL PROFILES OF LARVAE FROM THE F1 GENERATION. A Mustafa and S Winberg, Uppsala University, Uppsala, Sweden

INTRODUCTION: As in various other vertebrates, divergent stress coping styles usually referred to as proactive and reactive has been described in zebrafish (*Danio rerio*). Proactive individuals are aggressive, bold and usually characterized by high exploratory behavior, low hypothalamic-pituitary-interrenal (HPI) axis reactivity, routine formation etc. On the opposite, reactive individuals are shy, non-aggressive, less exploratory, more plastic in their behavior and respond to stress with a more pronounced activation of the HPI axis. In this study we screened wild caught zebrafish for boldness. Males and females displaying high and low boldness were identified and used in selective breeding. Here, we report divergent behavior of larvae from the F1 generation (of bold and shy strains of zebrafish). Moreover, the behavior of larvae from strains selectively breed for bold (proactive) and shy (reactive) behavioral profiles are compared to larvae obtained from random mating. **METHODS:** We screened the wild caught zebrafish from India for willingness to explore an unfamiliar environment, a traditional open field test and novel tank diving test to obtain the extremely bold and extremely shy male and female fish. Then we crossed the bold and shy parents identified through this behavioral screening. We also crossed unselected fish of same age. This way, we generated three groups of larvae derived from bold, shy and unselected parents, respectively. We performed the following behavioral test on larvae from these strains: a) A light-dark test in which larvae of each strain were kept in a 96 well plate and subjected to dark and light conditions. The behavioral activity was measured using the Daniovision system (Noldus IT). b) Social cue test. The social stimulus was a group of larvae (7-9) kept in small chamber in one of the arms of a U shaped chamber. A single test larvae was released in the other arm of the chamber and the activity and number of transition to the social zone (the zone in front of the group of larvae) were quantified using Ethovision (Noldus IT). Numerous other parameters like time spent in the social zone, latency to enter the social zone, distance moved and velocity in social zone were used to judge the boldness and shyness. All the experiments on larvae were performed on 8-day old larvae. **RESULTS AND DISCUSSION:** Our results show clearly divergent behavioral profiles of larvae derived from bold and shy parents. Larvae derived from the bold parents were more explorative and more attracted by conspecifics than larvae of the shy strain. We also see significant differences in how larvae of the bold and shy strain respond in the light/dark test. **RESEARCH SUPPORT:** Swedish Research Council Formas and the Facias Foundation.

ACUTE ALPHA-NETA EFFECTS ON ZEBRAFISH BEHAVIOR AND SEROTONIN METABOLISM. DA Meshalkina, EV Kysil, KA Antonova, MN Kislyk, EV Efimova and AV Kalueff, ISBS Fellow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: Alpha-NETA is a choline acetyltransferase inhibitor, causing motor phenotypes in rodents. To support its effect on zebrafish, we performed the analysis of its effects on the behavior and monoamine metabolism. **METHODS:** After a 20-min incubation with alpha-NETA solution (at 3, 0.3, and 0.03 mg/L), the fish behavior in novel tank test was video recorded 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). The significance of the associations was tested by the Kruskal-Wallis test with post-hoc Dunn analysis and FDR correction. **RESULTS AND DISCUSSION:** HPLC analysis of alpha-NETA treated brain samples showed decreased 5-HIAA content and lower 5-HIAA/5-HT ratio (from 0.328±0.014 in control to 0.226±0.024 at 3 mg/L dose, $p=0.026$). This action indicated enhanced 5-HT accumulation in the treated animals, that is relevant to decreased ACh synthesis, resulting from the inhibition with alpha-NETA. Analyses of zebrafish behavior in the novel tank test revealed a range of effects on their motor activity characteristics. Specifically, alpha-NETA caused a significant decrease in the mean movement velocity ($p=0.0037$) and distance traveled ($p=0.0064$), while not altering anxiety endpoints (time in the top of the tank or latency to enter the top) even at high doses. This supports the idea of motor and coordinational alpha-NETA effects, and its relevance for zebrafish as a choline acetyltransferase inhibitor. **RESEARCH SUPPORT:** The study was performed at the Environmental Safety Observatory Bioelectronic complex of SPbU, and is supported by the Russian Foundation for Basic Research (RFBR) grant 16-04-00851 A.

POPULAR ANTIFUNGAL DRUGS WITH ANTIGLUCOCORTICOID PROPERTIES, CLOTRIMAZOLE AND KETOCONAZOLE, CAUSE ANXIOLYTIC-LIKE BEHAVIOR AND MOTOR DISRUPTION IN ZEBRAFISH – A PILOT STUDY. KA Demin, TO Kolesnikova, SL Khatsko and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: Clotrimazole (Clo) and Ketoconazole (Ket) are imidazole derivatives used as antifungal agents, with a wide range of applications, including medical shampoos. Both drugs may disrupt steroidogenesis, and act as the glucocorticoid receptor (GR) antagonists. Interestingly, Ket antagonizes GR in a different way than another popular antiglucocorticoid agent, RU-486 (Svec 1988). GRs play an important role in the HPA axis response to stress. Zebrafish (*Danio rerio*) are a promising novel model organism, highly sensitive to multiple different stressors. The aim of this study was to characterize specific stress-induced behaviors in adult zebrafish following their exposure to antiglucocorticoid agents Clo and Ket. **METHODS:** A total of 20 wild-type short-fin zebrafish (1:1 male:female ratio) were used in this study, divided into 5 groups: Control group, 1.4 mg/l or 14 mg/l Clo-exposed groups, and 2.8 mg/l or 28 mg/l Ket-exposed groups. The novel tank test was used to assess zebrafish behavior for 5 min, following a 20-min pretreatment with Clo or Ket in a 0.5-L beaker. Time spent in upper half, latency to enter upper half, distance traveled (cm), maximal velocity (cm/sec), number of erratic movements, time spent freezing, and ataxia duration were analyzed in this pilot study (n=4) using the Mann-Whitney test vs. controls.

RESULTS: There was no significant difference in distance traveled, maximal velocity, the number of erratic movements, time freezing and ataxia in any group. The Ket 28 mg/l group showed significant increase in time spent in upper half, and fewer erratic movements. The Ket 2.8 mg/l and Clo 1.4 mg/l groups showed only the reduction in erratic movements. There was no significant difference in Clo 14 mg/l group behaviors from controls. **DISCUSSION:** The Ket 28 mg/l group resembled classical anxiolytic-like phenotype. The Ket 2.8 mg/l resembled this phenotype only partially, likely because of the low dose used. For Clo groups, both had 1 fish with ataxia. Low dose results in involuntary tale rise, and the higher dose additionally results in corkscrew-like swimming, with no other significant drug effects on behavior. It is possible that 1.4 mg/l dose (like Ket 2.8 mg/l) was too low, and the 14 mg/l dose was too high, to achieve the phenotype (note that Clo is known to be more potent as an antagonist than Ket; Loose al. 1983). In summary, zebrafish exposure to Ket may result in dose-dependent anxiolytic-like behavior, possible due to a GR antagonism and anti-steroidogenesis properties. Thus, Ket may become a cheap and promising tool to study GR-specific stress reactions, and these effects can be comparable to those evoked by the refrence drug RU-486. On the other hand, it is unclear whether Clo exposure may result in the same phenotype, necessitating further dose-dependent studies of its properties and further dissecting anxiety-related from toxicity-related responses. Finally, these pilot results are interesting from the environmental health and practical application standpoints, given the wide use of the two tested compounds in medicinal shampoos.

EFFECTS OF U-47700, A μ-OPIOID RECEPTOR AGONIST, ON ADULT ZEBRAFISH BEHAVIOR TESTED IN THE NOVEL TANK TEST. TO Kolesnikova, SL Khatsko, VA Shevyrin, OS Eltsov and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Russia

INTRODUCTION: Zebrafish (*Danio rerio*) is a popular animal model for toxicology and neurobiology research, as well as for CNS drug discovery. 3,4-dichloro-N-[(1R,2R)-2-dimethylamino)cyclohexyl]-N-methylbenzamide (U-47700) is a μ-opioid receptor agonist developed in 1978. U-47700 exerts opioid-like adverse effects in humans, and has analgesic properties similar to morphine. The aim of this study was to characterize in detail acute behavioral effects of U-47700 in adult zebrafish. **METHODS:** 95 adult wild-type shortfin zebrafish (1:1 male:female ratio) were housed 40 per 40-L tank, according to the standards of zebrafish care. All fish were experimentally naïve prior to testing. The novel lank test was used to assess zebrafish behavior for 5 min following a 20-min water bath exposure to 1, 5, 10, 25 and 50 mg/l of U-47700. We analyzed the latency (s) and number of top entries, time spent in the upper half, duration and frequency of freezing and the number of anxiety-like erratic movements. Additionally, we also evaluated the zebrafish skin coloration scores. **RESULTS AND DISCUSSION**: Overall, U-47700 did not alter fish behaviors at 1 and 5 mg/L, but at 10, 25 and 50 mg/L it significantly decreased the number of top entries and duration top swimming, compared to the control group. In addition, 50 mg/L elevated freezing frequency and duration vs. 5 mg/L. The top entry latency rose in 50 mg/L vs. control, 1 and 5 mg/L. Finally, zebrafish treated with the three high U-47700 doses (10, 25 and 50 mg/L) showed significantly darker skin coloration, compared to controls. The drug also caused ataxia and vertical swimming at the highest (50 mg/L) dose. Thus, U-47700 is likely to have pronounced psychoactive sedative-like properties with a strong analgesic action. **RESEARCH SUPPORT:** Ural Federal University, Ekaterinburg, Russia.

MODELING ANTIDEPRESSANT DISCONTINUATION SYNDROME (ADS) – PILOT STUDIES OF THE EFFECTS OF CHRONIC AMITRIPTYLINE DISCONTINUATION ON ZEBRAFISH. TO Kolesnikova, SL Khatsko, KA Demin, DA Meshalkina and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia

INTRODUCTION: Antidepressant withdrawal, or antidepressant discontinuation syndrome (ADS), occurs with all classes of antidepressant, and is particularly common for the selective serotonin reuptake inhibitors (SSRIs). While withdrawal from tricyclic antidepressants can also trigger ADS, some of them show a predominantly serotonergic profile, and in that sense are similar to SSRIs in their action. For example, amitriptyline is a tricyclic antidepressant with a strong serotonin transporter-inhibiting activity but rather minor norepinephrine transporter-inhibiting action. In general, ADS signs typically include flu-like symptoms, dizziness, imbalance, headache, sensory deficits, nausea and lethargy, with less frequent extrapyramidal syndromes and mania/hypomania (Haddad and Anderson, 2007). ADS have a generally rapid onset (e.g., within days of stopping the antidepressant), last for 1-2 weeks, but show a fast resolution when the drug is reinstated (Haddad and Anderson, 2007). With the growing use of antidepressant therapy globally, ADS becomes a serious biomedical problem, necessitating both clinical and pre-clinical experimentation. Here, we attempt to develop an ADS model based on an aquatic (zebrafish) species undergoing withdrawal from chronic antidepressant amitriptyline. **METHODS:** A total of 78 adult wild type short-fin zebrafish were housed in groups in tank filled with clear water, according to the standards of zebrafish care. All fish were experimentally naïve before testing. The novel tank test was used to assess zebrafish behavior for 5 min. In Experiment 1, we assessed zebrafish behavior after 14 days of chronic treatment of amitriptyline (0.05 mg/L). In Experiment 2, we observed zebrafish behavior 3 days after the withdrawal of amitriptyline. In both experiments, the latency (s) and number of top entries, time spent in the upper half (top), duration and frequency of freezing and the number of anxiety-like erratic movements were evaluated. **RESULTS AND DISCUSSION:** Overall, chronic 2-week amitriptyline treatment significantly reduced the number of top entries, but increased the duration of top swimming, decreased the number of erratic movements and shortened the latency of top entries, compared with water control fish. These effects were generally similar to acute effects of higher amitriptyline doses in zebrafish tested in the novel tank test (Demin et al, 2017). In Experiment 2, amitriptyline continued to lower the number of top entries and erratic movements, whereas the duration of top swimming was increased compared with control. Similar to Experiment 1, amitriptyline shortened the latency of top entries, also reducing the freezing duration. In addition, amitriptyline caused ataxia and vertical swimming in both Experiments 1 and 2, similar to effects of acute action of the higher doses of this drug (Demin et al, 2017). The present study was first to describe behavioral effects of chronic administration amitriptyline in adult

zebrafish, which were also strikingly similar to chronic administration of fluoxetine, an SSRI. In contrast, and despite our expectations, the ADS-like effects were not present in the drug-withdrawal group here, similar to our previous pilot attempts to model ADS for chronic fluoxetine (Kalueff et al, 2009-2012, unpublished data). Taken together, these findings suggest that amitriptyline is likely to have more prolonged serotonergic-like anxiolytic-like effects in zebrafish, but may necessitate a longer withdrawal period if it is able to cause ADS in zebrafish models. **RESEARCH SUPPORT:** Ural Federal University, Ekaterinburg, Russia

WHEN FISH TAKE A BATH: EXAMINING THE EFFECTS OF ALPHA-PYRROLIDINOPENTIOPHENONE (ALPHA-PVP), A BATH SALT "FLAKKA", IN ZEBRAFISH – PILOT STUDIES. TO Kolesnikova, SL Khatsko, OS Eltsov, VA Shevyrin, YuYu Morzherin and AV Kalueff, ISBS Fellow, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA

INTRODUCTION: Alpha-pyrrolidinovalerophenone (α-PVP) is a synthetic cathinone and the primary psychoactive alkaloid of khat. A psychotropic drug developed in the 1960s as a stimulant, α-PVP has not become a medication, but has recently reached drug market as an abused substance. Sold illegally as flakka", "bath salts" or "gravel", this drug is currently a strictly controlled substance in many countries worldwide. The psychopharmacological profile of α-PVP is poorly understood, but includes potent inhibition of the dopamine (DAT) and norepinephrine (NET) but little effects on the serotonin (SERT) transporters. A-PVP is more potent than cocaine and amphetamine as a DAT/NET blocker, strongly implicating it as a potent psychotropic drug with high abuse potential. In humans, α-PVP causes robust mental (agitation, aggression, hallucinations, delirium, reduced consciousness, confusion, anxiety and/or psychosis) and physiological effects (hypertension, tachycardia, mydriasis, fever, diaphoresis, miosis, seizures and/or hypokalemia), as well as insomnia, headache and lethality. In rodents, α-PVP activates locomotion, exploration and circular ambulation, also causing flat body posture, other atypical behaviors (e.g., stereotyped head circling and weaving), Straub tail and piloerection. **AIM:** Given the rich spectrum of pharmacological activity, strong behavioral/physiological effects of α-PVP in rodents and humans, as well as high potential for drug abuse, further studies are needed to understand the psychopharmacology of this and related compounds in various model organisms. The zebrafish *(Danio rerio)* is a novel, rapidly accepted model organism in psychopharmacological research. Here, we further characterize the effects of α-PVP in-vivo by assessing its acute behavioral effects in adult zebrafish. **METHODS:** Adult (5–7 month-old) wild type short-fin zebrafish (50:50 male:female ratio) were housed in groups of 15 fish per 20-L tank, filled with filtered system water maintained at 22–25 ℃. All fish used in this study were experimentally naïve, and observed in the novel tank test. Prior to testing, fish were pre-exposed in a 0.5-L plastic beaker for 20 min to either drug-treated or drug-free vehicle, 0.1% solution of dimethyl sulfoxide (DMSO) known to be devoid of own behavioral effects in zebrafish, and is commonly used in zebrafish drug studies. For treatment, fish were randomly divided in 4 groups (n=15): drug-free control, 1, 5 and 10 mg/L α-PVP. The standard 20-min pre-treatment time was based on our prior experience with various CNS drugs. Fish were then exposed to the novel tank test, as a standardized sensitive method to assess zebrafish anxiety and locomotion. Trials were recorded by a side-view web-camera for further analyses to manually score different behavioral endpoints, such as the number and duration of freezing bouts, number of complete, circle moves, erratic movements and erratic bottom movements. Other parameters, including maximal and average velocity, distance traveled, top entries, time spent in top, the latency to top entry and others, were collected using Noldus Ethovision XT10 (Netherlands). **RESULTS AND DISCUSSION:** Overall, α-PVP at 1, 5, 25 and 25 mg/L did not change key novel tank endpoints – the duration, frequency and latency of top entries, as well as freezing bouts and the number of erratic movements. However, α-PVP significantly reduced mean, frequency and cumulative duration of regular mobility (20-60% of the average) and low mobility/immobility (<20% of the average) in doses 25 and 50 mg/L, without changes in general velocity and distance traveled in any dose. The later profile was suggestive of a trend towards increasing the portion of faster (>80% of the average) locomotion in α-PVP-treated fish. Therefore, for additional analyses we decided to divide the lower half of the tank into 2 parts: bottom-top and bottom-bottom. We found that α-PVP at 25 and 50 mg/L significantly reduced the number of bottom-top and bottom-bottom entries, but did not affect the time spent in those zones of the tank. The latter profile would be suggestive of a less variable spatial spread of swimming patterns in α-PVP-treated (vs. control) zebrafish. Furthermore, we also noted frequent stereotypic-like side-to-side swimming in drug-treated fish in the same vertical plane. To examine this phenotype in detail, we divided the novel tank into two vertical halves by a virtual vertical line, finding, surprisingly, that the 25-mg/L dose significantly reduced the number of crossing in bottom-top and bottom-bottom parts of the tank. Taken together, our results suggest that α-PVP modulates zebrafish behavior, but does so in several ways that are difficult to characterize using the 'conventional' novel tank test analyses and endpoints. While seemingly unrelated to overt alterations in zebrafish anxiety levels, the drug profile observed here was interesting and unusual, and can be best described as a more rigid, stereotypic-like fish swimming near the tank bottom. Intriguingly, increased stereotypy in locomotion has previously been reported in humans and rodents following acute α-PVP administration, likely representing dopamine receptor-mediated phenotype. Thus, given potent DAT inhibition by this drug, future studies may need to explore putative hyper-dopaminergic mechanisms of similar α-PVP-evoked behavioral effects in zebrafish. Collectively, these pilot findings support zebrafish sensitivity to α-PVP and suggest that aquatic models based on these fish can be a sensitive tool to further examine the CNS effects evoked by α-PVP and related synthetic drugs of abuse.

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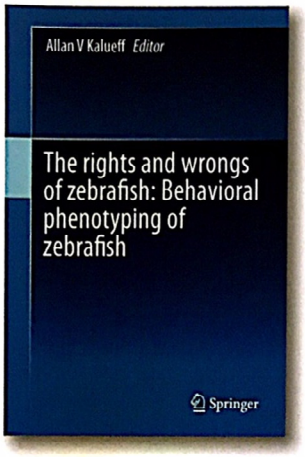

A.V. Kalueff (Ed.)

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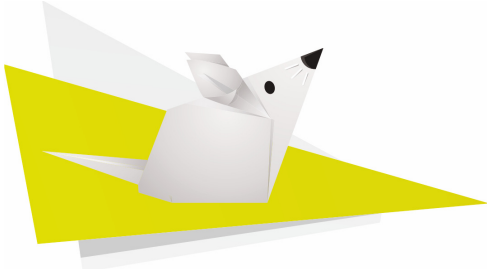

INVITATION LETTER

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)
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