STRESS, BRAIN AND BEHAVIOR

Program and Proceedings of the 25th Multidisciplinary International Neuroscience and Biological Psychiatry Conference "Stress and Behavior"

St-Petersburg, Russia
May 16-19, 2018

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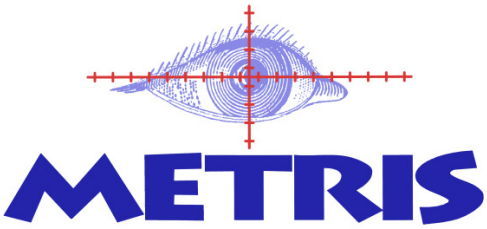

The International Stress and Behavior Society (ISBS)
Institute of Experimental Medicine (IEM)
Institute of Translational Biomedicine, St. Petersburg University
Centre for Physiology and Biochemical Research (CPBR)
The Russian Society for Biopsychiatry (RSBP)
The Ukrainian Society for Biological Psychiatry (USBP)

Program and Proceedings

25th Multidisciplinary International Neuroscience and Biological Psychiatry Conference

"Stress and Behavior"

St. Petersburg, Russia
May 16-19, 2018

CONFERENCE PROGRAM

Day 1. Wed, May 16, 2018

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

08.00-17.00 **REGISTRATION DESK OPEN**

09.00-09.15 **CONFERENCE OPENING AND WELCOMING ADDRESSES**
INDUCTION OF NEW ISBS FELLOWS
Prof AV Kalueff, ISBS President and Conference Chair (Russia, China)
Prof VM Klimenko, Program Committee Chair (Russia)

09.15-09.55 **PLENARY LECTURE 1: ROBUST ANTI-STRESS EFFECTS OF DOPAMINE D3 RECEPTOR ANTAGONISTS IN A LABORATORY ANIMAL MODEL OF POST-TRAUMATIC STRESS DISORDER.** EL Gardner, CR Ashby Jr, R Song, C Dixon, W Laurenzo and OV Rice, US National Institute on Drug Abuse, Baltimore, Maryland; Saint John's University, Queens, NY, USA; Beijing Institute of Pharmacology and Toxicology, Beijing, China; Furman University, Greenville, South Carolina, USA

09.55-10.20 **STATE OF THE ART IN BEHAVIORAL PHENOTYPING – TOOLS AND TECHNIQUES FOR RODENTS AND ZEBRAFISH.** A Willemsen, NOLDUS IT, Wageningen, Netherlands

10.20-10.40 **FACEREADER: FACIAL EXPRESSION ANALYSIS FOR STUDYING HUMAN BEHAVIOR.** T den Uyl, VicarVision, Amsterdam, Netherlands

10.40-14.00 **ISBS-ITBM SYMPOSIUM 1: ADVANCES IN UNDERSTANDING MOLECULAR MECHANISMS OF NEUROPSYCHIATRIC DISORDERS**
Chairs: RR Gainetdinov (Russia) and J-M Beaulieu (Canada)

10.40-10.50 **INTRODUCTION**

10.50-11.25 **NORADRENERGIC CONTROL OF RESILIENCE TO CHRONIC STRESS.** B Giros, Douglas Hospital Research Center, McGill University, Montreal, Canada

11.25-11.55 **CHRONIC BLOCKADE OF METABOTROPIC GLUTAMATE RECEPTOR 5 IN APPSWE/PS1DE9 AND 3XTG-AD MOUSE MODELS AMELIORATES ALZHEIMER'S DISEASE PATHOGENESIS.** SSG Ferguson, University of Ottawa Brain and Mind Institute, Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Canada

11.55-12.25 **FUNCTIONAL MAPPING OF CORTICAL DOPAMINE D2 RECEPTOR EXPRESSING NEURONS.** J-M Beaulieu, J Khlghatyan and C Quintana, Department of Pharmacology and Toxicology, University of Toronto, Medical Sciences Building, Toronto, Canada

12.25-12.45 ***COFFEE BREAK***

12.45-13.10 **DOPAMINE TRANSPORTER DEFICIENCY SYNDROME; PHARMACOLOGICAL CHAPERONES AND A NEW ANIMAL MODEL.** P Beerepoot, C Sutton, VM Lam and A Salahpour, Department of Pharmacology and Toxicology, University of Toronto, Toronto, Canada

13.10-13.30 **NEURONAL FUNCTIONS OF TRACE AMINE-ASSOCIATED RECEPTOR 5 (TAAR5).** S Espinoza, I Sukhanov, P Illiano, D Leo, TD Sotnikova and RR Gainetdinov, Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Genova, Italy; Skolkovo Institute of Science and Technology (Skoltech), Skolkovo, Moscow, Faculty of Biology and Soil Science, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

13.30-14.00 **PHENOTYPICAL, BEHAVIORAL AND PHARMACOLOGICAL CHARACTERIZATION OF THE DOPAMINE TRANSPORTER KNOCKOUT RATS.** RR Gainetdinov, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Skolkovo Institute of Science and Technology (Skoltech), Skolkovo, Moscow, Russia

14.00-15.00 **LUNCH BREAK (FREE TIME)**

15.00-15.30 **CONFERENCE PRESENTATION: THE SONOTRACK CALL CLASSIFICATION PROJECT: ENABLING PHENOTYPING BASED ON ULTRASOUND VOCALIZATIONS.** L Bachdasarian, R Bulthuis and G Piavchenko, Metris B.V., Hoofddorp, Netherlands; University of Orel, Orel, Russia

15.30-17.30 **SYMPOSIUM 2: ZUKOWSKA STRESS NEUROSCIENCE SYMPOSIUM**
Chairs: VM Klimenko (Russia), AV Kalueff (Russia, China)

15.30-15.40 **INTRODUCTION: PROFESSOR ZOFIA ZUKOWSKA**

15.40-16.00 **SWITCHING PREFRONTAL CORTEX NEURAL HEMISPHERIC ACTIVITY IN THE LEARNING PROCESS.** EV Filatova, AA Orlov, SV Afanasyev and AY Egorov, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

16.00-16.15 **AMYLOID β 25-35 ALTERS PHASIC SECRETORY ACTIVITY OF THE BRAIN DOPAMINERGIC PATHWAYS IN THE RATS.** VN Mukhin, V Sizov, K Pavlov, I Borovets and VM Klimenko, Institute of Experimental Medicine, Pavlov Department of Physiology, St. Petersburg, Russia

16.15-16.35 ***COFFEE BREAK***

16.35-16.55 **ASSESSMENT OF INDIVIDUAL RISK FACTORS FOR THE FORMATION OF ALCOHOL PREFERENCES IN RATS.** AY Egorov, IV Demianko and EV Filatova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Mechnikov Nord West State Medical University, Hertzen Russian State Pedagogical University, St. Petersburg, Russia

16.55-17.20 **NEUROIMAGING CHARACTERISTICS OF MOVEMENT DISORDERS.** D Kozić and K Ivošević, University of Novi Sad Faculty of Medicine, Novi Sad, Serbia

17.20-17.30 **GENERAL DISCUSSION**

17.30-18.00 **ISBS FELLOW LECTURE: STRESS-RESILIENCE AS A COMPLEX PHENOMENON.** VA Rozanov, St. Petersburg State University, St. Petersburg, Russia

18.00-18.15 **ART MEETS SCIENCE: INVITATION TO THE EXHIBITION.** D Raytchev, London, UK

18.15-19.15 **SOCIAL EVENT 1: RECEPTION AND MUSIC CONCERT - CO-SPONSORED BY THE ISBS AND THE INTSTITUTE OF TRANSLATIONAL BIOMEDICINE (ITBM) OF ST. PETERSBURG STATE UNIVERSITY: CELEBRATION OF 3 YEARS OF SUCCESS.**

19.30-22.30 **SOCIAL EVENT 2: BUS CITY TOUR (admissions)**

Day 2. Thur, May 17, 2018

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

08.30-17.00 **REGISTRATION DESK OPEN**

09.00-09.30 **ISBS SPECIAL LECTURE: RESILIENCE TO THE EFFECTS OF STRESS.** J Erskine, St George's University of London, London, UK

09.30-13.00 **SYMPOSIUM 3: ADDICTIVE BEHAVIORS AND STRESS: FROM CORRELATIONS TO MECHANISMS**
Chair: EA Budygin (USA)

09.30-09.40 **INTRODUCTION**

09.40-10.10 **THE ROLE OF DOPAMINE UPTAKE CHANGES IN COCAINE ADDICTIVE BEHAVIORS.** KD Bonin, Wake Forest University, Winston Salem, NC, USA

10.10-10.40 **DOPAMINERGIC MECHANISMS OF ALCOHOL ADDICTIVE BEHAVIORS.** EA Budygin, Wake Forest School of Medicine, Winston Salem, NC, USA

10.40-11.10 **CHRONIC ETHANOL AND HETEROSYNAPTIC PLASTICITY IN THE AMYGDALA.** BA McCool, MM McGinnis and M Morales, Wake Forest School of Medicine, Winston Salem, NC, School of Pharmacy and Pharmaceutical Sciences, Binghamton University, Binghamton, NY, USA

11.10-11.40 **PROBING THE NEURAL SUBSTRATES AND CIRCUITS OF VULNERABILITY TO ALCOHOL USE DISORDER AND COMORBID ANXIETY/STRESSOR-RELATED DISORDERS.** JL Weiner, SE Ewin, AN Karkhanis, JW Morgan, AG Almonte and SR Jones, Wake Forest School of Medicine, Winston Salem, NC, USA

11.40-12.00 ***COFFEE BREAK***

12.00-12.30 **ISBS SPECIAL LECTURE: EXTRACELLULAR VESICLE-INDUCED SICKNESS BEHAVIOR.** DC Anthony, Department of Pharmacology, University of Oxford, Oxford, UK

12.30-13.00 **INSTRUMENTATION FOR FAST-SCAN CYCLIC VOLTAMMETRY IN FREELY MOVING ANIMALS.** CJ McKinney, MD Verber and RM Wightman, Department of Chemistry, University of North Carolina, NC, USA

13.00-13.30 **CONFERENCE PRESENTATION: BEHAVIORAL TESTING STANDARD OF THE FUTURE.** J Fehmer, TSE Systems GmbH, Bad Homburg, Germany

13.30-14.00 **CONFERENCE PRESENTATION:** RWD Life Science, USA

14.00-15.00 **LUNCH BREAK (FREE TIME)**

15.00-18.00 **SYMPOSIUM 4: MODERATED POSTER SESSION**

SCHIZOPHRENIA WITH PERSECUTORY DELUSIONS AND SOMATIC PASSIVITY. LK Wei, Department of Psychiatry, National Health Group, Singapore City, Singapore

CORRELATIONS BETWEEN C-REACTIVE PROTEIN, RECENT LIFE-EVENTS STRESS, AND COGNITIVE FUNCTION IN PATIENTS WITH BIPOLAR DISORDER. LY Tang, HH Chang and PS Chen, Institute of Clinical Pharmacy and Pharmaceutical Sciences, School of Pharmacy, Department of Psychiatry, College of Medicine, National Cheng Kung University, Tainan, Taiwan

THE THIOREDOXIN-1 DOWNREGULATION IN NUCLEUS ACCUMBENS PROMOTES METHAMPHETAMINE-PRIMED REINSTATEMENT IN MICE. J Bai, MB Huang, C Yan, XY Yang, XS Zhou, W Lv, NN Guo and Y Li**,** Medical Faculty, Kunming University of Science and Technology, Kunming, China

INTERACTIONS OF SOCIAL STRESS AND *CRP* GENE POLYMORPHISM ON TREATMENT OUTCOME IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER. HH Chang and PS Chen, Institute of Clinical Pharmacy and Pharmaceutical Sciences, School of Pharmacy, Department of Psychiatry, College of Medicine, National Cheng Kung University, Tainan, Taiwan

THE INTERACTION OF OXYTOCIN AND SOCIAL SUPPORT IS ASSOCIATED WITH LONELINESS AND CORTISOL LEVEL IN MAJOR DEPRESSION. PS Chen, TY Tsai, HH Tseng, HH Chang, MH Chi, YK Yang, Department of Psychiatry, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

SUBFEBRILE STATE AND ANXIETY: EFFECTS OF DULOXETINE. A Miljatovic, Community Health Centre "Milutin Ivkovic", Belgrade, Serbia

EFFECT OF ATYPICAL ANTIPSYCHOTICS ON EYE MOVEMENTS IN SCHIZOPHRENIA DURING EARLY WEEKS OF TREATMENT. B Cetin-Ilhan, B Ilhan and BD Ulug, Konya Training and Research Hospital, Necmettin Erbakan University, Konya, Hacettepe University, Ankara, Turkey

RELATIONSHIP OF INJECTOR SHARING WITH CLINICAL CHARACTERISTICS AND SELF-HARMING BEHAVIOR IN A SAMPLE OF PATIENTS WITH HEROIN USE DISORDER. C Evren, İ Alnıak, V Karabulut, T Çetin, G Umut, R Ağaçhanlı and B Evren, Research, Treatment and Training Center for Alcohol and Substance Dependence, Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Ardahan State Hospital, Department of Psychiatry, Baltalimani State Hospital for Musculoskeletal Disorders, Istanbul, Turkey

RELATIONSHIP OF LIFETIME SUBSTANCE USE AND THE SELF-HARMING BEHAVIOR AMONG YOUNG ADULTS. B Evren, C Evren, E Dalbudak, M Topcu and N Kutlu, Department of Psychiatry, Baltalimani State Hospital for Muskuloskeletal Disorders, Research, Treatment and Training Center for Alcohol and Substance Dependence, Bakirkoy Training and Research Hospital for Psychiatry Neurology and Neurosurgery, Istanbul, Cankaya University Department of Psychology, Ankara, Turkey

THE EFFICACY OF VORTIOXETINE IN A MAJOR DEPRESSION CASE AND FOLLOW-UP OF PRURITUS ADVERSE EFFECT. B Yelken, Turkey

RELATIONSHIP BETWEEN CHILDHOOD TRAUMAS AND OBSESSIVE COMPULSIVE DISORDER. Birmay Çam İkiz**,** Manisa Mental Health Hospital Psychiatry Department, Manisa, Turkey

EFFECTS OF DEPRESSION AND ANXIETY LEVELS ON QUALITY OF LIFE IN TYROID CANCER PATIENTS. G Elboga, Gaziantep University Medical Faculty, Department of Psychiatry, Gaziantep, Turkey

THE FORWARD AND BACKWARD LOCOMOTION DURING ASYMMETRICAL SPINAL CORD STIMULATION. N Merkulieva, V Lyakhovetskii and P Musienko, St. Petersburg State University, Pavlov Institute of Physiology RAS, Russian Scientific Center for Radiology and Surgical Technologies, St. Petersburg, Russia

GAMBLING DISORDER AND DEPRESSION COMORBIDITY A CASE REPORT. MA Kocatas, Istanbul Silivri State Hospital, Istanbul, Turkey

DEVELOPMENT AND VALIDATION OF THE STROKE SCALE AMONG THE SYSTEM OF QUALITY OF LIFE INSTRUMENTS FOR CHRONIC DISEASES (QLICD-ST). CH Wan, CZ Xu, LH Chang, FQ Sun, P Quan and JJ Zhang**,** Research Center on Quality of Life and Applied Psychology, School of Humanities and Management, Guangdong Medical University, Dongguan; The First Affiliated Hospital of Kunming Medical University, School of Public Health, Kunming Medical University, Kunming, China

FACTOR OF EMOTIONAL VALENCE OF TV MESSAGE IN MEDIA RECEPTION. SV Tukaev, IG Zyma, YD Havrylets and VV Rizun, Taras Shevchenko Kyiv National University, Kyiv, Ukraine

PSYCHOEMOTIONAL DISTURBANCES IN RATS IN THE LITHIUM-PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY. IV Smolensky, OE Zubareva, SV Kalemenev, VV Lavrent`eva, AV

Dyomina and AV Zaitsev, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

CHANGES IN COGNITIVE FUNCTIONS AND ANXIETY LEVELS CAUSED BY INJECTING OF BACTERIAL LIPOPOLYSACCHARIDE IN EARLY POSTNATAL ONTOGENESIS. AV Dyomina, AA Karepanov, DV Krytskaya, AP Schwarz, SV Kalemenev and OE Zubareva, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Experimental Medicine, St. Petersburg, Russia

CHANGES IN GLUTAMATE RECEPTORS AND TRANSPORTER OF GENES' EXPRESSION IN THE RAT BRAIN AFTER LITHIUM-PILOCARPINE SEIZURES. AA Kovalenko, SV Kalemenev, OE Zubareva, AP Schwarz, AV Zaitsev, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia; Institute of Experimental Medicine, St. Petersburg, Russia

THE ACTIVITY OF MU- AND M-CALPAIN AFTER PSYCHOGENIC TRAUMA IN DIFFERENT STRUCTURES OF THE BRAIN. DU Krytskaya, MN Karpenko and SG Tsikunov, Institute of Experimental Medicine, St. Petersburg, Russia

MRNA EXPRESSION OF THE GLUTAMATE TRANSPORTER, NMDA AND AMPA RECEPTORS IN THE RAT BRAIN IN THE EXPERIMENTAL MODEL OF POST-TRAUMATIC STRESS DISORDER. GV Beznin, AA Kovalenko, MV Zakharova, VA Nikitina, AP Schwarz, SG Tsikunov and OE Zubareva, Institute for Experimental Medicine, Sechenov Institute for Evolutionary Physiology and Biochemistry RAS, St Petersburg, Russia

BIOINFORMATICS-BASED ANALYSES OF MOLECULAR NETWORKS IMPLICATED IN ABERRANT MOUSE GROOMING PHENOTYPES. AJ Friend and AV Kalueff, Tulane University School of Science and Engineering, New Orleans, ZENEREI Research Center, Slidell, LA, USA; St Petersburg State University, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

BEHAVIORAL EFFECTS OF TWO STRUCTURAL ANALOGS OF THIAZOLIDINE, KO-01 AND KO-04, IN ADULT RATS TESTED IN THE OPEN FIELD AND ELEVATED PLUS-MAZE TESTS: A PILOT STUDY. TO Kolesnikova, VG Borygina, AS Kraeva, SL Khatsko, KL Obydennov and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

BEHAVIORAL EFFECTS OF 4-(TRIFLUOROMETHYL)-2,4-DIHYDROCHROMENO[3,4-D][1,2,3]TRIAZOLE (CF3) AND 4-(TRICHLOROMETHYL)-2,4-DIHYDROCHROMENO[3,4-D][1,2,3]TRIAZOLE (CCL3) IN ADULT ZEBRAFISH TESTED IN THE NOVEL TANK TEST: A PILOT STUDY. TO Kolesnikova, SL Khatsko, VA Glinskikh, VYu Korotaev, IB Kutyashev, AYu Barkov and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

BEHAVIORAL EFFECTS OF CLOTRIMAZOLE (1-(2-CHLOROPHENY1)-DIPHENYLMETHYL-1H-IMIDAZOLE) IN ADULT ZEBRAFISH IN THE NOVEL TANK TEST. TO Kolesnikova, SL Khatsko, AV Zhdanov, MV Bytov, PE Prokhorova and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

TAAR5 IN THE REGULATION OF SENSORIMOTOR BEHAVIOR. D Kalinina, M Ptukha, N Merkulyeva, O Gorsky, Y Sysoev, A Volnova, R Gainetdinov and P Musienko, St. Petersburg State University, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Children's Surgery and Orthopedic Clinic, Department of Non-pulmonary Tuberculosis, Research Institute of Phthysiopulmonology; Russian Scientific Center for Radiology and Surgical Technologies, St. Petersburg State Chemical Pharmaceutical Academy, St. Petersburg, Russia

BRAIN BIOPSY AS A NEW TECHNIQUE TO ADDRESS DYNAMICS OF GENE EXPRESSION DURING STRESS IN MICE: THE ROLE OF SEROTONINERGIC SYSTEM. N Bazhenova, A Gorlova, G Ortega, N Markova, D Bonapartes, T Strekalova, K-P Lesch and DC Anthony, Institute of General Pathology and Pathophysiology, Moscow, Russia; Laboratory of Psychiatric Neurobiology, Sechenov First Moscow State Medical University, Moscow, Russia; Department of Neuroscience, Maastricht University, Maastricht, Netherlands; Division of Molecular Psychiatry, Clinical Research Unit on Disorders of Neurodevelopment and Cognition, Center of Mental Health, University of Wuerzburg,

Germany; Instituto de Medicina Molecular, Faculdade de Medicina de Lisboa, Universidade de Lisboa, Lisboa, Portugal; Department of Pharmacology, Oxford University, Oxford, UK

INVESTIGATION OF DEPRESSION-LIKE BEHAVIOR AND DESTRUCTIVE CHANGES IN THE DOPAMINERGIC AND NORADRENERGIC BRAIN SYSTEMS IN A MODEL OF THE PRECLINICAL-STAGE PARKINSON'S DISEASE IN AGED RATS. MB Pazi, AR Gazizova, DV Plaksina and IV Ekimova**,** Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

EFFECT OF BETULINIC ACID ON MOTOR BEHAVIOR AND NEURODEGENERATION IN THE NIGROSTRIATAL SYSTEM IN THE RAT MODEL OF PARKINSON'S DISEASE. MR Sadykova, MV Chernyshev, DV Plaksina, MA Guzeev and IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

GRP78 AFFECTS RECOVERY AFTER SLEEP DEPRIVATION IN RATS. VV Simonova, MA Guzeev, YuF Pastukhov and IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

N-HETEROCYCLIC BORNEOL DERIVATIVES ARE INHIBITORS OF MARBURG GLYCOPROTEIN-MEDIATED PSEUDOTYPE ENTRY. CAN THEY ABROGATE THE FILOVIRUS-INFLICTED STRESS? S Cheresiz, A Kononova, O Yarovaya, A Chepurnov, R Nikitina, A Pokrovsky, N Salakhutdinov and A Sokolova, Department of Medicine, Novosibirsk State University, Institute of Organic Chemistry, Institute of Clinical Immunology, Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia

OBTAINING FOUNDER MUTATIONS OF ZEBRAFISH SEROTONIN TRANSPORTER GENES FOR MODELLING AFFECTIVE DISORDERS – PROGRESS REPORT. MA Firulyova, EV Kysil, DA Meshalkina, PA Alexeeva and AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Almazov Medical Research Centre, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

MODELING WITHDRAWAL FROM CHRONIC FLUOXETINE TREATMENT IN ZEBRAFISH. KN Zabegalov, TO Kolesnikova, SL Khatsko, AV Zhdanov and AV Kalueff, Ural Federal University, Ekaterinburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

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

Day 3. Fri, May 18, 2018

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

08.45-17.00 **REGISTRATION DESK OPEN**

09.00-09.30 **ISBS SPECIAL LECTURE: A COMPETENCE MODEL-BASED ANALYSIS TO REDUCE PSYCHOSOCIAL RISKS AT WORK.** Ph Fauquet-Alekhine and L Rouillac, SEBE-Lab, Department of Psychological and Behavioral Sciences, LSE, London, UK; Laboratory for Research in Science of Energy, France and Germany; Nuclear Power Plant of Chinon, Avoine, France

09.30-11.40 **SYMPOSIUM 5: THE RUSSIAN SOCIETY OF PSYCHIATRISTS' SYMPOSIUM: PERSONALIZED PSYCHIATRY - THE POINT OF VIEW OF EARLY CAREER RESEARCHERS**
Chairs: NN Petrova, I Fedotov (Russia)

09.30-09.40 **INTRODUCTION.** NN Petrova and I Fedotov, Department of Psychiatry and Addictions, St. Petersburg State University, Committee for Working with Young Psychiatrists and Researchers, Psychiatry Department, Ryazan State Medical University, Early Career Psychiatrists' Council, the Russian Society of Psychiatrists, Ryazan, Russia

09.40-10.00 **PERSONALIZED PSYCHIATRY**. NN Petrova, School of Medicine, St. Petersburg State University, St. Petersburg, Russia

10.00-10.20 **BEHAVIORAL RISK FACTORS FOR HIV INFECTION.** EM Chumakov, NN Petrova, Department of Psychiatry and Addictions, St. Petersburg State University, Kaschenko First St. Petersburg Psychiatric Hospital, Section on Web-resources, the Early Career Psychiatrists' Council of the Russian Society of Psychiatrists, St. Petersburg, Russia

10.20-10.40 **GENETIC PREDICTORS OF TREATMENT-RESISTANT SCHIZOPHRENIA.** DN Sosin, MG Yanushko, MV Shamanina, MV Ivanov, St. Petersburg Bekhterev Psychoneurological Research Institute, Section on Scientific projects, the Early Career Psychiatrists' Council of the Russian Society of Psychiatrists, St. Petersburg, Russia

10.40-11.00 **BLOOD-BASED BIOMARKERS, COGNITIVE IMPAIRMENT AND THE COURSE OF SCHIZOPHRENIA.** M Dorofeikova, St. Petersburg Bekhterev Psychoneurological Research Institute, the Early Career Psychiatrists' Council of the Russian Society of Psychiatrists, St. Petersburg, Russia

11.00-11.20 **TOWARDS THE ZEBRAFISH-BASED MODELS FOR PERSONALIZED PSYCHIATRY - INSIGHTS FROM INDIVIDUAL, STRAIN AND GENDER DIFFERENCES, AND MODELING GENE X ENVIRONMENT INTERACTIONS.** AD Volgin, OV Yakovlev, KA Demin, MS de Abreu, PA Alekseeva, AJ Friend, TG Amstislavskaya and AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Almazov National Medical Research Center, Military Medical Academy, St Petersburg, Ural Federal University, Ekaterinburg, Russian Center for Radiology and Surgical Technologies, Pesochny, Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia; Bioscience Institute, University of Passo Fundo (UPF), Passo Fundo, Postgraduate Program in Pharmacology, Federal University of Santa Maria, Santa Maria, Brazil; Tulane University School of Science and Engineering, New Orleans, LA, USA; School of Pharmacy, Southwest University, Chongqing, China; The International Zebrafish Neuroscience Research Consortium (ZNRC), ZENEREI Research Center, Slidell, LA, USA

11.20-11.40 **ALTERED DEVELOPMENTAL MRNA EXPRESSION OF SHORT AND LONG D2 DOPAMINE RECEPTOR WITHIN PREFRONTAL CORTEX AND WORKING MEMORY DEFICIT IN THE RAT MODEL OF CHRONIC EARLY LIFE INFLAMMATION.** AP Schwarz, AYu Rotov, OI Chuprina, AN Trofimov, AM Ischenko, OE Zubareva and VM Klimenko, Institute of Experimental Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Research Institute of Highly Pure Biopreparations, St. Petersburg, Russia

11.40-12.00 ***COFFEE BREAK***

12.00-13.50 **SYMPOSIUM 6: NEURONUTRITIOLOGY**
Chairs: SA Apryatin, VA Rozanov (Russia)

12.00-12.10 **INTRODUCTION**

12.10-12.35 **EATING DISORDERS, STRESS AND SUICIDE.** VA Rozanov, St. Petersburg State University, St. Petersburg, Russia

12.35-13.00 **COMPARATIVE ANALYSES OF THE EFFECTS OF HIGH-FAT AND HIGH-CARBOHYDRATE DIET ON THE LEVEL OF ANXIETY, NEUROMOTOR AND COGNITIVE FUNCTION OF THE DOPAMINE TRANSPORTER KNOCKOUT RATS IN DIET-INDUCED OBESITY.** SA Apryatin, VA Shipelin, KV Mzhel'skaya, VS Evstratova, NV Trusov, NV Kirbaeva, RR Gainetdinov and IV Gmoshinski, Federal Research Centre of Nutrition and Biotechnology, Moscow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

13.00-13.20 **EFFECTS OF QUERCETIN ON NEUROMOTOR FUNCTION AND BEHAVIORAL RESPONSES OF THE ZUCKER RATS ON A HIGH-FAT AND HIGH-CARBOHYDRATE DIET.** KV Mzhel'skaya, VA Shipelin, AA Shumakova, AD Evstratova, DM Rezaeva, NV Trusov, NV Kirbaeva, SA Apryatin and IV Gmoshinski, Federal Research Centre of Nutrition and Biotechnology, Moscow, Russia

13.20-13.40 **CHANGES IN THE COMPOSITION OF INTESTINAL MICROBIOTA IN PATIENTS WITH MULTIPLE SCLEROSIS BY VARIOUS DISEASE-MODIFYING THERAPIES.** IN Abdurasulova, EA Tarasova, IV Kudryavtsev, AV Matsulevich, MK Serebryakova, EI Ermolenko, IG Nikiforova, AG Il'ves, EV Ivashkova, ID Stolyarov and VM Klimenko, Institute of Experimental Medicine, Institute of Human Brain RAS, St. Petersburg, Russia

13.40-13.50 **DISCUSSION**

13.50-15.00 **LUNCH BREAK (FREE TIME)**

15.00-17.30 **SYMPOSIUM 7: THE ROLE OF NEUROINFLAMMATION AND MITOCHONDRIAL DYSFUNCTION IN THE PATHOPHYSIOLOGY OF NEUROPATHOLOGICAL CONDITIONS: PREVENTIVE AND THERAPEUTIC IMPLICATIONS**
Chairs: T Strekalova (Netherlands, Russia), W Lim (Taiwan), D Anthony (UK)

15.00-15.10 **INTRODUCTION**

15.10-15.30 **RESILIENCE VERSUS SUSCEPTIBILITY TO THE DEPRESSIVE-LIKE SYNDROME IN ANIMAL MODELS OF DEPRESSION: METHODOLOGICAL AND CONCEPTUAL ASPECTS.** T Strekalova, Department of Neuroscience, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands; Laboratory of Psychiatric Neurobiology, Sechenov 1st Moscow Medical State University, Moscow, Russia

15.30-15.50 **MITOCHONDRIAL CONTROL OF INSULIN RECEPTOR ACTIVATION IN NEURONS.** IA Pomytkin, VG Pinelis, NA Semenova, ZI Storozheva, Laboratory of Psychiatric Neurobiology, Sechenov 1st Moscow Medical State University; Scientific Center of Children's Health; Emergency Children's Surgery and Traumatology Research Institute, Moscow, Russia

15.50-16.05 **INCREASED IMPULSIVITY AND MICROGLIA ACTIVATION IN THE PREFRONTAL CORTEX IN MICE HOUSED ON THE WESTERN DIET ARE ASSOCIATED WITH MULTIPLE BEHAVIORAL ABNORMALITIES.** E Veniaminova, M Oplatchikova, A Gorlova, D Pavlov, N Bazhenova, I Pomytkin, K-P Lesch, DC Anthony and T Strekalova, Laboratory of Psychiatric Neurobiology, Institute of Molecular Medicine, Sechenov University, Moscow, Russia; Department of Neuroscience, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands; Faculty of Biology, Lomonosov Moscow State University, Moscow, Russia; Department of Advanced Cell Technologies, Institute of Regenerative Medicine, Sechenov University, Moscow, Russia; Division of Molecular Psychiatry, Laboratory of Translational Neuroscience, Department of Psychiatry, Psychosomatics and

Psychotherapy, University of Wuerzburg, Wuerzburg, Germany; Department of Pharmacology, Oxford University, Oxford, UK

16.05-16.20 **BEHAVIORAL ALTERATIONS AND RESPONSE TO SYSTEMIC INFLAMMATION IN MICE WITH THE *FUS* GENE MUTATION, A NEW MODEL OF AMYOTROPHIC LATERAL SCLEROSIS.** A Trofimov, J de Munter, E Lysikova, E Veniaminova, A Gorlova, E Wolters, VM Klimenko, K-P Lesch and T Strekalova. Department of Neuroscience, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands; Laboratory of Psychiatric Neurobiology, Sechenov 1st Moscow Medical State University, Moscow, Institute of Experimental Medicine, St. Petersburg, Russia; Department of Psychiatry, University of Wurzburg, Wurzburg, Germany

16.20-16.40 **EFFECTS OF INTRACEREBROVENTRICULAR ADMINISTRATION OF NEURO-CELLS ON MOTOR HALLMARKS OF AMYOTROPHIC LATERAL SCLEROSIS IN THE *FUS*-TRANSGENIC MICE.** A Gorlova, J de Munter, E Walters, D Pavlov, N Bazhenova, E Veniaminova, DC Anthony and T Strekalova, Sechenov First Moscow State Medical University, Moscow, Russia; Lomonosov Moscow State University, Moscow, Russia; Maastricht University, Maastricht, Netherlands; Neuroplast Ltd, Maastricht, Netherlands; Oxford University, Oxford, United Kingdom

16.40-17.00 ***COFFEE BREAK***

17.00-17.30 **ISBS SPECIAL PLENARY LECTURE: DEEP BRAIN STIMULATION IN EXPERIMENTAL STRESS ANIMAL MODEL OF DEPRESSION.** LW Lim, Li Ka Shing Faculty of Medicine, the University of Hong Kong, Hong Kong

17.30-17.45 **THE EFFECTS OF CAFFEINE AND STRESS ON PSYCHOSIS-LIKE EXPERIENCE.** C Ágoston, Z Demetrovics, Doctoral School of Psychology, Institute of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary

17.45-18.00 **IMPACT OF SEVERE PEDIATRIC EPILEPSY (DRAVET SYNDROME) ON PARENTAL STRESS AND ANXIETY.** T Leonova, S Auvin, S Caharel, N Coqué, Nabbout, M Robert, A de Saint Martin and A Piquard-Kipffer, Université de Lorraine, Hôpital Robert-Debré, Agro-Paris-Tech, Hôpital Necker, Université de Strasbourg, France; Université du Québec en Outaouais, Canada

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

Day 4. Sat, May 19, 2018

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

09.45-14.00 **REGISTRATION DESK OPEN**

10.00-10.30 **ISBS PRESIDENTIAL LECTURE: ZEBRAFISH NEUROBEHAVIORAL MODELS, STRESS AND ENVIRONMENTAL ENRICHMENT.** KA Demin, AD Volgin, OV Yakovlev, MS de Abreu, PA Alekseeva, AJ Friend, TG Amstislavskaya and AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Almazov National Medical Research Center, Military Medical Academy, St Petersburg, Ural Federal University, Ekaterinburg, Russian Center for Radiology and Surgical Technologies, Pesochny, Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia; Bioscience Institute, University of Passo Fundo (UPF), Passo Fundo, Postgraduate Program in Pharmacology, Federal University of Santa Maria, Santa Maria, Brazil; Tulane University School of Science and Engineering, New Orleans, LA, USA; The International Zebrafish Neuroscience Research Consortium (ZNRC), ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

10.30-15.15 **SYMPOSIUM 8: LAPIN SYMPOSIUM ON TRANSLATIONAL BIOLOGICAL PSYCHIATRY**
Chair: AV Kalueff (Russia, China)

10.30-10.45 **INTRODUCTION: PROFESSOR IZYASLAV LAPIN**

10.45-11.00 **LONG-TERM EFFECTS OF PRENATAL HYPOXIA ON EMBRYONIC DAYS E14 OR PROLONGED PRENATAL HYPERHOMOCYSTEINEMIA ON THE NUMBER AND LOCALIZATION OF CORTICAL NEURONS AND GLIA DEPEND ON THE TIME PATTERN OF PRENATAL STRESS.** DS Vasilev, NL Tumanova and AD Shcherbitskaia, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg State Pediatric Medical University, St. Petersburg, Russia

11.00-11.15 **PHARMACOLOGICAL SCREENING OF MAFEDINE, A NOVEL ALPHA2 ADRENORECEPTOR AGONIST, IN ZEBRAFISH.** YI Sysoev, DA Meshalkina, SV Okovitiy, PE Musienko and AV Kalueff, St. Petersburg State Chemical Pharmaceutical University, Institute of Translational Biomedicine (ITBM), St. Petersburg State University, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

11.15-11.30 **INTRANASAL EXPOSURE TO MANGANESE INDUCES ACTIVATION OF CALPAINS IN RAT BRAIN.** IS Oblamskaya, VA Maistrenko, EA Skomorohova, MN Karpenko and VM Klimenko, Institute of Experimental Medicine, St. Petersburg, Russia

11.30-11.45 **WHEN FISH TAKE A BATH-2: EXAMINING THE EFFECTS OF ACUTE AND CHRONIC TREATMENT OF ALPHA-PYRROLIDINOPENTIOPHENONE (ALPHA-PVP), A BATH SALT "FLAKKA", IN ADULT ZEBRAFISH.** TO Kolesnikova, SL Khatsko, OS Eltsov, VA Shevyrin and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

11.45-12.00 **BEHAVIORAL EFFECT OF 2-(4-FLUOROPHENYL)-4H,5H,6H,7H-8Λ^5--[1,2,3]TRIAZOLO[1,5-A]PYRIDIN-8-YLIUM-3-OLATE (C-66) IN MICE IN THE OPEN FIELD AND ELEVATED PLUS-MAZE TESTS.** TO Kolesnikova, AS Kraeva, VG Borygina, SL Khatsko, TV Gluhareva, Y Nein, IA Kotov and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

12.00-12.30 ***COFFEE BREAK***

12.30-12.50 **THE STUDY OF EMOTIONAL INTELLIGENCE OF A PRIMARY SCHOOL TEACHER IN THE CONTEXT OF PROFESSIONAL CHOICE PROBLEM.** MN Anderson, Pushkin Leningrad State University, St. Petersburg, Russia

12.50-13.05 **THE ASSOCIATION BETWEEN THE BRAIN-DERIVED NEUROTROPHIC FACTOR GENE POLYMORPHISMS AND AGITATION OR EARLY TRAUMATIC EXPERIENCE IN PATIENTS WITH POST-TRAUMATIC STRESS DISORDER.** N Pivac, M Konjevod, L Tudor, M Nikolac Perkovic, D Svob Strac, G Nedic Erjavec, S Uzun and O Kozumplik, Division of Molecular Medicine, Rudjer Boskovic Institute, Clinic for Psychiatry Vrapce, Zagreb, Croatia

13.05-13.20 **BLASTOCYSTS INVASION IN PATIENTS WITH MULTIPLE SCLEROSIS IN ST PETERSBURG.** EA Tarasova, IN Abdurasulova, AV Matsulevich, EI Ermolenko, IG Nikiforova, AG Il'ves, EV Ivashkova, ID Stolyarov and VM Klimenko, Institute of Experimental Medicine, Institute of Human Brain RAS, St. Petersburg, Russia

13.20-13.35 **STRESS AND ANXIETY IN PETS: ADOPTION OF THE HUMANE THERAPEUTIC APPROACH.** KK Ganina, EA Karelina, SA Tarasov, Research and Production Company "Materia Medica Holding", Institute of General Pathology and Pathophysiology, Moscow, Russia

13.35-13.50 **INFLUENCE OF SHORT-TERM PHYSICAL EXERCISES ON THE STRENGTH OF VISUAL ILLUSIONS.** VA Lyakhovetskii, VJu Karpinskaia, II Shoshina, Pavlov Institute of Physiology RAS, Russian Scientific Center for Radiology and Surgical Technologies, St. Petersburg State University, St. Petersburg, Russia

13.50-14.05 **DAILY HASSLES, STRESS AND PSYCHOLOGICAL WELL-BEING: GENDER DIFFERENCES.** S Savenysheva, St. Petersburg State University, St. Petersburg, Russia

14.05-14.20 **MODERATING ROLE OF SELF-ACCEPTANCE FOR PERCEIVED STRESS AND LOCUS OF CONTROL IN ADULTS.** O Strizhitskaya, L Golovey, St. Petersburg State University, St. Petersburg, Russia

14.20-14.35 **EVALUATION OF DENTAL ISSUES IN ADMITTED PATIENTS IN PSYCHIATRIC EMERGENCY: ALBANIAN EXPERIENCE.** F Elezi, S Tomori, A Braho, E Sotiri, E Myslymi, Emergency Unit, Psychiatric Service, Neuroscience Pole, Neuropediatry Service, University Hospital Center "Mother Teresa", Tirana, Albania

14.35-14.50 **RELATIONS BETWEEN HAIR CORTISOL AND SELF-REPORTED CHRONIC STRESS AND HEALTH IN YOUNG AND AGE WOMEN.** OM Razumnikova, AE Ilinykh, AA Yashanina and NV Asanova, Department of Psychology and Pedagogic of Novosibirsk State Technical University, Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia

14.50-15.05 **OBJECTIVE TOTAL SLEEP TIME IS LONGER THAN SUBJECTIVE TOTAL SLEEP TIME IN PATIENTS WITH SLEEP DISORDERS.** J-S Lee, Pusan National University Yangsan Hospital, Yangsan, South Korea

15.05-15.15 **DISCUSSION**

15.15-15.30 **CONFERENCE CLOSING**

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

POST-CONFERENCE SOCIAL EVENTS SUN, MAY 20, 2018

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

Day 1. Wed, May 16, 2018

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

CONFERENCE OPENING AND WELCOMING ADDRESSES
INDUCTION OF NEW ISBS FELLOWS
Prof AV Kalueff, ISBS President and Conference Chair (Russia, China)
Prof VM Klimenko, Program Committee Chair (Russia)

PLENARY LECTURE 1: ROBUST ANTI-STRESS EFFECTS OF DOPAMINE D3 RECEPTOR ANTAGONISTS IN A LABORATORY ANIMAL MODEL OF POST-TRAUMATIC STRESS DISORDER. EL Gardner, CR Ashby Jr, R Song, C Dixon, W Laurenzo and OV Rice, US National Institute on Drug Abuse, Baltimore, Maryland; Saint John's University, Queens, NY, USA; Beijing Institute of Pharmacology and Toxicology, Beijing, China; Furman University, Greenville, South Carolina, USA

INTRODUCTION: Post-traumatic stress disorder (PTSD) is a debilitating stress-induced anxiety disorder. We have shown that selective dopamine (DA) D3 receptor antagonists attenuate stress responses in laboratory animal models of drug addiction. Here, we asked whether highly-selective DA D3 receptor antagonists attenuate PTSD-like behavior in a laboratory animal model. **METHODS:** We subjected male Sprague-Dawley rats to modified Single Prolonged Stress (SPS): forced swim for 20 mins, restraint for 2 hrs, and inescapable foot shock for 20 mins (1.5 s every 20 sec). A distinctive tone was paired with the stress-inducing conditions. After 14 days without any stressors, we tested the animals in the presence of tone and assessed PTSD-like behavior (freezing). Effects of the DA D3 receptor antagonists SB-277011A or YQA-14 on the tone-evoked PTSD-like behavior were then assessed. **RESULTS AND DISCUSSION:** We found increased tone-evoked freeze time ($p<0.001$) 14 days after SPS exposure. SB-277011A at 6 mg/kg significantly ($p<0.0001$) decreased tone-evoked freeze time. YQA-14 at 6.25 mg/kg ($p<0.01$) or 12.5 mg/kg ($p<0.001$) significantly decreased tone-evoked freeze time. These results show that D3 receptor antagonism prior to re-exposure to stress-associated cues attenuates expression of PTSD-like fear-conditioned responses. DA D3 receptor antagonists may present a new approach for treatment of PTSD and other stress-induced behavioral pathologies. **RESEARCH SUPPORT:** This research was supported by funds of the Intramural Research Program, National Institute on Drug Abuse, U.S. National Institutes of Health; the National Basic Research Program of China; the Natural Science Foundation of China; and by internal funding at Furman University.

STATE OF THE ART IN BEHAVIORAL PHENOTYPING – TOOLS AND TECHNIQUES FOR RODENTS AND ZEBRAFISH. A Willemsen, NOLDUS IT, Wageningen, Netherlands

Behavioral phenotyping has been booming in the past decade, in an effort to characterize mutant mice in terms of their behavior. This is indispensable when working on brain processes or medical conditions with a behavioral component. There is a wide variety of tools and technologies available. The lion's share is still focusing on rodents. There are two main approaches in rodent research. The first is to apply batteries of short-term tests like mazes, open field, rotarod and gait analysis. Each test focuses on a different aspect of the phenotype. In spite of its transparent appearance this approach has serious methodological issues. Tests are typically short and stressful. Variation in the time and circumstances of testing is very hard to avoid, and it may have a big influence on the outcomes. Habituation and the order of tests are likely to influence the results. Researchers recognized these issues and developed holistic test approaches, where the animal is kept under standardized conditions and tested in its home environment. The result is a multi-dimensional profile of the animal. Test environments can be configured in many ways, with food rewards, lickometers, operant devices and much more. In the past few years there is an increasing interest in the integration of telemetry, eeg, optogenetics and other technologies. This adds physiological dimensions to the test. A third and radically different approach is using zebrafish models. They have big advantages in throughput and cost, and there are fewer legal and ethical concerns to their use. Zebrafish advocates state that their fidelity as models for humans is comparable to that of rodents, and sometimes even better. The range of available behavioral tests is much smaller than for rodents, but it is rapidly increasing.

FACEREADER: FACIAL EXPRESSION ANALYSIS FOR STUDYING HUMAN BEHAVIOR. T den Uyl, VicarVision, Amsterdam, Netherlands

Emotions play an important role in our decision making process. Measuring emotions can provide key insights into understanding human behavior for many research disciplines, as the face often shows more than what people would explicitly answer. Emotions can be measured in a non-intrusive way by analyzing facial expressions using tools such as FaceReader. FaceReader, released in 2007, is the world's first commercial solution for automatically measuring facial expressions. The very first version of FaceReader was capable of automatically analyzing basic emotions (neutral, happy, sad, angry, disgusted, surprised and scared) from video, live, or from an image. Since then a lot of engineering has been done, and development is still going on. This talk will present some of FaceReader's most recent functionalities and the possibilities they offer for scientific research. This includes action unit classification for measuring subtle expressions, automatic heart rate detection using a normal webcam, and measuring complex emotional states such as interest, boredom and confusion.

ISBS-ITBM SYMPOSIUM 1: ADVANCES IN UNDERSTANDING MOLECULAR MECHANISMS OF NEUROPSYCHIATRIC DISORDERS

Chairs: RR Gainetdinov (Russia) and J-M Beaulieu (Canada)

NORADRENERGIC CONTROL OF RESILIENCE TO CHRONIC STRESS. B Giros, Douglas Hospital Research Center, McGill University, Montreal, Canada

INTRODUCTION: Dopamine (DA) neurons in the ventral tegmental area (VTA) have been shown to play a key role in controlling stress susceptibility and resilience. However, upstream mechanisms responsible for the functional control of these neurons remain unknown. Noradrenergic (NE) neurons in the locus cœruleus, implicated in the pathophysiology of depression, have direct anatomical and functional connections within the VTA. **METHODS:** We investigated the role of these NE neurons using conditional knockout of the Vesicular Monoamine Transporter type-2 (VMAT2). VMAT2lox/lox mice were crossed with DBH (Dopamine Beta Hydroxylase) cre mice, to generate a specific removal of VMAT2 only in NE neurons; without VMAT2, these NE neurons are not able anymore to accumulate, and therefore release, NE into synaptic space. To generate a "mirror" model, we bi-laterally injected a virus expressing the Channel Rhodosin 2 (ChR2) in the locus Coeruleus of DBHcre transgenic mice. Laser-optical stimulation in the VTA can triggers a direct circuit-specific NE release in these mice. **RESULTS AND DISCUSSION:** We investigated the role of these NE neurons in regulating susceptibility to chronic social defeat (CSD) versus resilience via inhibitory control of VTA-DA neurons. Whereas the genetic absence of NE release totally suppressed resiliency, the pharmacological or optogenetical stimulation of NE release in the VTA could promote resilience in vulnerable mice. We therefore characterized a new neural circuit, from the LC to the VTA, that underlies resilience against chronic emotional stress, providing a rationale for the use of NE releaser in depression or PTSD and future direction to develop therapeutic treatments. **RESEARCH SUPPORT:** Natural and Engineering Research Council of Canada (RGPIN 385732-2012).

CHRONIC BLOCKADE OF METABOTROPIC GLUTAMATE RECEPTOR 5 IN APPSWE/PS1DE9 AND 3XTG-AD MOUSE MODELS AMELIORATES ALZHEIMER'S DISEASE PATHOGENESIS. SSG Ferguson, University of Ottawa Brain and Mind Institute, Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Canada

Metabotropic glutamate receptor 5 (mGluR5) has been implicated in the pathogenesis of a number of neurodegenerative diseases, including Alzheimer's disease (AD). Proposed to act as an extracellular scaffold for beta amyloid (Aβ), mGluR5 has been suggested to function as a receptor for the soluble oligomeric Aβ most closely linked to neuronal death and cognitive decline. The binding of Aβ has been shown to impair the lateral diffusion of mGluR5 and increase mGluR5 at the cell surface, leading to over activation of the receptor. This over activation of mGluR5 in the AD brain, has been implicated in: (1) the elevation of intracellular Ca2+, through the potentiation of NMDAR activity by mGluR5, (2) increased release of neurotoxic Aβ oligomers caused by increasing fragile X mental retardation protein (FMRP) mediated translation of amyloid precursor protein (APP), and (3) alteration of autophagy. This presents the potential for mGluR5 to be a therapeutic target for the treatment of AD. CTEP is an orally bioavailable, highly selective negative allosteric modulator for mGluR5. Chronic CTEP treatment of both APPswe/PS1DE9 and 3xtg-AD mice improves memory and learning and also reduces both oligomeric and fibrillar Aβ in both mouse models. Chronic CTEP treatment also normalizes cell surface mGluR5 expression and reduces elevated GSK3b expression resulting in reduced expression of a ZBTB16-Cullin3-Roc1 E3-ubiquitin ligase involved in the regulation of ATG14-dependent autophagy. Consistent with this a significant reduction in the expression of p62 a marker of autophagy. Taken together, these data indicate that mGluR5 antagonists currently in clinical trials for the Fragile X mental retardation, major depressive disorder and Parkinson's disease are candidates for repurposing

for the treatment of Alzheimer's disease.

FUNCTIONAL MAPPING OF CORTICAL DOPAMINE D2 RECEPTOR EXPRESSING NEURONS. J-M Beaulieu, J Khlghatyan and C Quintana, Department of Pharmacology and Toxicology, University of Toronto, Medical Sciences Building, Toronto, Canada

BACKGROUND: Dopamine D2 receptor (Drd2) gene variants have been identified as risk factors for schizophrenia. Moreover, Drd2 is a direct target of antipsychotics and contributes to the action of mood stabilizers. Cortical functions of Drd2 are of interest, considering the involvement of cortical dopamine in cognitive functions and emotional processing in schizophrenia and mood disorders. Thus, multimodal characterization and cortex wide mapping of Drd2 expressing cell types is critical to understand the functions of this receptor in the regulation of mental disorders symptoms. **METHODS:** We used digital reporter mice expressing a Cre activated HA-ribosomal tag specifically in Drd2 positive (Drd2+) cells to generate a comprehensive map of these neurons and their projections. Furthermore, these mice allowed for the characterization of cortical Drd2+ cells translatomes, under basal condition and in response to chronic antipsychotic. Finally, chemogenetic was used to validate functional roles of Drd2+ neurons suggested by their projection pattern. **RESULTS:** Comprehensive mapping identified previously unappreciated cortical clusters of Drd2+ cells in limbic and sensory areas. Translational profiling underscored the heterogeneity of cortical Drd2+ neurons and allow identifying the impact of antipsychotic treatment on transcripts related to Drd2 signaling and/or neuropsychiatric disorders. Chemogenetic manipulation of mPFC Drd2+ neurons revealed their direct involvement in the regulation of anxiety related behaviors, as suggested by their projection to the basolateral amygdala. **CONCLUSIONS:** Comprehensive map of cortical Drd2 expressing neurons provides a valuable resource pointing to the involvement of certain brain regions and cell types in particular symptoms of neuropsychiatric disorders and response to medications.

DOPAMINE TRANSPORTER DEFICIENCY SYNDROME; PHARMACOLOGICAL CHAPERONES AND A NEW ANIMAL MODEL. P Beerepoot, C Sutton, VM Lam and A Salahpour, Department of Pharmacology and Toxicology, University of Toronto, Toronto, Canada

INTRODUCTION: Hereditary dopamine transporter deficiency syndrome (DTDS) is a genetic condition caused by loss-of-function mutations in the dopamine transporter (DAT). The disorder is characterized by parkinsonism-dystonia and raised cerebrospinal fluid levels of dopamine metabolites. No treatment is currently available and patients generally do not survive past adolescence. When expressed in vitro, the DAT missense mutations result in reduction of dopamine uptake as well as preventing DAT protein maturation. In this study, we aimed to identify pharmacological chaperones of DAT as a potential treatment for DTDS. This approach has been used previously to rescue misfolding mutations causing cystic fibrosis and Nephrogenic diabetes insipidus. **METHODS/RESULTS:** We have recently shown that ibogaine and bupropion can increase surface expression and activity of wild type and DTDS causing mutants (A314V and R445C). Importantly, ibogaine and bupropion treatment increases mature protein and uptake of mutants suggesting that these compounds are pharmacological chaperones of DAT. We are currently testing a number of bupropion and ibogaine analogs in order to identify higher potency and efficacy compounds. Our results already show that noribogaine has better efficacy than ibogaine for increasing DAT surface expression. To complement these studies, we have recently generated a mouse model of DTDS by knocking in the A313V mutant which can be rescued by bupropion and ibogaine in cells. Our characterization so far shows that A313V-KI DAT mutant mice have an 80% reduction in striatal and midbrain mature DAT protein levels compared to WT animals. Importantly, we also detect the presence of immature DAT protein in the midbrain samples of the A313V mutants while no immature band is observed in WT animals. Behaviorally, A313V-KI mice display mild hyperactivity and blunted response to amphetamine in agreement with their reduced DAT levels. Using these animals, we will soon be able to verify whether the A313V mutant can be rescued by bupropion in vivo. **CONCLUSION:** Our results suggest that pharmacological chaperones are a viable approach for the treatment of DTDS. The new A313V-KI mouse will be an important tool to allow us to better understand the physiological consequences of DTDS mutations and identify pharmacological agents for the treatment of this disease.

NEURONAL FUNCTIONS OF TRACE AMINE-ASSOCIATED RECEPTOR 5 (TAAR5). S Espinoza, I Sukhanov, P Illiano, D Leo, TD Sotnikova and RR Gainetdinov, Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Genova, Italy; Skolkovo Institute of Science and Technology (Skoltech), Skolkovo, Moscow, Faculty of Biology and Soil Science, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: Trace amine-associated receptors (TAARs) are a class of G protein-coupled receptors 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 function in the central nervous system 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. **METHODS AND RESULTS:** 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. Similarly to TAAR1, TAAR5 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. Furthermore, TAAR5-KO mice showed significant differences in depression and anxiety-related tasks. **CONCLUSION:** TAAR5 is expressed not only in olfactory system but also in certain brain areas and may be involved in the control of emotional behaviors.

PHENOTYPICAL, BEHAVIORAL AND PHARMACOLOGICAL CHARACTERIZATION OF THE DOPAMINE TRANSPORTER KNOCKOUT RATS. RR Gainetdinov, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Skolkovo Institute of Science and Technology (Skoltech), Skolkovo, Moscow, Russia

INTRODUCTION: Dopamine (DA) controls many vital physiological functions and is critically involved in several neuropsychiatric disorders such as schizophrenia and attention deficit hyperactivity disorder (ADHD). The major function of the plasma membrane dopamine transporter (DAT) is the rapid uptake of released DA into presynaptic nerve terminals leading to control of both the extracellular levels of DA and the intracellular stores of DA. **METHODS AND RESULTS:** Here, we present a newly developed strain of rats (DAT-knockout, DAT-KO rats) in which the gene encoding the DAT has been disrupted by using zinc finger nuclease technology (ZFN). Male and female DAT-KO rats develop normally but weigh less than heterozygote and wild-type rats and demonstrate pronounced spontaneous locomotor hyperactivity. While striatal extracellular DA lifetime and concentrations are significantly increased, the total tissue content of DA is markedly decreased demonstrating the key role of DAT in the control of DA neurotransmission. Hyperactivity of DAT-KO rats can be counteracted by amphetamine, methylphenidate, the partial Trace Amine-Associated Receptor 1 (TAAR1) agonist RO5203648 and haloperidol. DAT-KO rats also demonstrate a deficit in working memory and sensorimotor gating tests, less propensity to develop obsessive behaviors and show strong dysregulation in frontostriatal BDNF function. **CONCLUSIONS:** DAT-KO rats could provide a novel translational model for human diseases involving aberrant DA function and/or mutations affecting the DAT or related regulatory mechanisms. The DAT knockout rats should be an excellent and improved tool for the study and development of drugs used in the management of dopaminergic disfunctions. Our goal is to provide a complex and translational model for several human diseases involving aberrant DA function or mutations affecting DAT or altered DAT regulatory mechanisms in vivo such as schizophrenia, ADHD and newly discovered Dopamine Transporter Deficiency Syndrome (DTDS). Other animal models of DTDS and potential approaches to treat this disorder will be also discussed.

CONFERENCE PRESENTATION: THE SONOTRACK CALL CLASSIFICATION PROJECT: ENABLING PHENOTYPING BASED ON ULTRASOUND VOCALIZATIONS. L Bachdasarian, R Bulthuis and G Piavchenko, Metris B.V., Hoofddorp, Netherlands; University of Orel, Orel, Russia

Modern preclinical testing requires not only shorter lead times, but also completer and more consistent test results. To achieve this further automation and collection of multi-modal data for example, behavioral characterization, physiology measurements and detailed characterization of vocalizations is highly needed in animal testing. Although ultrasonic vocalizations (USV) of rodents could potentially be used for phenotyping and new animal models practical applications have been limited by manual classification of calls and a lack of proper definitions. A recording can have 1000 calls in 10 mins and multiple syllables per call, leading to manual analysis times of several weeks. Metris developed software that enables fully automatic classification of Ultrasonic Vocalization of mice in 15 distinct categories (such as Short, Flat, Up, Down, Chevron, U-Shape, Trailing, Step Up, Step Down, Step Double (Split), Complex-3, Complex-4, etc.). In addition the software calculates a large number of bio

acoustic parameters that can be used to further profile each call and its syllables. Where manual classification of calls limits the recording duration to several minutes, in contrast automatic classification enables detailed analysis of very long recordings and also enables integration with other high throughput systems, allowing true phenotyping. Automatic analysis of Ultrasonic Vocalizations (USV) of rodents is also expected to lead to more standardized and better definitions of the vocalizations. Based on this larger databases can be built up which are crucial in developing new animal models for investigating complex social behavior and emotional parameters such as pain, stress, anxiety, fear and social defeat.

SYMPOSIUM 2: ZUKOWSKA STRESS NEUROSCIENCE SYMPOSIUM

Chairs: VM Klimenko (Russia), AV Kalueff (Russia, China)

INTRODUCTION: PROFESSOR ZOFIA ZUKOWSKA

Prof. ZOFIA M. ZUKOWSKA (1949-2012) received her M.D. and Ph.D., trained in cardiovascular medicine at the Warsaw Medical Academy (Poland). She pursued post-doctoral training at the NIH, working with such renowned scientists as Irwin I. Kopin, Scientific Director of NINDS, and Julie Axelrod, a Nobel Laureate. During this research period, her interest in stress and neuropeptides became galvanized. For the 25 years, she was a professor (and, later Chair) of the Department of Physiology and Biophysics at Georgetown University, before moving to the University of Minnesota as the Director of Stress Physiology Center. Her research examined how stress affects cardiovascular and metabolic health and diseases, and the role of peptides, in particular neuropeptide Y (NPY), a sympathetic neurotransmitter and stress mediator. She was the first to determine that NPY mediates stress-induced prolonged vasoconstriction and vascular mitogenic and pro-atherosclerotic effects (via Y1 receptors) and potent angiogenic actions (via Y2 receptors), establishing the role of NPY in ischemia, retinopathy, tumors and obesity. Professor Zukowska (or Zosia, as she was known and admired by many) was a good friend and a strong supporter of the ISBS, serving as a regular plenary speaker at our conferences. Her scientific vision, extraordinary creativity, kindness to colleagues, and the talent to be daring, continue to inspire all her ISBS colleagues and their research. This regular ISBS symposium continues Zofia's scientific legacy in the field of biological psychiatry of stress.

SWITCHING PREFRONTAL CORTEX NEURAL HEMISPHERIC ACTIVITY IN THE LEARNING PROCESS. EV Filatova, AA Orlov, SV Afanasyev and AY Egorov, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: It is known that hemispheric interactions play the important role as well as different manifestations of hemispheric asymmetry in the cognitive functioning. The goal of the study was to evaluate neuronal activity simultaneously in both hemispheres of rat frontal cortex during learning. **METHODS:** Neuronal activity was recorded simultaneously from two symmetrical points of rat medial frontal cortex (17 points in the left hemisphere and 16 - in the right one). The recording was conducted in the process of learning the behavioral problem of choosing the side of reinforcement in a two-ring maze. The collective neuronal activity in both hemispheres was compared in initial and in final stages of the learning. **RESULTS AND DISCUSSION:** Comparison of neuronal activity during correct (+) or error (-) trials of the right-side (R) and left-side (L) choices was conducted. Six pairs of comparison were evaluated: L+R+; L-R-; L-R+; L+R-; L+L-; R+R-. In the beginning of the learning differences in compared pairs were observed in the left hemisphere and no differences in the right one. During the learning, when the percentage of correct trials has increased, the differences in neural responses appear in the right hemisphere and decrease in the left one. It is supposed that the observed opposite tendency of the rearrangement of collective impulse activity is associated with the different role of the hemispheres in the constructing of behavior internal model. **RESEARCH SUPPORT:** This research was supported by Russian State Scientific Program № AAAA-A18-118012290427-7.

AMYLOID β 25-35 ALTERS PHASIC SECRETORY ACTIVITY OF THE BRAIN DOPAMINERGIC PATHWAYS IN THE RATS. VN Mukhin, V Sizov, K Pavlov, I Borovets and VM Klimenko, Institute of Experimental Medicine, Pavlov Department of Physiology, St. Petersburg, Russia

INTRODUCTION: It is known that dysfunction of the mesocorticolimbic or nigrostriatal dopaminergic pathways of the brain is observed in and may underlie some clinical syndromes of Alzheimer's disease, namely cognitive impairments, apathy and parkinsonism. According to the literature, the dysfunction can be caused by impairment of normal metabolism of amyloid β in the brain. It has been experimentally proved that amyloid β reduces basal level of extracellular dopamine and suppresses its long-term (tonic) changes in the dorsal and ventral striatum. Short-term (phasic) changes of secretory activity have not been studied well. There are few studies performed ex vivo. At the same time, it is the phasic changes that initiates formation and loss of memory trace, which is primarily disturbed in Alzheimer's disease. The aim of this study was to investigate acute effects of increasing of the amyloid β level in the rat brain on short-term (phasic) changes in dopamine secretion in vivo. **METHODS:** To increase the level of amyloid β in the brain solution of aggregated amyloid β fragment 25-35 was intracerebroventricularly administered in urethane-anesthetized rats. Amplitude of electrically evoked dopamine release was registered in the anterior medial dorsal striatum, core and shell of nucleus accumbens before, and many times within an hour after amyloid β administration. **RESULTS AND DISCUSSION:** Statistical analysis showed that amyloid β decreased electrically evoked dopamine release in the dorsal striatum and increased in the nucleus accumbens shell within the first hour after administration. No changes discovered in the nucleus accumbens core. Downregulation of the nigrostriatal system which we found is consistent with other studies. However, the reduction of phasic secretory activity was shown for the first time. Strengthening of the phasic activity of the mesolimbic system in the n. accumbens shell in response to acute increase in the level of beta-amyloid was also found for the first time. Previously, only chronic effects of beta-amyloid or tonic changes in dopamine have been studied. In contrast to our result, these studies revealed weakening of the secretory activity of the mesolimbic system in the n. accumbens shell. **CONCLUSION:** Acute elevation of amyloid beta level in the rat brain downregulates phasic secretory activity in the nigrostriatal dopaminergic pathway and upregulates this in the mesolimbic pathway in the n. accumbens shell.

ASSESSMENT OF INDIVIDUAL RISK FACTORS FOR THE FORMATION OF ALCOHOL PREFERENCES IN RATS. AY Egorov, IV Demianko and EV Filatova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Mechnikov Nord West State Medical University, Hertzen Russian State Pedagogical University, St. Petersburg, Russia

INTRODUCTION: It was shown earlier that alcohol preference in rats after social isolation and latter voluntary consumption was associated with social rank and anxiety level. It remains unclear which factors will be important for shaping the future alcohol preference beyond a stressful situation. The aim of this study was to search for and evaluate individual risk factors in the formation of alcohol preferences in rats. **METHODS:** 15 adult Wistar male rats weighing 160-240 grams contained by three individuals in a cage under standard laboratory conditions. For 2.5 months, rats were soldered by free individual selection of 10% alcohol or water in the \"two-bottle\" test after a daily water deprivation. Behavioral indicators were assessed in the \"Open field\", \"Social interactions\" and \" Marble Burying. \" tests at the beginning of the study, in 2 weeks and at the end of the study. **RESULTS AND DISCUSSION:** At the end of the experiment, according to the results of the last \"two-bottle\" test all rats was ranked into three groups: Preferring alcohol (PA - 26% and above alcohol consumption from the whole drunk liquid - 5 rats); 2) slightly preferring (SP 1-11% - 6 rats); and not preferring (NP - 0% - 4 rats). In general, SP and NP rats have demonstrated similar dynamics of the level of ethanol preferences with the exception of the first ”two-bottle” test. In contrast to PA and NP rats, SP rats actively have tried alcohol at its first presentation, but in the second test they have significantly reduced consumption. While NP rats have dramatically increased the alcohol consumption in subsequent tests. Significant differences were observed for NP rats who have preferred alcohol at the end of the experiment, which have demonstrated low research activity, a low time spent in the center of the open field, a low percentage of alcohol consumed in the first test. On the contrary, SP rats have shown a considerable time spent in the open field center, which reflects their low anxiety, as well as a high percentage of alcohol drunk in the first “two-bottle” test, and a significant difference between the first two alcohol samples. The analysis of individual parameters recorded at the end of the experiment has shown that the SP rats differ from the others in the higher level of social interactions, in the larger number of buried balls, in higher motor and research activity, which may indicate to the activation effect of ethanol low doses. Thus, it can be assumed that the low-drinking rats, who actively try alcohol at the beginning of the experiment, and then significantly reduce its intake, are less anxious and more adaptive. **RESEARCH SUPPORT:** This research was supported by Russian State Scientific Program AAAA-A18-118012290373-7.

NEUROIMAGING CHARACTERISTICS OF MOVEMENT DISORDERS. D Kozić and K Ivošević, University of Novi Sad Faculty of Medicine, Novi Sad, Serbia

To illustrate and discuss the spectrum of magnetic resonance imaging (MRI) features in different movement disorders. Abnormal movements can be classified as hyperkinetic or hypokinetic. Hyperkinesias occur due to involvement of the subthalamic nucleus (ballism) or striatum (chorea, athetosis, or dystonia). Hypokinesias (bradykinesia) occur due to the involvement of the substantia nigra and pedunculopontine nucleus. Conventional MRI may show morphological abnormalities, while advanced imaging modalities may detect changes on subcellular level. Primary (idiopathic) movement disorders are those with no detectable underlying cause like in idiopathic Parkinson's disease. Syndromes with findings other than pure movement disorder are called “plus syndromes” - progressive supranuclear palsy, multiple system atrophy and corticobasal degeneration. Heredodegenerative disorders are those with a well-defined hereditary basis such as neurodegeneration with iron accumulation, seen in Huntington's disease, Wilson's disease, pantothenate kinase-associated neurodegeneration and frontotemporal dementia with parkinsonism. Secondary movement disorders are those with known identifiable causes such as tumors, stroke, injuries, vascular malformations, toxins, drugs and metabolitic disorders. Although the diagnosis and classification of movement disorders is still mainly clinical, MRI is unavoidable additional supportive diagnostic method.

ISBS FELLOW LECTURE: STRESS-RESILIENCE AS A COMPLEX PHENOMENON. VA Rozanov, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: While stress-vulnerability is extensively studied, mechanisms of resilience to stress are much less clear. **METHODS:** To integrate knowledge in the interdisciplinary manner and to describe stress-resilience as a multi-layered phenomenon. **RESULTS AND DISCUSSION:** Resilience is a complex and multilayered phenomenon having several dimensions – biological, personal and social. The essence of this concept is often represented in reasoning that among people who experience life-threatening events (for instance, soldiers at war or victims of the natural catastrophe) majority do not develop PTSD, though a substantial portion does (in case of being at war this portion may reach 20-25%). Resilience sometimes is understood as specific behavioral, emotional and cognitive pattern, that leads to “bending and not breaking” or even “active resistance” to adversity through coping mechanisms. Brain plasticity, especially in the early life periods, and programming of stress-reactivity systems, mainly HPA, is thought to be main underlying factors of such trait or ability. Though studies of resilience are still at an early stage, recent investigations are trying to identify genetic, epigenetic, developmental, psychological, and neurochemical factors that underlie resilience, especially in development. There may exist predispositions to resilience, though it is largely the result of development and, sometimes, even of training. Several systems of the brain, including noradrenergic, dopaminergic and serotoninergic, glutamate/GABA system, HPA-system, system of neurotrophins (BDNF) and some other mediators of emotions and behavioral responses represented by their specific genetic background factors and supported by neural circuitry are thought to be main biological mechanisms for resilience. Reversible structural changes or even their absence after stress in such brain regions as hippocampus, amygdala and prefrontal and orbitofrontal cortex in animal studies are associated with better behavioral, emotional and cognitive outcomes after severe stress, suggesting that the same structures that are responsible for vulnerability are also involved in resilience. Among neurophysiological processes that may be involved in the ability to remain active and maintain resilient character traits and adaptive social responses to stress, besides HPA and SAS, neural circuits for reward and fear are discussed. Well-balanced HPA reactivity, efficient control from the side of hippocampus, more precise differentiation between dangerous and not significant threats, quick soothing of noradrenergic structures, endurable reward systems that maintain optimism and hope, reasonable modulation of amygdala activity and effective control from PFC that helps to suppress fear – all are linked to resilience. All these peculiarities may be caused by different factors – genetic predispositions, epigenetic programming during early life stages and further in life enhancement of the predisposed and programmed functions or behaviors due to effective coping, experience accumulation, training and distinct life goals setting.

ART MEETS SCIENCE: INVITATION TO THE EXHIBITION. D Raytchev, London, UK

ISBS SPECIAL LECTURE: RESILIENCE TO THE EFFECTS OF STRESS. J Erskine, St George's University of London, London, UK

INTRODUCTION: Resilience to the effects of stress is a variable that is often overlooked in studies of the effects of stress on behavior and individuals. Indeed our models of health provision (both physical and mental health) focus almost entirely on waiting until individuals develop issues and then seeking to treat these via pharmacotherapy and psychological interventions. This method of treating dis-ease is costly and ineffective. Furthermore science is beginning to unravel ways of living that evidence has shown can reduce the likelihood individuals will become sick in the future. This project seeks to implement a resilience training course in University students and examine the impacts. **METHODS:** Review the scientific literature on evidence based factors that improve human resilience to the destabilising effects of stress. Distil the evidence down into interventions that could be implemented, taught and practiced in university students. Design and implement a program delivered in a classroom setting. Trial the intervention by collecting mental health data before and after students undergo the training and longer term follow up. **RESULTS AND DISCUSSION:** The project represents ongoing work. The literature has been reviewed and evidence based interventions have been selected. One necessary precondition was that these could be delivered, taught and trailed with individuals in a classroom setting. At present the interventions are being delivered. However the statistics regarding the cohorts baseline mental health has been computed and suggests higher than anticipated levels of burnout, stress, and poor mental health. Implications of this project for the study of stress and its effects on organisms are discussed. **RESEARCH SUPPORT:** St George\'s, University of London.

SYMPOSIUM 3: ADDICTIVE BEHAVIORS AND STRESS: FROM CORRELATIONS TO MECHANISMS

Chair: EA Budygin (USA)

THE ROLE OF DOPAMINE UPTAKE CHANGES IN COCAINE ADDICTIVE BEHAVIORS. KD Bonin, Wake Forest University, Winston Salem, NC, USA

INTRODUCTION: Changes in dopamine (DA) neurotransmission are strongly associated with reinforcing effects of addictive drugs. For many years it has been known that these substances including cocaine cause an increase in extracellular DA concentration in the ventral striatum. However, the temporal structure of these changes was not clear. Furthermore, the behavioral consequences of neurochemical alterations were not fully understood. For example, does cocaine-induced DA uptake inhibition influence drug seeking and self-administrative behaviors? We attempted to answer these important questions combining advanced behavioral, neurochemical and mathematical approaches. **METHODS:** Electrically-evoked DA concentrations in rat nucleus accumbens were measured using voltammetry. Subjects were secured in a stereotaxic frame following urethane (1.5 g/kg, i.p.) anesthesia. Electrical stimulation was obtained using a bipolar stimulating electrode that was inserted into the ventral tegmental area. Voltammetric recordings occurred at the carbon fiber electrode every 100 ms by applying a triangular waveform (-0.4 to +1.3V, 400 V/s). Cocaine (0.75 and 1.0 mg/kg, i.v.) was intravenously infused into naïve rats using inter-infusion intervals, which were predetermined from rats that escalated cocaine self-administration rates under a fixed ratio 1 schedule. For the mathematical model, which describes cocaine-induced DA uptake changes, MATLAB was used to fit the experimental data using a least-squares minimization procedure. **RESULTS AND DISCUSSION:** This study clearly demonstrated that cocaine-induced DAT inhibition may provide the accumbal DA dynamic, which strongly correlates with the cyclic regularity of cocaine intake. Furthermore, DA transporter (DAT) inhibition thresholds corresponding to self-administration behavior are plastic and are shifted upward during escalated cocaine-taking behavior. This shift may reflect the development of a diminished level of the reinforcing effectiveness of cocaine following a history of high intake. These observations indicate that a tight correlation exists between the level of DAT inhibition and cocaine self-administration. Furthermore, experiments also revealed the existence of facilitated DA uptake in rat nucleus accumbens after escalated cocaine self-administration. Moreover, a mathematical model was created that quantitatively describes the dynamics of DA uptake and permits accurate predictions of the level of DAT inhibition. Therefore, a computational interpretation of cocaine-induced DA alterations during cocaine self-administration was offered. **RESEARCH SUPPORT:** This Research was supported by NIH grant AA022449.

DOPAMINERGIC MECHANISMS OF ALCOHOL ADDICTIVE BEHAVIORS. EA Budygin, Wake Forest School of Medicine, Winston Salem, NC, USA

INTRODUCTION: During the last several decades, a large body of evidence has demonstrated an important role for mesolimbic dopamine (DA) signaling in the etiology of alcohol use disorder. Surprisingly, despite much effort, it is still unclear how DA controls the initiation and suppression alcohol drinking. This knowledge is crucial for the development of effective pharmacotherapies aimed at treating alcohol addiction. **METHODS:** In this work, we applied a new viral technology to restrict the expression of ChR2 to DA cells in the ventral tegmental area (VTA) of Long Evans rats, driving ChR2-EYFP expression by a tyrosine hydroxylase promoter. The viral construct was microinjected into the VTA of rats and evident expression of ChR2-EYFP was observed in the VTA and nucleus accumbens. Fast-scan cyclic voltammetry was used to confirm that the level of the expression was sufficient to mimic tonic and phasic patterns of accumbal DA release. Optogenetically-evoked DA was identified by the background-subtracted cyclic voltammograms. Ethanol consumption was assessed using an intermittent home-cage drinking procedure, which we and others have previously shown to engender relatively high levels of ethanol intake. Ethanol seeking (or motivational) behavior was evaluated using an operant drinking paradigm that procedurally separates appetitive and consummatory behaviors. **RESULTS AND DISCUSSION:** Using an intermittent, two-bottle choice protocol, we found that optogenetic shifting of DA release into tonic mode significantly reduced ethanol intake and latency to the first lick. However, enhancing phasic DA signaling through opto-activation of VTA DA cell bodies had no effect on ethanol drinking. Limitations of these first studies included the fact that the intermittent drinking regimen does not provide a clear separation of appetitive and consummatory drinking behaviors, which may be differentially regulated by DA. Therefore, we further explored the relationship between specific patterns of accumbal DA release and ethanol drinking behaviors using an operant drinking paradigm. In these experiments, while the viral construct was delivered to the VTA, opto-stimulation was applied directly to nucleus accumbens. We found that tonic stimulation of accumbal DA terminals significantly decreased the number of lever presses while phasic stimulation had no effect on ethanol drinking behaviors. However, using extinction probe trials, in which subjects had 20 min to lever press in a non-reinforced session, phasic activation significantly increased in the number of lever presses. In addition, forcing accumbal DA transmission into a tonic pattern dramatically decreased ethanol seeking in this paradigm. These data provide the first evidence that different patterns of accumbal DA release can bidirectionally regulate ethanol seeking behavior. **RESEARCH SUPPORT:** This Research was supported by NIAAA grant AA022449.

CHRONIC ETHANOL AND HETEROSYNAPTIC PLASTICITY IN THE AMYGDALA. BA McCool, MM McGinnis and M Morales, Wake Forest School of Medicine, Winston Salem, NC, School of Pharmacy and Pharmaceutical Sciences, Binghamton University, Binghamton, NY, USA

INTRODUCTION: Ethanol abuse produces marked changes in behavior and neurobiological function that is believed to represent interactions between drug and the stress of the exposure. Among the behavioral manifestations of this ethanol/stress interaction are profound increases in anxiety-like behaviors that drive subsequent ethanol abuse. The lateral/basolateral amygdala plays a critical role in the regulation of anxiety-related behaviors in both drug naïve and ethanol exposed animals. Previous work from our lab has catalogued a number of synaptic alterations to chronic ethanol that could together explain why a dependence-like exposure enhances the expression of anxiety. The current study was designed to understand how these alterations interact to produce this maladaptive outcome. **METHODS:** Male and female Sprague-Dawley adolescent rats were subjected to an ethanol dependence-like chronic ethanol exposure using chronic intermittent ethanol (CIE) vapor inhalation. Animals in the home cage were housed in air-tight Plexiglas chambers and exposed to ethanol vapor for 12 hours each day for 7 to 10 consecutive days; blood ethanol levels measured at the end of the exposure were in the range from 150 to 200mg/dL. Control animals (CON) were identically housed but received only room air during the exposure period. For some experiments, we expressed Channel Rhodopsin in brain regions known to send robust glutamatergic projections to the lateral/basolateral amygdala to measure the effects of this chronic ethanol exposure on defined terminal populations. Whole-cell patch clamp recordings were made from individual BLA principal neurons within acute brain slices prepared from CON or CIE-treated animals 24-72h after the last ethanol exposure. Glutamatergic synaptic responses were pharmacologically isolated using 10microM picrotoxin in the extracellular solution and evoked using either by electrical stimulation of stria terminalis and external capsule or by illumination of these fiber tracks with 473nm light. **RESULTS AND DISCUSSION:** We found that CIE facilitation of glutamate synaptic function was input, exposure duration, and sex-dependent. Glutamatergic synapses arising from the stria terminalis in slices from male animals expressed a presynaptic form of synaptic facilitation characterized by increased release probability measured with paired electrical stimuli. On the other hand, external capsule synapses expressed a postsynaptic facilitation defined by increased amplitude of asynchronous excitatory postsynaptic

currents (EPSCs) evoked using strontium substitution for calcium in the extrasynaptic recording solution. These distinct pre- and post-synaptic adaptations were expressed in a specific temporal sequence with ≤3 days CIE producing presynaptic facilitation a stria synapses and longer exposures (≤ 7 days) producing postsynaptic facilitation at external capsule synapses. This temporal sequence was conserved at glutamatergic synapses onto female BLA principal neurons although the exposure durations required to produce these effects were increased relative to males. Prelimbic (PrL) cortical inputs arrive to the BLA along the stria terminalis and dorsal agranular insular (AI) cortical inputs course into the BLA along the external capsule. Using ChannelRhodopsin, we found that CIE enhanced light-evoked glutamatergic responses arising from PrL and AI terminal fields in the BLA with PRL inputs expressing presynaptic and AI inputs expressing postsynaptic facilitation again in a 'pre- then post-' temporal sequence. These findings suggest that chronic ethanol facilitates glutamate function in a way that mimics heterosynaptic plasticity in this brain region. **RESEARCH SUPPORT:** This research was supported by NIH/NIAAA grants R01 AA01445, R01 AA023999, T32 AA007565, P50 AA026117, F31 AA025514, and F32 AA024949.

PROBING THE NEURAL SUBSTRATES AND CIRCUITS OF VULNERABILITY TO ALCOHOL USE DISORDER AND COMORBID ANXIETY/STRESSOR-RELATED DISORDERS. JL Weiner, SE Ewin, AN Karkhanis, JW Morgan, AG Almonte and SR Jones, Wake Forest School of Medicine, Winston Salem, NC, USA

INTRODUCTION: Individuals suffering from anxiety or stressor-related disorders are two to three times more likely to develop alcohol use disorder (AUD) than the general population. Moreover, this dual diagnosis is associated with greater symptom severity of both disorders and poor treatment outcomes. Despite the frequent co-occurrence of these disorders, the neural substrates and circuits underlying this comorbidity are unclear. **METHODS:** To address this gap in our knowledge, we have established a rodent adolescent social isolation (aSI) model and shown that, in male rats, this model elicits robust, long-lasting alterations in many behavioral risk factors for anxiety/stressor disorders or AUD. Relative to rats that were group-housed throughout adolescence (aGH), aSI rats exhibit enduring increases in anxiety-like behaviors, deficits in fear extinction, and escalated alcohol intake and preference. We also identified a number of neural adaptations that contribute to the maladaptive behaviors promotes by this model, including long-lasting alterations in dopamine release dynamics in the nucleus accumbens and increased measures of neuronal excitability in the basolateral amygdala (BLA). **RESULTS AND DISCUSSION:** This talk will focus on new data demonstrating that a central mechanism responsible for aSI-associated dysregulation of accumbal dopamine involves an increase in kappa opioid receptor signaling and that this upregulation may play a causal role in the maladaptive drinking behavior promoted by this model. Our studies also reveal that aSI increases synaptic excitability in the ventral, but not dorsal, domain of the hippocampus (vHC), a brain region that receives strong excitatory input from the BLA. Chemogenetic data will also be presented which demonstrate that silencing the BLA-vHC circuit significantly decreases anxiety-like behaviors and alcohol drinking. Collectively, these findings suggest that aSI leads to the expression of many behaviors that may be considered risk factors for AUD and comorbid anxiety/stressor-related disorders. These data also reveal novel neural substrates and circuits that may contribute to the frequent comorbidity between these disorders, shedding light on potential targets for the development of novel and much-needed treatments for individuals suffering from these dual diagnoses. **RESEARCH SUPPORT:** Supported by NIH grants P50AA26117, R37AA17531, R01AA10422.

ISBS SPECIAL LECTURE: EXTRACELLULAR VESICLE-INDUCED SICKNESS BEHAVIOR. DC Anthony, Department of Pharmacology, University of Oxford, Oxford, UK

In recent years interest has increased in the involvement of inflammation in the aetio-pathophysiology of a number of neuropsychiatric disorders, including major depressive disorder (MDD) (Miller and Raison 2015). Furthermore, autoimmune and infectious diseases often present with stereotypical behavioral disturbances – partially overlapping with MDD – collectively termed 'sickness behavior' (Miller and Raison 2015). While many studies have shown that low grade peripheral inflammation can induce specific region-dependent proinflammatory cytokine expression in the brain that has been show to contribute to MDD-like behaviors, the mechanism by which signals from the periphery achieve selective expression of cytokines in the brain remains unclear. Some have suggested that circulating cytokines, such as IL-1b, my act on the luminal surface of brain endothelial cells, but the receptors for these cytokines tend to be abluminal and the concentration of free circulating cytokines is often below the limits of detection the commonly employed sickness behavior models. A novel mechanism of signal transmission that could transform our understanding of periphery-to-brain interaction was described recently: this is the intercellular communication mediated by extracellular vesicles. Extracellular vesicles (EVs) are a heterogeneous group of membrane vesicles that are secreted by numerous cell types, including cells of the immune system (Buzas et al. 2014). The content, or so-

called cargo, of EVs comprises different molecules including lipids, proteins, and various species of RNA (Buzas et al. 2014). When EVs are released from their cells of origin they enter the extracellular space; from here they can be transported remotely. At their destination organ, EVs transfer their cargo to recipient cells and can exert functional effects in those cells (Valadi et al. 2007). We have shown that EVs containing a specific inflammatory cargo are able the induce MDD-relevant changes in behavior in the absence of any other stimuli and, therefore, are a new target for therapeutic intervention.

INSTRUMENTATION FOR FAST-SCAN CYCLIC VOLTAMMETRY IN FREELY MOVING ANIMALS. CJ McKinney, MD Verber and RM Wightman, Department of Chemistry, University of North Carolina, NC, USA

INTRODUCTION: Fast-Scan Cyclic Voltammetry (FSCV) has proven to be a powerful electrochemical technique for probing concentrations of neurotransmitters in the brains of freely moving and behaving animals. Real-time FSCV measurements have allowed changes in dopamine concentration to be correlated with specific behaviors, particularly those associated with the brain's reward system. **METHODS:** We will cover the history of the FSCV technique from an instrumentation standpoint, including a discussion of the standard three-electrode potentiostatic techniques along with the two-electrode techniques typically used for FSCV. We will look at the various circuit topologies, including the sense resistor method, the virtual ground method, and the driven virtual ground method. The relationship between electrode parameters, scan speeds, and circuit operation will be addressed. A breakdown of the software used for experiment control and data acquisition as well as for data analysis will be discussed. We will also discuss some of the "best practices" to be followed when performing actual FSCV measurements. **RESULTS AND DISCUSSION:** Simulations will be shown that can be used to predict circuit behavior based on electrode characteristics. The specifications of the particular circuit topologies that we have chosen will be presented. We will also discuss some recent results obtained using our FSCV instrumentation along with future directions for instrument development. **RESEARCH SUPPORT:** This research was supported by grant DA032530 from NCBI-NIH.

CONFERENCE PRESENTATION: BEHAVIORAL TESTING STANDARD OF THE FUTURE. J Fehmer, TSE Systems GmbH, Bad Homburg, Germany

TSE Systems has over 130 years of expertise in developing and manufacturing sophisticated life science research equipment. Today, using the latest technology, we are world's leading provider of highly customizable metabolic and behavioral phenotyping equipment. Complex behavioral paradigms can be achieved with our IntelliCage system. It allows the evaluation of behavior and cognitive performance of individual mice or rats while they are living in a social group of up to 16 cage mates. This unique principle fosters normal social behavior in an enriched, highly standardized home cage environment, thereby ensuring a high level of animal welfare and minimizing the need for human intervention or single test apparatuses. The IntelliCage decreases the variability of stress reactions in mice and therefore provides consistent data across laboratories. It has been used to transfer standard mouse tests to assess e.g. exploratory behavior, activity, spatial learning, operant/associative learning, memory and animal tests of anxiety. The preprogrammed tasks are evaluated seamlessly by specialized integrated fully automated operant conditioning corners. Each animal is equipped with a RFID transponder/unique tag number and recognized as it enters the conditioning corner. Also the transponders allow the selection of specific animals out of the group, via an animal gate the IntelliCage expands to a multi-area system, where fully customizable arenas and mazes can be added to create the PhenoWorld, the behavioral testing standard of the future.

CONFERENCE PRESENTATION: RWD Life Science, USA

SCHIZOPHRENIA WITH PERSECUTORY DELUSIONS AND SOMATIC PASSIVITY. LK Wei, Department of Psychiatry, National Health Group, Singapore City, Singapore

BACKGROUND: Schizophrenia is a chronic, severe, and disabling brain disorder that has affected people throughout history. The symptoms of schizophrenia may be divided into the following four domains which include positive symptoms - psychotic symptoms, such as hallucinations, which are usually auditory; delusions; and disorganized speech and behavior. Negative symptoms - decrease in emotional range, poverty of speech, and loss of interests and drive; the person with schizophrenia has tremendous inertia. Cognitive symptoms - neurocognitive deficits and fourthly mood symptoms where patients often seem cheerful or sad in a way that is difficult to understand; they often are depressed. **CASE PRESENTATION:** This is a case of a 31 year old Chinese female who has a background history of schizophrenia which was diagnosed 2 years ago where she experienced persecutory delusions. During the initial diagnosis she experienced persecutory delusions such as the FBI spying on her and following her and nurses poisoning her. She was tried on multiple medications such as Olanzapine, Risperidone, Clozapine, IM Paliperidone and had 6 cycles of ECT. After titration of all these medications for one year, she returned back to her baseline and was discharged on Risperidone 2mg ON. However after 1 year, she relapsed again presenting with persecutory delusions of bed bugs embedded with nano bots collecting tissue samples from her and poisoning the water supply leading to her drinking bottled water only. Medications were titrated and she seemed stable and was allowed for outing sessions by herself during the day. She went for a few outing sessions and came back stable. However on the 5th outing, she came back vomiting and said that 30 tablets of Paracetamol tablets had been forcefully shoved down her throat by a group of people she was unfamiliar with. She described it as traumatic as she could feel a force holding her jaw tight, opening her mouth and could feel a hand pushing the tablets down her throat. She insisted that she had no intention of wanting to harm self and that it was the doing of a group of people that had caused the incident. A thorough medical workup was done which showed deranged LFTs. Her ALT and AST levels were more than 3000U/L which warranted medical management. After 5 days of medical management her LFTs returned back to baseline. She was restarted on Risperidone 2mg but continued to have persecutory delusions of people following and spying on her at a lesser intensity. Her somatic passivity symptoms were still present but with reduced intensity. **CONCLUSION:** In conclusion, schizophrenia with somatic delusions is an understudied and under reported phenomenon that is poorly understood in the medical literature. It poses challenges to the treatment provider. In the clinical setting, the psychiatrist is faced with the task of developing a therapeutic relationship with the patient to engage them in treatment and rule out any medical complications or comorbidities. Further exploration and investigation into schizophrenia with somatic delusions is necessary to better understand its psychiatric manifestations and consequences.

CORRELATIONS BETWEEN C-REACTIVE PROTEIN, RECENT LIFE-EVENTS STRESS, AND COGNITIVE FUNCTION IN PATIENTS WITH BIPOLAR DISORDER. LY Tang, HH Chang and PS Chen, Institute of Clinical Pharmacy and Pharmaceutical Sciences, School of Pharmacy, Department of Psychiatry, College of Medicine, National Cheng Kung University, Tainan, Taiwan

INTRODUCTION: Bipolar disorder (BD), a psychiatric illness characterized by extreme mood swings, was often associated with cognitive deficits. Accumulating evidence suggested that inflammation and life events stress may play a role on the pathogenesis of BD. According to previous studies, levels of C-reactive protein (CRP), an inflammatory marker, were increased in BD patients. Besides, stressful life events were more prevalent in BD compared with controls. In this study, we aimed to investigate the correlations between CRP, recent life events stress, and cognitive function in BD patients. **METHODS:** One hundred and twelve controls without psychiatric disorder history and fifty-eight BD patients who met DSM-V criteria were enrolled by trained psychiatrists. Levels of plasma CRP were measured by ELISA, and the recent life events stress was assessed through the Taiwan version of the Life Events Scale (LES). The Wisconsin Card Sorting Test (WCST) and the continuous performance test (CPT) were used to measure cognitive function. **RESULTS AND DISCUSSION:** The BD patients had significantly higher plasma CRP levels (384.16±476.39 vs. 145.63±199.63 ng/mL, $p< 0.001$), worse cognitive performance (the number of completed categories of WCST: 2.22±1.69 vs. 3.00±1.53, $p= 0.004$; unmasked CPT: 3.87±0.99 vs. 4.56±0.39, $p< 0.001$; masked CPT: 3.50±1.16 vs. 3.97±0.83, $p= 0.043$), but similar exposure of LES compared with controls. In addition, the correlation between the CRP level and the exposure of LES was found in BD patients ($r= 0.338$, $p= 0.008$) but not in controls ($r= 0.146$, $p= 0.130$). Moreover, there was a significant interaction of the CRP level and the exposure of LES on unmasked CPT in BD patients ($p= 0.028$). Further studies are needed to confirm our results and to elucidate their causal relationships. **RESEARCH SUPPORT:** This research was supported by the Ministry of Science and Technology of Taiwan (MOST 106-2320-B-006-040).

THE THIOREDOXIN-1 DOWNREGULATION IN NUCLEUS ACCUMBENS PROMOTES METHAMPHETAMINE-PRIMED REINSTATEMENT IN MICE. J Bai, MB Huang, C Yan, XY Yang, XS Zhou, W Lv, NN Guo and Y Li**,** Medical Faculty, Kunming University of Science and Technology, Kunming, China

INTRODUCTION: Relapse of drug abuse after abstinence is a major challenge to the treatment of addicts. Thioredoxin-1 (Trx-1) is an important neuroprotecting protein, and is involved in resisting morphine-induced rewarding effects. In the present study, we aim to investigate the role of Trx-1 in the nucleus accumbens (NAc) in METH-primed relapse by using a reinstatement procedure in mice. **METHODS:** Adeno-associated virus vectors expressing shRNA-mTrx-1 (AAV-shRNA-mTrx-1) were bilateral microinjected into the NAc after METH-CPP extinction. Conditioned place preference (CPP) was used to assess the rewarding effect, and withdrawal syndrome, and reinstatement of METH. Western blot analysis were used to detect expression of N-methyl-D-asparate (NMDA) receptor 2B subunit (NR2B), the phosphorylation levels of extracellular signal-regulated kinase (p-ERK) and cAMP-response element binding protein (p-CREB) in the NAc. **RESULTS AND DISCUSSION:** The results showed that NAc Trx-1 downregulation promoted the reinstatement of METH-CPP primed by a lower dose of METH. The levels of NR2B, p-ERK, and p-CREB were increased after re-exposing lower dose METH in NAc in AAV-shRNA-mTrx-1 mice, but were not changed in the NAc of control and negative mice. These data suggest that increased levels of NR2B, p-ERK, and p-CREB in the NAc in downregulation of Trx-1 may be responsible for the primed reinstatement, thus, downregulation of Trx-1 in NAc may result in the mice more sensitivity to relapse induced by lower dose METH. **RESEARCH SUPPORT:** This study was supported by National Natural Science Foundation of China (Nos. 81660222, U1202227) and Yunling Scholar in Yunnan Province.

INTERACTIONS OF SOCIAL STRESS AND *CRP* GENE POLYMORPHISM ON TREATMENT OUTCOME IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER. HH Chang and PS Chen, Institute of Clinical Pharmacy and Pharmaceutical Sciences, School of Pharmacy, Department of Psychiatry, College of Medicine, National Cheng Kung University, Tainan, Taiwan

INTRODUCTION: Major depressive disorder (MDD) is a severe mood disorder, and about 50% of the patients do not response to antidepressants treatment. Social stresses are suggested to be associated with MDD and with regulation of inflammatory genes expression, such as C-reactive protein (CRP). In addition, the polymorphisms of CRP gene that may be corresponding to MDD and to inflammatory status could be associated with the antidepressant treatment outcome in MDD patients. In the current study, we aimed to investigate whether the social stress and CRP gene polymorphisms influence antidepressant treatment outcome in Taiwanese MDD patients. **METHODS:** We enrolled 96 community controls and 67 MDD patients. Social support scales (SSS), and World Health Organization Quality of Life (QOL) Taiwan version was assessed to collect the life social stresses at baseline. The polymorphisms of CRP gene (rs2794520) were genotyped. The 17-item Hamilton Rating Scale for Depression (HAMD) scores were collected at baseline and after 6 weeks of treatment. **RESULTS AND DISCUSSION:** At baseline, MDD patients had lower SSS and QOL scores than those in community controls (96.3 ± 20.8 vs. 115.6 ± 13.4, $p<0.001$; 75.7 ± 11.6 vs. 96.4 ±9.8, $p<0.001$, respectively). The polymorphisms of CRP gene were not associated with MDD or community controls. After 6 weeks of antidepressant treatment, patients with higher SSS and QOL scores had better treatment response ($p= 0.015$ and $p= 0.020$). Moreover, interactions of SSS scores and polymorphisms of CRP gene influenced antidepressant treatment outcome ($p= 0.001$). MDD patients with higher SSS scores and TT genotype of CRP rs2794520 had better antidepressant response. Therefore, the interactions of social stress and CRP gene polymorphism influenced treatment outcome in MDD. Future studies are needed to elucidate the mechanisms. **RESEARCH SUPPORT:** This research was supported by the Ministry of Science and Technology of Taiwan (MOST 106-2320-B-006-040).

THE INTERACTION OF OXYTOCIN AND SOCIAL SUPPORT IS ASSOCIATED WITH LONELINESS AND CORTISOL LEVEL IN MAJOR DEPRESSION. PS Chen, TY Tsai, HH Tseng, HH Chang, MH Chi, YK Yang, Department of Psychiatry, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan

INTRODUCTION: Oxytocin, a neuropeptide, facilitates the buffering effects of social support in alleviating stress response. This study sought to probe the associations between the oxytocin level–social support interaction, loneliness and serum cortisol level among a sample of drug-naïve patients with major depressive disorder (MDD). **METHODS:** Cross-sectional analysis using data from twenty-six (M:F=3:23, age: 45.54±12.97) Taiwanese patients with MDD. Serum oxytocin and cortisol levels were assessed using immunoassay kits. The UCLA

Loneliness Scale and Measurement of Support Function questionnaire were adopted. **RESULTS AND DISCUSSION:** Higher social support, but not a higher serum oxytocin level, was associated with lower loneliness, controlled for age. The effect of interaction between social support and the serum oxytocin level was significantly associated with a lower UCLA loneliness score (β=–0.50, p=0.017) and a lower serum cortisol level (β=–0.52, p=0.020) after adjusting for age. The significance remained after further adjusting for sex and depression severity. The interaction between oxytocin and social support is a more consistent alleviating factor, rather than oxytocin or social support alone, on loneliness and HPA axis hyperactivity in depressive patients. **RESEARCH SUPPORT:** This research was supported by the Ministry of Science and Technology, Taiwan (NSC 101-2314-B-006-064, MOST 105-2321-B-006-020 and MOST 106-2030-B-006-052).

SUBFEBRILE STATE AND ANXIETY: EFFECTS OF DULOXETINE. A Miljatovic, Community Health Centre "Milutin Ivkovic", Belgrade, Serbia

INTRODUCTION: Prolonged subfebrile state is a state of elevated body temperature measuring between 37.1 C and 37. 5 C ,lasting between 3 months and several years. In addition to the elevated temperature, more than 50 % of patients reports fatigue, muscle and joint pain, headache, exhaustion, perspiration. Certain research suggests that a considerable percentage of these patients also show symptoms of anxiety. **METHODS:** A total of 35 patients aged 19- 55 with a diagnosis of prolonged subfebrile state were included in the study. The criteria for participation in the study were as following :1 elevated body temperature -between -37.1 C and 37.5 C lasting a minimum of 3 months, and ,2) basic laboratory parameters within normal ranges, including sedimentation, KKS with lekocyte formula, fibrinogen, C reactive protein. All patients were tested using the HAM-A scale and 16 item Anxiety Sensitivity Index (ASI) self-report scale. Visits for these patients were organized at the beginning of treatment with duloxetine (week 0), after 4 weeks, after 6 weeks and after 12 weeks from the beginning of treatment. Patients have received 30 mg of duloxetine per day for 12 weeks, without concomitant therapy. At the initial visit, the minimum score on the HAM-A scale was 18. The minimum score on the ASI self-report scale was 33. **RESULTS AND DISCUSSION:** All data was statistically elaborated. Patients whose subfebrile state lasted for more than a year had a significantly higher anxiety score on both -HAM-A and ASI scales. There were 14 such patients. During the study, it was found that there was a significant degree of reduction of anxiety on both scales in patients treated with duloxetine ,6 and 12 weeks after administration of the drug, compared to the initial visit. 25% of total number of patients with the diagnosis of prolonged subfebrile state who were later administered duloxetine has become afebrile. **RESEARCH SUPPORT:** This research was supported by Goodwil pharma Belgrade.

EFFECT OF ATYPICAL ANTIPSYCHOTICS ON EYE MOVEMENTS IN SCHIZOPHRENIA DURING EARLY WEEKS OF TREATMENT. B Cetin-Ilhan, B Ilhan and BD Ulug, Konya Training and Research Hospital, Necmettin Erbakan University, Konya, Hacettepe University, Ankara, Turkey

INTRODUCTION: There is no study investigating eye movement parameters during the very first weeks of antipsychotic (AP) treatment in Schizophrenia, which is indeed the period to expect any transient (efficacy vs. side) effects. **METHODS:** The recovery of frontal functions was followed over oculomotor and clinical measures, bi-weekly during the 6 weeks after the onset of atypical antipsychotic (AAP) treatment, on 25 washed-out schizophrenia patients as compared to matched controls. Test protocol included visually-guided saccade (VGS), anti-saccade (AS), memory-guided saccade (MGS) and smooth-pursuit (SP) tasks, together with clinical scales of PANSS and CGI. Saccadic latency, gain, peak velocities, AS error rates, and SP gains, were investigated. **RESULTS AND DISCUSSION:** Significant recovery was observed in clinical scales for all individual patients. AS and MGS reaction times, and AS error rates, which were higher at baseline were found to decrease to normal levels at only 2nd week of treatment, suggesting early recovery in frontal functions with improved inhibitory functioning. Even though AS and MGS gains were both found to be lower, only MGS gains increased to the level of controls at 6th week, which might be associated with milder working memory improvement specifically in recalling positional information. VGS peak velocities were found to start decreasing at 2nd week relative to gain, possibly due to a short-term side effect of AAPs over low-level saccadic systems. Our results show that the effects of AAP treatment in schizophrenia could be observed much earlier than it has been reported previously, over the parameters of standard eye movement tasks. Our findings are also consistent with the view that AAPs might interfere with the mechanisms for eye movement control via their associated prefrontal centers, more likely than TAP treatments.

RELATIONSHIP OF INJECTOR SHARING WITH CLINICAL CHARACTERISTICS AND SELF-HARMING BEHAVIOR IN A SAMPLE OF PATIENTS WITH HEROIN USE DISORDER. C Evren, İ Alnıak, V Karabulut, T Çetin, G Umut, R Ağaçhanlı and B Evren, Research, Treatment and Training Center for Alcohol and Substance Dependence, Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Ardahan State Hospital, Department of Psychiatry, Baltalimani State Hospital for Musculoskeletal Disorders, Istanbul, Turkey

INTRODUCTION: It has been reported that injecting heroin users have different demographic and clinical features from the patients using other routes. Features such as starting substance and opioid use at an earlier age, use of multiple substances (Alaei et al., 2017), more frequent additional physical and psychiatric pathology (Novak and Kral, 2011), poor treatment compliance and frequent relapse (Dayal and Balhara, 2017) are more prevalent in injecting heroin users. The aim of the present study was to evaluate the relationship of injector sharing (IS) with clinical characteristics and self-harming behavior in patients with heroin use disorder (HUD). **METHODS:** A sample of 219 male patients diagnosed with HUD who were currently in opioid maintenance treatment (OMT) participated in the study. All patients were evaluated using the *Form specially computed for the present study, which included some demographic and clinical variables.* **RESULTS:** The rate of IS in our sample was 24.7%. Current age, duration of education and marital status did not differ between those with IS and those without. Age at first heroin use was lower and duration of heroin use was higher among patients who share injectors. Individuals who share injectors were more likely than the other group to be unemployed, to have a criminal record, history of incarceration and probation. Multiple substance use, Hepatitis C virus (HCV) seropositivity, history of suicide attempts and self-mutilation were significantly more common in the IS (+) group. **DISCUSSION:** Patients who share injectors were clinically more severe, such that they started using heroin at earlier age, their duration of heroin use was higher, they were using multiple substance, they had higher rates of criminal record, HCV seropositivity and self-harming behavior.

RELATIONSHIP OF LIFETIME SUBSTANCE USE AND THE SELF-HARMING BEHAVIOR AMONG YOUNG ADULTS. B Evren, C Evren, E Dalbudak, M Topcu and N Kutlu, Department of Psychiatry, Baltalimani State Hospital for Muskuloskeletal Disorders, Research, Treatment and Training Center for Alcohol and Substance Dependence, Bakirkoy Training and Research Hospital for Psychiatry Neurology and Neurosurgery, Istanbul, Cankaya University Department of Psychology, Ankara, Turkey

INTRODUCTION: The aim of the present study was to evaluate the relationship of substance use (particularly alcohol use [AU], cannabis use [CU] and any substance use [ASU] other than alcohol and cannabis) in the last year and CRAFFT Screening Interview items with the self-harming behavior (SHB), while controlling the effect of neuroticism and extraversion among young adults. **METHODS:** The study was conducted with online survey among 457 volunteered university students in Ankara and people who play games on the Internet and who are in the e-mail database of a company located in Istanbul that organizes e-sports tournaments. Participants were evaluated by applying the CRAFFT Screening Interview and the Eysenck Personality Questionnaire Revised-Abbreviated Form (EPQR-A). **RESULTS:** Mean of age was did not differ between those with SMB (24.34±4.94) and those without (24.23±5.16). Rates of AU, CU, ASU and all six items of Part B of the CRAFFT Screening Interview were higher among those with SHB. In first logistic analysis, taking Part B of the CRAFFT Screening Interview as independent variables, AU and CU predicted SHB together with neuroticism. ASU was not a predictor, nor the extraversion. In the second logistic analysis second item (Ever using alcohol or drugs to relax, feel better about the self, or fit in) of the Part B of the CRAFFT Screening Interview predicted SHB together with neuroticism. **DISCUSSION:** These findings suggest that the SHB is related with AU, CU and high neuroticism. Also ever using alcohol or drugs to relax, feel better about the self, or fit in is related with SHB, together with high neuroticism.

THE EFFICACY OF VORTIOXETINE IN A MAJOR DEPRESSION CASE AND FOLLOW-UP OF PRURITUS ADVERSE EFFECT. B Yelken, Turkey

INTRODUCTION: Many of the Major Depression Disorder (MDD) patients respond poorly to antidepressant therapy (1). Vortioxetine is a multi-modal agent combining serotonin transporter inhibition with modulation of selected population of HT receptors. In vitro studies have shown that Vortioxetine is antagonist at 5-HT3, 5-HT7 and 5-HT1D, partial agonist at 5-HT1B, agonist at 5-HT1A and inhibitor of the serotonin transporter (2). By this multi-modal effect mechanism, Vortioxetine manages to treat a broad range of depressive symptoms (3). This presentation discusses the efficacy observed when the treatment was switched to Vortioxetine in a MDD case who has been on antidepressant therapy on and off for 11 years, and the follow-up treatment of itching adverse effect. **METHODS:** CASE 34 year old female, married patient-a civil servant-admitted to psychiatry outpatient

clinic, with the complaint of no improvement in her depressive symptoms. Her history revealed that first symptoms started when she was 23 years old and she has been treated for the symptoms such as; significant pessimism, loss of pleasure in activities, disrupted appetite and sleep habits, unwillingness, restlessness, dysmnesia, distractibility, hopelessness, irritability, poor self confidence, depressive affect and unwillingness to get out of home. The patient has been prescribed 200 mg sertraline in the past year. Since she has been considered resistant to treatment, lamotrigine 200 mg and aripirazole 10 mg have been added in the past 4 months. However, it was observed that she did not benefit from the treatment; her depressive thoughts and affect continued and her HDS was 30. Since the patient was considered not benefiting from sertraline, the medication was stopped gradually in 10 days and at the same time vortioxetine 10 mg was started. No significant adverse effects of vortioxetine was observed, except a strong itching on scalp and interdigital spaces which started on the fourth day of the treatment. The patient was prescribed hydroxyzine hcl once-daily for this adverse effect, and stopped after 7 days when her complaints cleared. After 30 days, improvement in depressive thoughts and affect, increase in functionality, getting out more, decrease in symptoms such as restlessness and amnesia, was observed. Vortioxetine was increased to 20 mg on the 60th day of the treatment. Significant improvement was observed with an HDS score of 12. No pruritus or other side effects of was observed. **RESULTS AND DISCUSSION:** Antidepressant efficacy of vortioxetine has been shown in 11 randomized, double-blind placebo-controlled short-term (6/8 week) studies and five open-label extension Long-term (□52 weeks) studies (4). According to the results of three studies which switched the therapy to vortioxetine in case of inadequate response to first-line therapy, vortioxetine had a statistically significantly higher remission rate than agomelatine (5). In short term studies, nausea-vomiting is the only dose dependent frequently reported adverse effect (i≥5% and more than two fold of placebo). Pruritus is among the frequent adverse effects (≥ 1/100 to < 1/10) (6). In this case, pruritus has been controlled with the addition of short term antihistamine therapy. Because of its novel therapeutic effect vortioxetine can be considered as a new alternative in the treatment of MDD.

RELATIONSHIP BETWEEN CHILDHOOD TRAUMAS AND OBSESSIVE COMPULSIVE DISORDER. Birmay Çam İkiz**,** Manisa Mental Health Hospital Psychiatry Department, Manisa, Turkey

INTRODUCTION: Some relationship between traumatic experiences in childhood and depression, psychotic disorders, anxiety disorders, and post-traumatic stress disorder has previously been shown. While there are studies that show that childhood traumas are more common in patients with obsessive-compulsive disorders than in healthy individuals, there are also studies reporting that the frequency of childhood traumas between the two groups is not much different. In this study, we aim to investigate the relationship between childhood traumas and obsessive compulsive disorder. **METHOD:** 101 patients diagnosed with Obsessive Compulsive Disorder (OCD) according to SCID-I and 100 healthy control subjects were included in the study. (38 males, 63 females, mean age=38±2.01) All patients were evaluated using the Sociodemographic Information Form, Childhood Mental Trauma Scale (CTQ 28), Yale Brown Obsessive Compulsive Scale (Y-BOCS), Beck Depression Scale (BDI) and Beck Anxiety Scale (BAE). The obtained results were analyzed in the SPSS 15.0 statistics software. **RESULTS AND DISCUSSION:** In the OCB group, the average of the CTQ total score, emotional abuse, emotional neglect and physical neglect scores were found to be significantly higher with respect to the control group (p=0.04). A significant positive correlation was found between CTQ total score and Y-BOCS total score, BDI and BAE total scores ($r = 0.319$, $p<0.01$; $r = 0.270$, $p<0.01$; $r = 0.169$, $p<0.01$). Also, a significant positive correlation was identified between Y-BOCS total score and emotional neglect and emotional abuse subscale scores ($r = 0.328$, $p<0.01$, $r = 0.265$, $p<0.01$, respectively). In multiple linear regression analysis, it was discovered that the emotional neglect score alone could predict the Y-BOCS total score. Our study showed that there is a relationship between OCD and childhood traumas. It is important to include traumatic experiences from childhood in OCD treatment protocols.

EFFECTS OF DEPRESSION AND ANXIETY LEVELS ON QUALITY OF LIFE IN TYROID CANCER PATIENTS. G Elboga, Gaziantep University Medical Faculty, Department of Psychiatry, Gaziantep, Turkey

INTRODUCTION: Radioactive iodine-131 therapy shows significant differences from other malignancies in terms of therapy response and period in thyroid cancer patients. The aim of this study was to evaluate the possible anxiety and depression levels and the effect of this condition on the quality of life in the study group. **METHODS:** A total of 100 thyroid cancer patients who received radioactive iodine treatment after total thyroidectomy were included in the study, taking into consideration that at least one month has passed since the treatment they received. The half of the patients were followed 1-5 months after the treatment and the others who followed for 6 months or more after the treatment. Beck Anxiety Inventory, Beck Depression Inventory, and Short Form-36 were used to assess the anxiety, depression levels and quality of life. **RESULTS AND DISCUSSION:** The

Beck Anxiety Inventory mean score was 18.71 ± 13.56; The Beck Depression Inventory mean score was 12.58 ± 9,40. There was a negative and significant relationship between all subscales except for physical role weakness of the quality of life scale and anxiety, depression levels ($r = -0.52$, $p < 0.01$) ($r = -0.55$, $p < 0.01$). Anxiety and depression levels were high in cases with low quality of life subscale scores. Patients with thyroid cancer, usually with good prognosis, have mild depressive symptoms that are associated with moderate anxiety and mental distress due to uncertainty and anxiety at the beginning of the treatment. Anxiety and depression levels were found high in cases of low quality of life. Possible accompanying anxiety and depression symptoms will cause deterioration of the quality of life and negative effects on the treatment process and follow-up if the necessary precautions are not taken.

Keywords: Anxiety, Depression, Quality of Life, Thyroid Cancer, Radioactive Iodine Treatment

THE FORWARD AND BACKWARD LOCOMOTION DURING ASYMMETRICAL SPINAL CORD STIMULATION. N Merkulieva, V Lyakhovetskii and P Musienko, St. Petersburg State University, Pavlov Institute of Physiology RAS, Russian Scientific Center for Radiology and Surgical Technologies, St. Petersburg, Russia

INTRODUCTION: The control of the stepping direction is an important aspect of locomotor behavior. It was shown earlier that decerebrated cats are able to walk forward (FW) or backward (BW) adapting stepping pattern to the direction of treadmill belt during electrical spinal cord stimulation (ES). However, the spinal cord region triggering by ES the BW locomotion was rather narrow (predominantly the L6 segment) in comparison to FW one (L3-S2 segments). It allows supposing the particular properties of the neuronal populations controlling FW and BW locomotion. In the present work, we compared locomotor generating capacities of the FW and BW networks when they were triggered by laterally displaced ES electrode. **METHODS:** Five adult cats were used for this study. Animals were decerebrated at precollicular-postmammilar level. Locomotion FW and BW was evoked by ES of the dorsal surface over the L6 segment: (i) at the midline of the spinal cord, or (ii) at the point located 0.2 mm lateral to the midline. All parameters of the ES were identical (5Hz, 0.5 ms, 100-150μA) when stimulated different mediolateral locations. We recorded the limb movements by means of two mechanical sensors synchronized with the EMG activity. The kinematic parameters of the stepping, self-similarity and step asymmetry, characterizing the intra-limb and inter-limb coordination respectively, were calculated. **RESULTS AND DISCUSSION:** ES of L6 segment at the midline evoked FW and BW stepping having similar asymmetry level of stepping and EMG pattern, but the self-similarity of the BW locomotion was lower than the FW one. Oppositely, the ES of the L6 point laterally displaced lead to the dramatic changing of the BW locomotor pattern: the step asymmetry increased 6 times in relation to the BW locomotion evoked by ES in the midline point, and the self-similarity decreased significantly too. The pattern of FW locomotion remained almost unchanged. Thus, FW and BW walking have a different degree of intra-limb and inter-limb coordination following lateral displacement of ES electrode. Based on this evidences, we propose that the BW locomotion is less stable for disturbing than the FW one due to specific structural and functional differences of FW and BW networks. **RESEARCH SUPPORT:** This research supported by RFBR grants №16-04-01791 and №17-04-01822.

GAMBLING DISORDER AND DEPRESSION COMORBIDITY A CASE REPORT. MA Kocatas, Istanbul Silivri State Hospital, Istanbul, Turkey

INTRODUCTION: Gambling disorder is a psychopathology including behavioral and cognitive determinants. Several studies have shown that pathological gambling is highly co-occur with substance use, personality and mood disorders. **METHODS:** In this paper 43 years of male patient discussed, who took psychotrop medication in psychiatric services, complaining about spending and lost money and time, destroy his family because of gambling.He often gambles when feeling distress, over four years. After he lost his job and his family left the house, he is depressed and use antidepressant medication. But he has still anhedonia and depression symptoms, and also still gambling. He was diagnosed with gambling disorder and depression using by psychiatric evaluations and psychometric tests. **RESULTS AND DISCUSSION:** After behavioral cognitive therapy and psychiatric medication, we assessed the reduction of depression symptoms and prominently gambling. This case emphasized the role of cognitive behavioral therapy in gambling disorder with depression.

DEVELOPMENT AND VALIDATION OF THE STROKE SCALE AMONG THE SYSTEM OF QUALITY OF LIFE INSTRUMENTS FOR CHRONIC DISEASES (QLICD-ST). CH Wan, CZ Xu, LH Chang, FQ Sun, P Quan and JJ Zhang**,** Research Center on Quality of Life and Applied Psychology, School of Humanities and Management, Guangdong Medical University, Dongguan; The First Affiliated

Hospital of Kunming Medical University, School of Public Health, Kunming Medical University, Kunming, China

INTRODUCTION: Generic assessments are less responsive to subtle changes due to stroke, making it challenging to fully understand the impact of stroke on stroke survivals' quality of life (QOL). Objective: To develop and valid a scale of the Quality of Life Instruments for Chronic Diseases to be used among stroke survivals (GLICD-ST). **METHODS:** We applied programmed decision procedures and theories on instrument development to develop the scale. One hundred stroke survivals participated in measuring QOL three times before and after treatments. We assessed the validity, reliability, and responsiveness of GLICD-ST using correlation analysis, factor analysis, multi-trait scaling analysis, and t test analysis. **RESULTS:** The QLICD-ST comprised of four domains, physical (9 items), psychological (11), social (8), and stroke specific domain (15). All domains but social domain demonstrated excellent internal reliability (Cronbach's alpha values for each domain and the overall scale > 0.80, 0.65 for social domain). Majority of domains were moderately correlated with similar domains of SF-36 (r range, 0.3 to 0.5). Excellent test-retest reliability for all domains and overall scale were observed (Pearson r ranged between 0.70 and 0.80). Most domains were responsive moderately or highly to the changes associated with treatments with standardized response means ranging from 0.47 to 1.07. **CONCLUSIONS:** The QLICD-ST is valid with encouraging levels of validity, reliability and responsiveness, and can be used to measure the QOL for Chinese stroke survivals. Additional studies in diverse stroke populations are needed. **RESEARCH SUPPORT:** Supported by the National Natural Science Foundation of China (71373058, 81460519). **Keywords:** stroke, quality of life, validity, reliability, responsiveness.

FACTOR OF EMOTIONAL VALENCE OF TV MESSAGE IN MEDIA RECEPTION. SV Tukaev, IG Zyma, YD Havrylets and VV Rizun, Taras Shevchenko Kyiv National University, Kyiv, Ukraine

INTRODUCTION: The media effects represent a complex subject for research. Now the issue of great importance is to detect unique traits in reactions to emotionally accented Mass Media in the conditions similar to the natural setting of TV news program. **METHODS:** The aim of current study was to investigate the neurodynamics of human brain while watching negative TV news (4 plots each 1-1,5 minutes long) interrupted by a pause for three 30 seconds-long TV commercials (food and drink). 86 healthy volunteers (women and men) aged 17 to 26 years participated in this study. We estimated the spectral power density of all frequencies from 0.2 to 45 Hz. **RESULTS AND DISCUSSION:** All participants characterized the TV news as unpleasant and activating, the ads – as rather pleasant and relaxing. We demonstrated that the viewing TV news and TV ads caused activation changes in the information-analytical cognitive processes of neural networks. They increased actualization of attention (depression alpha2 rhythm), short-term memory with an emotional component (increase in theta1,2 in the central-posterior and right frontal areas only for negative TV news), as well as semantic-cognitive and emotional processes (depression alpha3 and exaltation of beta1,2 bands). Increasing the number of viewed TV news plots with ads interruption in spite of their negative emotional content led to the development of intellectual processes of adaptation (no changes in the reactivity of the theta-rhythm and activity reduction of cognitive beta1,2 and alpha3 neural networks). Depression of alpha1,2-bands (external attentional system) demonstrates the activity of the descending control systems. We revealed the most significant changes in EEG while watching TV ads after TV news and the absence of such changes in the functional activity of brain under prolonged viewing of TV ads. It was demonstrated inhibitory effect of ads viewing on the activation of cognitive neural networks in response to watching TV news despite their negative emotional orientation. Our results suggest that violence and ads in TV videos exert significant influence on the psychological condition of the participants. The general trends show that violent video cause more significant emotional impact on mental state.

PSYCHOEMOTIONAL DISTURBANCES IN RATS IN THE LITHIUM-PILOCARPINE MODEL OF TEMPORAL LOBE EPILEPSY. IV Smolensky, OE Zubareva, SV Kalemenev, VV Lavrent`eva, AV Dyomina and AV Zaitsev, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Temporal lobe epilepsy (TLE) is the most frequent form of partial epilepsy and can be accompanied by different comorbid behavioral impairments, both cognitive and psychoemotional. Developing new therapeutical approaches to treat not only the seizures but also comorbid behavioral disturbances needs deep and wide studying of their mechanisms in adequate animal models. **METHODS:** The most valid rat model of TLE is lithium-pilocarpine model with i/p administration of lithium chloride (127 mg/kg) followed by metilscopolamine (1 mg/kg) and pilocarpine (40 mg/kg) next day. Two experimental groups of rats with long (two hours and more) and strong convulsions tested one two weeks later (latent phase of epilepsy, LP), another in two months later (chronic phase, CP). Control group received only injections of lithium chloride and was tested either two weeks (one half), or

two months (another half) later. Every animal in all groups was exposed to a large set of behavioral tests – open field, elevated plus maze, forced swimming test, sucrose preference, Y-maze and resident-intruder test. Both experimental groups were compared with control using Mann-Whitney U test in IBM SPSS Statistics 23. **RESULTS AND DISCUSSION:** We found that both in latent and chronic phases of epilepsy rats demonstrated elevated motor activity in open field – maximal speed (control 29±1.6 cm/s, LP 40±2 cm/s ($p = 0.004$), CP 43±2 cm/s, ($p < 0.0001$)), average speed (control 0.3±0.03 cm/s, LP 0.4±0.04 cm/s ($p = 0.03$), CP 0.4±0.04 ($p = 0.007$)) and distance (control 514±55 cm, LP 764±64 cm ($p = 0.03$), CP 772±67 cm, ($p = 0.007$)) were significantly higher in experimental groups. Both groups also spent significantly more time in open arms of elevated plus maze (control 16±5 s, LP 84±26 s ($p = 0.004$), CP 117±24 s ($p = 0.005$)). Moreover, in chronic phase time of looking out of close arms, time in the center and number of dips from open arms were also increased compare to control. All changes in EPM should be explained by motor hyperactivity, rather than reduced anxiety. Resident-intruder, sucrose preference and Y-maze tests were carried out in chronic phase of epilepsy. Experimental rats drink more liquid in general ($p < 0.01$) and water ($p < 0.01$), but don`t prefer water or sucrose ($p = 0.2$). Rats doesn`t differ by coefficient of alternation in Y-maze, which reflects operative space memory, but rats in chronic phase of epilepsy have more entries in arms of maze equally to results in open field. In resident-intruder test experimental rats have three times decreased sniffings and grooming of intruder (control – 92±15 s, LP 31±12 s, p=0,007), reflecting disturbances in communicative behavior. Also they have more grooming time (control – 12±2 s, LP 54±12 s, p=0,006), reflecting increased anxiety in novel environment. There were no differences in defensive and aggressive behavior. **RESEARCH SUPPORT:** This work is supported by Russian Scientific Foundation (grant 16-15-10202).

CHANGES IN COGNITIVE FUNCTIONS AND ANXIETY LEVELS CAUSED BY INJECTING BACTERIAL LIPOPOLYSACCHARIDE IN EARLY POSTNATAL ONTOGENESIS. AV Dyomina, AA Karepanov, DV Krytskaya, AP Schwarz, SV Kalemenev and OE Zubareva, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: “Developmental” hypothesis of neuropsychiatric disorders formation is widely discussed. According to this hypothesis, the higher aptitude to psychopathology may be caused by the influence of infective agents, stress and another negative factors on developing nervous system. In the present study, this assumption was tested in experiment with a neonatal rat model of infection. **METHODS:** The aim of the study was the investigation of particular behavioral changes in male mature rats, with were injected by bacterial lipopolysaccharide (25 and 50 mcg/kg) on the 15th, 18th and 21th day of life. There were two control groups in test, one of them was intact, and other one was influenced by the apyrogenic saline. The behavioral testing of animals was performed after the end of their puberty (at the age of 3 months). The following tests were used: “Open field” with low and high lighting (testing of research and motor activity, level of anxiety), “Elevated plus maze” (level of anxiety), “Sucrose preference test” (anhedonic behavior measurement), Y-maze test (testing of working memory). **RESULTS AND DISCUSSION:** We observed that mature rats from experimental group were overactive in “Open field” with high light (an increase of locomotion in time and the number of hole observation was revealed) and had an abnormally low level of anxiety in “Elevated plus maze” (reduced time spent in closed arms, increased activity in open arms). These changes are characteristic of animals, which were influenced by 50 mcg/kg dose of bacterial lipopolysaccharide. In the remaining tests, no significant behavioral changes were detected. To sum up, we concluded the infection diseases in the early postnatal life can lead to behavioral disorders in adulthood. **RESEARCH SUPPORT:** The work is supported by the Russian Foundation for Basic Research, grants 17-04-02116, 16-04-00998.

CHANGES IN GLUTAMATE RECEPTORS AND TRANSPORTER GENES’ EXPRESSION IN THE RAT BRAIN AFTER LITHIUM-PILOCARPINE SEIZURES. AA Kovalenko, SV Kalemenev, OE Zubareva, AP Schwarz, AV Zaitsev, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia; Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Temporal lobe epilepsy (TLE) is a severe neurological disease. The pathogenetic mechanisms of this pathology have not been studied enough, which causes difficulties in its treatment. The development of TLE is believed to be associated with an imbalance between inhibitory (GABA) and excitatory (glutamate) systems in different regions of the brain, and one of the reasons for the development of cognitive impairments may be a disruption in the functional activity of the NMDA and AMPA receptors associated with a change in their subunit composition. This research aims to study gene expression of subunits of NMDA and AMPA receptors, and glutamate transporter in the cells of various regions of the rat brain after lithium-pilocarpine seizures. **METHODS:** We used a lithium-pilocarpine model, which is considered to be the best model of TLE. The experiments were performed

on six-week-old male Wistar rats. One day before intraperitoneal (i.p.) administration of pilocarpine (30 mg/kg), the rats were injected with LiCl (127 mg/kg, i.p) and one hour before the pilocarpine administration, the rats were injected with methylscopolamine (1 mg/kg, i.p.). The control animals were injected with saline instead of pilocarpine. Animals with prolonged seizures usually develop spontaneous convulsions in the chronic phase of the model. In this study, the rats with long (180 or more minutes) seizures were taken for the analysis. The rats were sacrificed by decapitation one week after the injection of pilocarpine (in the latent phase of the model). Analysis of gene expression of NMDA and AMPA receptor and glutamate transporter EAAT2 was performed by quantitative RT-PCR in the dorsal and ventral hippocampus, medial prefrontal, temporal and entorhinal cortex. **RESULTS AND DISCUSSION:** We found that seizures cause the changes in the expression of receptor and glutamate transporter genes, which depend on the region of the brain. Expression of the GluN1 and GluA2 genes decreased in the temporal cortex. The mRNA level of GluN2a decreases in the ventral hippocampus, temporal and entorhinal cortex. Expression of the GluN2b gene did not change; however, we detected changes in the GluN2a/GluN2b expression ratio. It significantly decreased in the temporal cortex and ventral hippocampus. The increase in the production of EAAT2 mRNA was detected in the medial prefrontal cortex and the dorsal hippocampus. The revealed changes can underlie the epileptic processes in the brain and the associated behavioral impairments. **RESEARCH SUPPORT:** Supported by RSF project No. 16-15-10202.

THE ACTIVITY OF MU- AND M-CALPAIN AFTER PSYCHOGENIC TRAUMA IN DIFFERENT STRUCTURES OF THE BRAIN. DU Krytskaya, MN Karpenko and SG Tsikunov, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Posttraumatic stress disorder (PTSD) is a mental health problem that some people develop after witnessing a life-threatening event. In model PTSD in rats, induced psychogenic trauma of the threat to life, it was revealed the development of diffuse neuronal death in the hippocampus, the hypothalamus and the cerebral cortex, which is also the case for neurodegenerative diseases. Hyperactivity of intracellular calcium-dependent cysteine proteases-calpains, which are involved in the process of activation of the caspase-12-dependent and apoptosis-inducing factor-mediated caspase-independent apoptotic pathways, is one of the markers for neurodegeneration. The development of PTSD can be explained by the hyperactivity of calpains in the cells of the CNS. The aim of the present work was to determine the activation of calpains in the striatum, the hippocampus and the prefrontal cortex on the 1st, 3rd, 10th and 50th days after extremely traumatic life events. **METHODS:** Psychogenic trauma was modeled on 20 male Wistar rats; they experienced the death of a relative of the actions of a predator – a Python molurus. 10 intact animals were used for control. The calpain activity was determined by the method of casein zymography in the gel. The significance of the differences between the activity calpain during different periods was assessed by one-way ANOVA with subsequent application of the Fisher criterion. **RESULTS AND DISCUSSION:** After the application of psychogenic trauma, the development of stress reaction was confirmed by determining the concentration of corticosterone in animal blood serum by ELISA. 1 day after application of the vital stress: an increase in the level of corticosterone was detected. In the prefrontal cortex, the activity of mu-calpain at an early date and on the 50th day after the application of psychogenic trauma did not change. The activity of m-calpain on the 1st day after the application of psychogenic trauma was increased, on the 10th day didn't differ from the control, and on the 50th day again increased, which probably indicates the chronicle process. The activity of mu-calpain and m-calpain in the hippocampus at an early date and on the 50th day didn't change. On the 3rd day after application of psychogenic stress the activity of mu-calpain in the striatum was increased in relation to activity on the 1st and 10th day, but not differing from the control. To 10 days has also been a decrease in the activity of m-calpain of the striatum cells. By the 50th day, the activity of striatum protease was restored to normal. Thus, we found a specific reaction to each of the analyzed calpain isoform caused by psychogenic trauma. The most pronounced and prolonged changes were revealed for m-calpain cells of the prefrontal cortex.

MRNA EXPRESSION OF THE GLUTAMATE TRANSPORTER, NMDA AND AMPA RECEPTORS IN THE RAT BRAIN IN THE EXPERIMENTAL MODEL OF POST-TRAUMATIC STRESS DISORDER. GV Beznin, AA Kovalenko, MV Zakharova, VA Nikitina, AP Schwarz, SG Tsikunov and OE Zubareva, Institute for Experimental Medicine, Sechenov Institute for Evolutionary Physiology and Biochemistry RAS, St Petersburg, Russia

INTRODUCTION: Posttraumatic stress disorder (PTSD) is a severe psychiatric disorder that can develop as a result of a traumatic event threatening a person's life. This disorder is related to changes of glutamatergic transmission in brain cells. The predator stress in rats is one of the experimental models of PTSD. **METHODS:** We used the model of predator (python) stress to investigate the changes in mRNA expression of NMDA (GluN1, GluN2A, GluN2B) and AMPA (GluA1, GluA2) receptor

subunits and EAAT2 (glutamate transporter) in the brain analyzed in rats 6, 24 hours, 3, 9 and 25 days after stress. **RESULTS AND DISCUSSION:** The most prominent changes were observed 25 days after stress. EAAT2 mRNA expression was increased in the ventral hippocampus. mRNA expression of GluA1 and GluA2 subunits of AMPA receptors was downregulated in the dorsal hippocampus but upregulated in the ventral hippocampus. The changes in mRNA expression of GluN2B subunits of NMDA receptors were also region-specific. It was increased in the ventral hippocampus and the medial prefrontal cortex, but decreased in the dorsal hippocampus. GluN2A mRNA was upregulated in the amygdala. Observed changes may be one of the mechanisms underlying delayed stress-induced neuropsychiatric disorders. **RESEARCH SUPPORT:** This research was supported by the Russian Foundation for Basic Research, Project No 17-04-02116 A.

BIOINFORMATICS-BASED ANALYSES OF MOLECULAR NETWORKS IMPLICATED IN ABERRANT MOUSE GROOMING PHENOTYPES. AJ Friend and AV Kalueff, Tulane University School of Science and Engineering, New Orleans, ZENEREI Research Center, Slidell, LA, USA; St Petersburg State University, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

BEHAVIORAL EFFECTS OF TWO STRUCTURAL ANALOGS OF THIAZOLIDINE, KO-01 AND KO-04, IN ADULT RATS TESTED IN THE OPEN FIELD AND ELEVATED PLUS-MAZE TESTS: A PILOT STUDY. TO Kolesnikova, VG Borygina, AS Kraeva, SL Khatsko, KL Obydennov and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

INTRODUCTION: Thiazolidine, and especially its fused analogs, are a poorly studied class of heterocyclic compounds. Therefore, preclinical screening of their potential pharmacological properties and safety is important. Mammals are widely used in-vivo animal models in neurotoxicology and CNS drug discovery. Here, we characterize acute behavior effects of two thiazolidine analogs, methyl 2-[(2Z,5Z)-4-oxo-2-[(phenylcarbamoyl)methylidene]-1,3-thiazolidin-5-ylidene]acetate (KO-01) and 2-[(2Z,5Z)-2-[(benzylcarbamoyl)methylidene]-4-oxo-1,3-thiazolidin-5-ylidene]acetic acid (KO-04), in adult rats tested in the Open field (OF) and Elevated plus-maze (EPM) tests. **METHODS:** A total of 49 white adult (6 months old) female rats were used for this study. Experiment 1 assessed KO-01 at 10 and 50 mg/kg, and Experiment 2 tested KO-04 at 5, 25 and 50 mg/kg vs. controls (n=7 per group). The drugs were dissolved in a 1-% solution of starch mucus and injected intraperitoneally. After a 30-min period, animals were individually placed in OF and then EPM for 5 min in each test. The OF testing scored the number of squares crossed and the duration, latency and frequency of wall-leaning, rearing, freezing and hole-poking behaviors. The EPM session accessed time spent in closed and open arms, the number of entries to closed/open arms, locomotor activity, as well as the frequency, duration and latency of freezing, vertical wall-learning and self-grooming behaviors. Data was analyzed using the Kruskal-Wallis test ($p < 0.05$). **RESULTS AND DISCUSSION:** This study is the first report examining behavioral effects of KO-01 and KO-04 in rodents. Overall, KO-01 at all doses tested did not change horizontal, vertical and exploratory activity of rats in both OF and EPM tests. KO-04 at 50 mg/kg significantly decreased the number and duration of vertical rearing in the EPM closed arms ($p=0.0395$), with no effects in the OF. Interestingly, our earlier pilot studies in rats (Kolesnikova et al., 2016) have identified sedative psychoactive properties of other KO-series substances, which represent structural analogs of an antiepileptic drug, ralitoline (which possesses strong anticonvulsant properties in various animal models of epilepsy). However, structurally similar to it drugs KO-01 and KO-04 tested here did not show overt psychoactive profiles, and their effects on epilepsy are yet to be studied. Because chemical analyses of multilevel neighborhoods of atoms (MNA) descriptors suppositional properties of tested KO-series substances suggest these group of agents as potential drugs active in phobic disorders, allergy and epilepsy, it is necessary to further probe the potential of these substances as new medicines.

BEHAVIORAL EFFECTS OF 4-(TRIFLUOROMETHYL)-2,4-DIHYDROCHROMENO[3,4-D][1,2,3]TRIAZOLE (CF3) AND 4-(TRICHLOROMETHYL)-2,4-DIHYDROCHROMENO[3,4-D][1,2,3]TRIAZOLE (CCL3) IN ADULT ZEBRAFISH TESTED IN THE NOVEL TANK TEST: A PILOT STUDY. TO Kolesnikova, SL Khatsko, VA Glinskikh, VYu Korotaev, IB Kutyashev, AYu Barkov and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

INTRODUCTION: Mesoionic 1,2,3-triazoles and its fused analogs are poorly understood, necessitating their in-depth screening in vivo. The zebrafish (Danio rerio) is a popular aquatic model for toxicology,

neurobiology and CNS drug discovery research. Here, we characterize acute behavioral effects of 4-(trifluoromethyl)-2,4-dihydrochromeno[3,4-d][1,2,3]triazole (CF3) and 4-(trichloromethyl)-2,4-dihydrochromeno[3,4-d][1,2,3]triazole (CCL3) in adult zebrafish tested in the novel tank test of anxiety and activity. **METHODS:** A total of 71 adult (5-7 months old) wild type short-fin zebrafish were involved in the study. All fish were experimentally naïve and housed in groups of 40 in a 40-L tank filled with filtered water according to the standards of zebrafish care. Experiment 1 assessed CF3 at 25 and 50 mg/L vs. controls (n=17-19 per group). Experiment 2 tested CCl3 at 10, 25 and 50 mg/kg vs. controls (n=10-17 per group). The novel tank test was used to assess zebrafish behavior for 5 min following a 20-min pretreatment with CF3 or CCl3. We analyzed the latency (s) and the number of top entries, time spent in the upper part of the tank (s), the duration and frequency of freezing bouts and the number of anxiety-like erratic movements. **RESULT AND DISCUSSION:** In Experiment 1, CF3 at 25 mg/L significantly reduced the number and latency of top entries, but did not change top duration vs. control. CF3 at 50 mg/L also decreased the number of entries to top and erratic movements. The latency to enter the top was significantly shorter at 50 mg/L, and fish spent more time in top. In Experiment 2, CCl3 at 10 and 25 mg/L significantly decreased top entries, at 25 mg/L increased time in top, lowered the frequency and duration of freezing and erratic movements, and shortened the top latency (the latter also at 10 mg/L). 10 mg/L CCl3 significantly decreased top duration and did not alter zebrafish freezing behavior, whereas 50 mg/L was toxic as all fish died during the 20-min pretreatment. Overall, 1,2,3-triazoles fused analogs likely have psychoactive/psychostimulant properties (possibly, due to their chemical similarity with amphetamine). Interestingly, no toxic effects of all tested doses were found in rat fibroblast cell cultures in vitro, yet potent drug CNS effects (and toxicity at higher doses) were seen here in zebrafish. Clearly, further research is necessary to better understand the effects of these substances in vivo, as well as their potential for abuse and therapy in humans.

BEHAVIORAL EFFECTS OF CLOTRIMAZOLE (1-(2-CHLOROPHENY1)-DIPHENYLMETHYL-1H-IMIDAZOLE) IN ADULT ZEBRAFISH IN THE NOVEL TANK TEST. TO Kolesnikova, SL Khatsko, AV Zhdanov, MV Bytov, PE Prokhorova and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

INTRODUCTION: Clotrimazole (1-(2-chloropheny1)-diphenylmethyl-1H-imidazole) is a synthetic antimycotic imidazole drug used for treating candidiasis and other mycoses. Its side-effects include gastrointestinal disorders, altered liver enzymes, dysuria and depression (Waugh, 2008). Transient mental disorders, hallucinations and confusion may also be a consequence of using clotrimazole. Zebrafish (Danio rerio) is a powerful aquatic in vivo model in neurobehavioral research. This model organism has biochemical similarity to humans, utilizes cortisol as main stress hormone, and shows robust, easily interpretable behavioral phenotypes (that in many cases generally parallel rodent behavioral domains). Here, we assess the effects of clotrimazole on adult zebrafish behavior assessed in the novel tank test of anxiety and activity. **METHODS:** A total of 100 wild type short-fin zebrafish (4-6 month-old, ≈50:50 male:female ratio) were used for this study. All fish were naïve before testing, and housed in groups of 40 in a 40-L glass tanks, according with standards of zebrafish care. The present study exposed each fish to 1, 5, 10, 15, 20 mg/L (n=15-16) or 25 mg/L (n=7) of clotrimazole for 20 min prior to the novel tank testing, to assess the duration and frequency of freezing, latency and frequency of top entries, time spent in top, the number of erratic movements, total velocity, rotation frequency, angular velocity and total distance moved. **RESULTS AND DISCUSSION:** Overall, clotrimazole significantly reduced erratic movements at 15, 20 and 25 mg/L (the latter dose also reduced the number, mean and duration of high mobility states). However, there were no significant differences in basic behavioral patterns, such as the frequency and duration of freezing, the number and latency of top entries and time spent in top. Thus, clotrimazole does not appear to act behaviorally as a typical glucocorticoid receptor antagonist in zebrafish acutely, since it did not cause anxiolytic effects in this model. These results are also in line with rodent data on stress-like behavior evoked by higher doses of this agent. However, our findings emphasize the need to further assess safety and environmental health impacts of this component, especially due to its use in medical shampoos.

TAAR5 IN THE REGULATION OF SENSORIMOTOR BEHAVIOR. D Kalinina, M Ptukha, N Merkulyeva, O Gorsky, Y Sysoev, A Volnova, R Gainetdinov and P Musienko, St. Petersburg State University, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Children's Surgery and Orthopedic Clinic, Department of Non-pulmonary Tuberculosis, Research Institute of Phthysiopulmonology; Russian Scientific Center for Radiology and Surgical Technologies, St. Petersburg State Chemical Pharmaceutical Academy, St. Petersburg, Russia

INTRODUCTION: Trace amines (TAs), although structurally similar to classic biogenic amines, are compounds that are present in mammalians in very low (nanomolar) concentrations. Therefore, the

role of TAs in vertebrates remained unclear for decades before the discovery of a group of mammalian trace amine-associated receptors (TAARs) in 2001. Since then various functions of TAARs, especially TAAR1, were clarified, but the role of TAARs in regulation of sensorimotor behavior is still poorly understood. **METHODS:** In this study we examined the behavior of male TAAR5-KO mice (n = 9), and wild type (WT) C57BL mice (n = 10+28) in two experiments. During the first experiment locomotor activity of TAAR-5 KO (n=9) and WT (n=10) was assessed using the Open Field (OF) test (duration – 10 mins; distance, velocity, movement and time in the inner zone were the characteristics used to assess locomotor activity) and the static rod (circular cross section rods are fixed to a laboratory shelf 80 cm above the floor such that the rods horizontally protrude into space – 20, 15, 10 mm diameter, 100 cm long. Time of orientation and time of traverse were examined). In the second experiment WT mice were treated i/p 5 mg/kg (n=10), 10 mg/kg α-NETA (n=10) or 0.9% NaCl as control (n=8). After the injection mice were tested using the OF test and the Elevated Plus Maze (EPM; time spent in open arms and in closed arms, frequency of location change and movement were analyzed) test (5 mins each). **RESULTS AND DISCUSSION:** The first experiment showed that distance moved by TAAR5-KO mice was longer compared to the WT (7175±410 cm vs 5487±448 cm, $p<0.05$). TAAR5-KO mice had a greater number of intersections of the central zone compared to the WT (67.6±6.7 vs 50.6±3.6), a higher velocity (17.13±0.97 cm vs 1.17±1.09 cm) and moved more (1.45±0.14 s vs 0.96±0.08 s). TAAR5-KO mice in static rod test passed the rod faster ($p< 0.01$, t-test) in comparison with the WT (9.7±0.9 s vs 6.9±0.4 s). Although they spent more time for the orientation (e.g. time taken to orientate 180° from the starting position towards the target box), however TAAR5-KO mice show a lower percentage of falls from the rod compared to the WT group (16% vs 60%). The second experiment showed a smaller number of intersections of the central zone in mice that got 5 mg/kg of α-NETA (15.40±1.61 vs 23.50±2.84 in WT) in OF and lower frequencies of movement (149.9±13.49 vs 199.3±19.81) and non-movement (150.4±13.48 vs 198.81±19.79) in mice that got 10 mg/kg α-NETA in EPM. Overall, we assume that TAAR5 involved to regulation of locomotor behavior and posture balance and therefore TAAR5-KO mice tend to demonstrate an overall increase of activity and better balance control. However the future studies are required.

BRAIN BIOPSY AS A NEW TECHNIQUE TO ADDRESS DYNAMICS OF GENE EXPRESSION DURING STRESS IN MICE: THE ROLE OF SEROTONINERGIC SYSTEM. N Bazhenova, A Gorlova, G Ortega, N Markova, D Bonapartes, T Strekalova, K-P Lesch and DC Anthony, Institute of General Pathology and Pathophysiology, Moscow, Russia; Laboratory of Psychiatric Neurobiology, Sechenov First Moscow State Medical University, Moscow, Russia; Department of Neuroscience, Maastricht University, Maastricht, Netherlands; Division of Molecular Psychiatry, Clinical Research Unit on Disorders of Neurodevelopment and Cognition, Center of Mental Health, University of Wuerzburg, Germany; Instituto de Medicina Molecular, Faculdade de Medicina de Lisboa, Universidade de Lisboa, Lisboa, Portugal; Department of Pharmacology, Oxford University, Oxford, UK

INTRODUCTION: The aim of the study was to apply a newly developed method of biopsy of prefrontal cortex in wildy type male C57 BL6J mice and mice with genetically compromised expression of TPH2, tryptophan hydroxilase two, the neuronal-specific enzyme of serotonin synthesis, during rat exposure stress. As serotonin is known to play a crutial role in the regulation of stress response and associated with neuronal plasticity and emotional beahviour, including aggerssion, we studied the expression of several elements of serotominergic system in the proefrontal coretx of mice prior and following rat exposure rat in mice. **MATERIAL AND METHODS:** TPH2 heterozygous male mice bred on C57 BL6J background and their wild type littermates we subjected to a 20-min stereotactic microsurgery, where a small amount of tissue was retrieved from a prefrontal cortex via customized needle. Thereafter they were subjected to a 5-day rat expsoure predation stress, studied in the resident-intruder test, and killed for a rutine diseection of the priefrontal coretx. RT PCR was run to atud< expression of genes of interest that are invloved in stress response, neuroplasticity and sertoninergic regulation. **RESULTS AND DISCUSSION:** TPH2 heterozygous mice displayed markedly increased scores of aggressive behavior, while wild type showed their reduction. Stressed mutant mice had significantly upregulated AMPA receptor gene and diminished 5-HT6 receptor expression in comparison to wild type mice. Expression of 5-HT1a, 5-HT2a, GSK3 beta and c-fos did not differ bwteen two genotypes. We found that expression of investigated genes incluidng SERT was comparable between material that was collected via biopsy and via regular brain dissection. **CONCLUSIONS:** Our findings point to the involvement AMPA and 5-HT6 receptors in the mechainsms of excessive aggression associated with partial genetic reduction of brain serotonin synthesis that is triggered by stress. They also suggest the utility of brain biopsy as a new technique that enebles to study dynamics of gene expression in the prefrontal cortex of small rodents.

INVESTIGATION OF DEPRESSION-LIKE BEHAVIOR AND DESTRUCTIVE CHANGES IN THE DOPAMINERGIC AND NORADRENERGIC BRAIN SYSTEMS IN A MODEL OF THE PRECLINICAL-STAGE PARKINSON'S DISEASE IN AGED RATS. MB Pazi, AR Gazizova, DV

Plaksina and IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Parkinson's disease (PD) is a chronicle, progressive neurodegenerative disorder characterized by a range of motor and non-motor disturbances (neuropsychiatric, vegetative, sensory), which may antedate the development of motor phenomena by several years or more. One of the most significant neuropsychiatric symptoms of the clinical stage of PD is anhedonia, which is diagnosed on average in 45.7% of PD clinical stage cases [Assogna et al., 2011]. Pathomorphological and neurochemical mechanisms underlying depressive symptoms of PD remain unclear. The risk of developing PD over the next 4-6 years is approximately twice higher for patients with depression and signs of anhedonia [Szatmari et al., 2017]. Therefore, neurologists suggest using depression as a predictor of the possible development of PD. The aim of this study was to evaluate the presence of behavioral signs of anhedonia (the major symptom of depression) and destructive changes in the ventral tegmental area (VTA) and locus coeruleus in the model of preclinical PD stage in rats induced by intranasal LC administration. **METHODS:** The work was carried out on aged (20 months) male Wistar rats. To mimic preclinical stage of PD specific ubiquitin-proteasome system inhibitor lactacystin (LC) was injected intranasally twice within a 7-day interval. Sucrose preference test was used to reveal anhedonia. An immunohistochemical assay was applied to analyze the pathomorphological changes in VTA, ventral striatum (VS) and locus coeruleus. **RESULTS AND DISCUSSION:** 21 days after the first LC injection, 30% of LC-treated rats developed anhedonia that manifested through reduced sucrose preference by 55%. Immunohitochemical assay indicated that hedonistic deficit was accompanied by neurodegeneration in mesolimbic system and locus coeruleus: the study demonstrated the loss of 30 % of neurons in VTA and 23% of their axons in VS, as well as loss of 30% of locus coeruleus neurons. That corresponds to the subthreshold neurodegeneration level compared to the level in clinical PD stage (60-70%). Conclusion: The obtained data indicate that the appearance of depression signs in the form of anhedonia may be a non-motor symptom of the preclinical stage of PD, marking the onset of neurodegeneration in the dopaminergic mesolimbic brain system and the noradrenalinergic system of locus coeruleus. The obtained results can be applied in the development of the technology of preclinical diagnosis and therapy of PD. **RESEARCH SUPPORT:** The research was supported by Russian Science Foundation Grant (project №16-15-00278). Morphological studies were conducted on the basis of the center for collective use of the IEPhB RAS.

EFFECT OF BETULINIC ACID ON MOTOR BEHAVIOR AND NEURODEGENERATION IN THE NIGROSTRIATAL SYSTEM IN THE RAT MODEL OF PARKINSON'S DISEASE. MR Sadykova, MV Chernyshev, DV Plaksina, MA Guzeev and IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Parkinson’s disease (PD) is a progressive neurodegenerative disorder characterized by extensive neurodegeneration of dopamine (DA)-ergic neurons of the substantia nigra pars compacta (SNpc), which leads to motor disorder. The mechanisms underlying the disease are not clearly understood. To the present moment, researchers have found an association between attenuation in ubiquitin–proteasome system (UPS) activity and the development of this disease. Betulinic acid (BA) is a naturally occurring compound, which can increase chymotrypsin-like activity of proteasome [Huang et al., 2007]. Preventive injection of BA in the model of Alzheimer's disease in rats alleviate disorders in memory, emotional behavior and electrophysiological parameters of hippocampal neurons [Navabietal et al., 2018]. In this work, we aimed to test the BA as a possible anti-Parkinson drug in the rat model of PD developed on the basis of a decrease in proteasome activity of the SNpc. **METHODS:** Experiments were carried out in male Wistar rats (7 months). To create a model of neurodegeneration of nigrostriatal system bilateral microinjections of the proteasome inhibitor lactacystin (LC) were performed to the SNpc twice with 7-days interval. BA was injected i/p 2 h after each LC microinjections and 7 days after the last LC microinjection. On the 21st day after the first LC injection the following behavioral tests were used: a) the open field test to assess locomotor deficit measured by travelled distance (cm), velocity (cm/min) and vertical activity (the number of rearings); b) the beam-walking test to asses sensomotor deficit measured by the number of errors and the duration of the walk. After all the behavioral tests animals were sacrificed for immunohistochemical studies. Antibodies against tyrosine hydroxylase (TH; the rate-limiting enzyme of DA biosynthesis) were used for labeling of the dopamine-(DA)-ergic neurons in SNpc. **RESULTS AND DISCUSSION:** On the 21 days after the first LC injection the behavioral analysis in the open field test revealed a decrease in the travelled distance, velocity and the number of rearings in rats treated with LC compared to the control. BA therapy prevented this negative effect. The similar tendency was revealed in the beam-walking test: BA therapy prevented an increase in the duration of the walk. However, this drug did not arrest an increase in the number of errors induced by LC administration. It was found that in LC-treated rats the number of survived DA-ergic neurons in the SNpc was decreased by 58% compared with the controls. After the BA administration, the number of survived DA-ergic neurons was close to control values. Thus, BA therapy has a neuroprotective effect and can correct motor dysfunctions in the clinical stage

of the model of Parkinson's disease. The study was performed within the state assignment of FASO of Russia (theme No.AAAA-A18-118012290427-7).

GRP78 AFFECTS RECOVERY AFTER SLEEP DEPRIVATION IN RATS. VV Simonova, MA Guzeev, YuF Pastukhov and IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: GRP78 (78 kDa glucose-regulated protein) serves as a sentinel for up-regulation of several signaling pathways collectively called the unfolded protein response (UPR). Sleep deprivation (SD) induces the UPR and the increase in protein/mRNA levels of GRP78 in the brain [Cirelli et al., 2004; Terao et al., 2006]. Stress-induced UPR deals with the adverse consequences of SD protecting cells from proteotoxic damage [Naidoo, 2009]. GRP78 over-expression leads to 30% increase in recovery sleep after SD in parallel with the delay of protective UPR [Naidoo et al., 2007]. The present study aimed to determine whether preventive administration of GRP78 affects sleep-wake cycle during the recovery period after SD. **METHODS**: The study was carried out in 6-7-month-old male Wistar rats (n=4). Total sleep deprivation (SD) was performed during the first 6 h of a light phase. Grp78 or vehicle had been intranasally administered prior to the start of SD. Electrophysiological data were recorded continuously (24 h) using a DSI telemetric system. Statistical significance accessed by Mann-Whitney U-test was considered to be present when $p<0.05$. **RESULTS AND DISCUSSION**: Under control conditions, SD induces an increase in the total time of both slow-wave and REM sleep during the 2nd-5th hrs interval of the recovery period. Slow-wave activity (0.5-4 Hz) is 12% higher during the first 3 hrs after SD. Administration of GRP78 alters neither temporal nor spectral characteristics of SWS rebound after SD. However, GRP78 seems to attenuate REM sleep need in sleep-deprived rats: REM sleep rebound is delayed by 1 h compared to the vehicle group. Hence, results of the study suggest the involvement of GRP78 in molecular mechanisms of REM sleep homeostasis. The study was performed within the state assignment of FASO of Russia (theme No.AAAA-A18-118012290427-7).

N-HETEROCYCLIC BORNEOL DERIVATIVES ARE INHIBITORS OF MARBURG GLYCOPROTEIN-MEDIATED PSEUDOTYPE ENTRY. CAN THEY ABROGATE THE FILOVIRUS-INFLICTED STRESS? S Cheresiz, A Kononova, O Yarovaya, A Chepurnov, R Nikitina, A Pokrovsky, N Salakhutdinov and A Sokolova, Department of Medicine, Novosibirsk State University, Institute of Organic Chemistry, Institute of Clinical Immunology, Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia

INTRODUCTION: Virus infection is a clearly defined cellular stress, as evidenced by the stress granules formation, similarly to the cell response to many stressors (heat shock, UV, oxidative stress, hypoxia, nutrient deprivation, etc). Unlike other classes of antivirals, entry blockers are physically preventing the viral nucleocapsids from penetrating into the host cell cytoplasm, potentially, halting the downstream cellular stress responses at the earliest point. Pathogenesis of filoviral hemorrhagic fevers (EBOV and MARV diseases) involves early events, which determine the disease morbidity including the toxic effects of viral glycoproteins and triggering the early pathologic activation of coagulation cascade, complement system, and excessive cytokine release ("cytokine storm"). Can the activity of antifiloviral entry inhibitors abrogate these cellular and systemic stress reactions? **METHODS:** ~170 original small molecule compounds from several groups of derivatives were screened for their entry blocking activity using a biologically safe (BSL 2 level) MARV-GP-VSIV(Luc) pseudotype system. **RESULTS AND DISCUSSION:** For all compounds, the 50% inhibitory concentration (IC50) was determined for MARV-GP-VSIV(Luc) entry. Further, the selectivity index (SI) was calculated as a ratio of compound toxicity to inhibitory activity (CC50/ICMarV50). As a reference filovirus entry inhibitor, we chose a ion channel inhibitor, verapamil. Borneol derivatives showed varying toxicities and antiviral activities. Six hit compounds with potent MARV-GP-VSIV(Luc) entry blocking activity were identified in the group of N-heterocyclic borneols. The derivative containing a methylpiperidine moiety exhibited the best antiviral activity with IC50 3 times lower than the reference compound, verapamil (4 vs . 13 μM/mL). Our study demonstrates the efficient MARV entry inhibition by some N-heterocyclic bornyl esters. Preliminary experiments also show the inhibition of an infectious MARV strain in an in vitro infection of cultured Vero cells. Although MARV GP is clearly the pharmacological target, the mechanisms of inhibition remain to be elucidated. Whether the antifiloviral entry blockers can abrogate the virus-inflicted cellular stress underlying the morbidity of these hemorrhagic fevers will require further experiments with animal protection). **RESEARCH SUPPORT:** This work was supported by Foundation by the Russian Foundation Research (N 15-03-00193A). The biological study was supported by the task N 17.5484.2017/BY.

OBTAINING FOUNDER MUTATIONS OF ZEBRAFISH SEROTONIN TRANSPORTER GENES FOR MODELLING AFFECTIVE DISORDERS – PROGRESS REPORT. MA Firulyova, EV Kysil, DA

Meshalkina, PA Alexeeva and AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Almazov Medical Research Centre, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

INTRODUCTION: Serotonin transporter is a target molecule for most antidepressant treatment approaches. Its mutations are known to enhance the possibility of affective disorders in human that underpins using of the knockout rodents for modeling of the depressive-like behavior. Modeling of the affective disorders in zebrafish is experiencing a sharp need in serotonin transporter (sert) mutant lines, but meets the problem of duplicated sert gene, resulting in two isoforms: sertA and sertB which functions have not been characterized yet. The present work aimed to generate the mutated animals that will become founders of the knockout sertA-/- and sertB-/- lines. **METHODS:** Sequences of sgRNA for first exon mutations were generated with a Chopchop resource (http://chopchop.cbu.uib.no/). Their genes were synthesized in vitro, cloned under T7-promoter and transcribed in vitro with HiScribe™ T7 High Yield RNA Synthesis Kit (NEB, MA, USA). The obtained sgRNA were mixed with a Cas9 mRNA to get 100 ng/μL of sgRNA and 300 ng/μL of Cas9 mRNA in the mixture. Another approach was to clone the gene for sgRNA under U6-promoter in the px330 plasmid. Each zebrafish egg was microinjected with the mixture on 1/10 of its volume with the IM-300 microinjector (Narishige, Japan). The resulting embryos were raised according to the standard protocols and their fin probes were collected at one month of age for sert genotyping. The region, containing probable mutation was PCR amplified with Phusion polymerase (Thermo Scientific, MA, USA) and blunt-end cloned into pBluescript II SK- plasmid for sequencing. At the same time, we performed the preliminary real-time PCR with temperature gradient to identify the specimens with poorly annealing primer, corresponding to the sgRNA site. **RESULTS AND DISCUSSION:** For each gene (sertA and sertB) we microinjected nearly 500 eggs. Preliminary screening with real-time PCR revealed nearly 20% of specimen having abnormal product kinetics that may be indicative for the presence of mutations. Sequencing of the cloned inserts is in progress. In the search process we aim to find long deletions, easily detectable by PCR to facilitate further genotyping of the animals. **RESEARCH SUPPORT:** The research was supported by the Russian Foundation for Basic Research (RFBR): grant 18-315-00375 mol_A. The work was conducted at the SPBU Centre for Molecular and Cell Technologies (PCR, cloning and sequencing) and the SPBU Department of Zoology (microinjections of zebrafish eggs).

MODELING WITHDRAWAL FROM CHRONIC FLUOXETINE TREATMENT IN ZEBRAFISH. KN Zabegalov, TO Kolesnikova, SL Khatsko, AV Zhdanov and AV Kalueff, Ural Federal University, Ekaterinburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

INTRODUCTION: Antidepressants are used as one of the major pharmaceuticals in the treatment of depression. Antidepressant discontinuation syndrome (ADS) is poorly investigated set of symptoms which often occurs in patients after withdrawal of antidepressant treatment, and includes gastrointestinal disturbances, insomnia, headaches, anxiety and flu-like symptoms. ADS can last from several days to several weeks. However, such syndrome differs from conventional drug withdrawal syndrome, as antidepressants do not cause abuse. Here, we used zebrafish undergoing chronic fluoxetine treatment with subsequent withdrawal, to model ADS in zebrafish. **METHODS:** A total of 100 adult wild type zebrafish with 50/50 male-female ratio were kept in group of 40 in 40-L tank filled with filtered water in accordance with zebrafish care standards. Zebrafish behavior analysis was conducted by the using novel tank test with 5 min video recording after 2 weeks of chronic fluoxetine treatment at 0.01 and 0.05 mg/L (n=20), as well as 2 days after withdrawal of 2-week fluoxetine at the above doses (n=20). We assessed the latency (s) and number of top and bottom entries, time spent in the upper half (top) of the tank, duration and frequency of freezing and the number of anxiety-like erratic movements. **RESULTS AND DISCUSSION:** Fish treated with fluoxetine at both doses display decreased freezing duration, increased top duration in comparison with control untreated fish. Additionally, 0.05 mg fluoxetine treatment increased bottom latency, and decreased freezing frequency and the latency to top entries. Resembling results observed in groups with 2 days withdrawal, so the fish of these groups have increased top duration, therewith, fish treated with fluoxetine in dose of 0,05 mg have decreased bottom entries, freezing frequency and duration, top latency, and increased bottom latency. In general, zebrafish anxiety- and stress-like behavioral endpoints are decreased top duration, increased freezing frequency and duration, and increased number of erratic movements (Egan et al. 2009). Fluoxetine successfully attenuates anxiety- and stress like behavior in zebrafish by increasing top duration, decreasing freezing and the number of erratic movements (Singer et al., 2016). In such manner, the results of chronic treatment with fluoxetine confirm the anxiolytic effects of this drug. Increased anxiety is strongly marked symptom in ADS as it was shown in rodent studies (Sah et al., 2012). Despite this fact, discontinuation groups display anxiolytic behavioral hallmarks similarly to chronic treatment groups. It probably related to long washout period fluoxetine due to its long half-life. Thus, we should develop our research protocol with account of such specifics. **RESEARCH SUPPORT:** Ural Federal University, Ekaterinburg, Russia.

Day 3. Fri, May 18, 2018

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

ISBS SPECIAL LECTURE: A COMPETENCE MODEL-BASED ANALYSIS TO REDUCE PSYCHOSOCIAL RISKS AT WORK. Ph Fauquet-Alekhine and L Rouillac, SEBE-Lab, Department of Psychological and Behavioral Sciences, LSE, London, UK; Laboratory for Research in Science of Energy, France and Germany; Nuclear Power Plant of Chinon, Avoine, France

INTRODUCTION: Studies and surveys regarding safety and health at work indicate an "increasing number of workers exposed to psychosocial risks at work and affected by work-related stress" (EASHW, 2012: 9). Consequences such as anxiety, insomnia, boredom, emotional instability, depression, psychosomatic diseases, cardiovascular problems, increased alcohol consumption, drug abuse affect mental health (Teasdale, 2002: 252). This is intimately linked with subjects' perception of well-being, itself associated to perception of competencies (Sheldon and Elliot, 1999; Judge et al., 2005). Attainment-to-well-being effects are mediated by daily activity-based experiences of competence (Mark & Smith, 2008; Nieuwenhuijsen, 2010): increasing a positive perception of competencies participates to improving mental health. Studies carried out to define how perceived competence could be characterized at work (Karasek, 1979; Sheldon & Elliot, 1999; Mann et al. 2004; Oomens et al., 2007; Bowling et al., 2010; Ankudinov et al., 2015; Bentley et al., 2015) concluded that four criteria were relevant: level of skill, possibility to learn new things or to develop special abilities or to be creative, and the repetitive nature of tasks, designated under the concept of "skill discretion". Quantified results related high skill discretion to reduced risk of depressive disorders and other mental disorders, and low skill discretion to increased risk (Joensuu et al. 2010), highlighting the direct and indirect contribution of perceived competencies to mental health. **METHODS:** We here suggest an innovative model-based method that helps for identification of factors deteriorating mental health at work when related to skill discretion. The Square of Perceived Action model (SPEAC model) structures competencies and defines what is needed to summon competencies successfully in action (Fauquet-Alekhine, 2016). Performing an activity by putting competencies successfully in action is considered possible provided that four poles are effective: Having to act, Knowing to act, Wanting to act, Being able to act. Having to act refers to the motives and goals needed for the professional to be involved in action and legitimates responsibility and risk-taking. Knowing to act is that the professional knows to implement in situation (knowledge and know-how). Wanting to act refers to the desire, the willingness and the personal commitment of the professional. Being able to act reflects the context of the situation of work, the external resources of the professional. "Putting competencies successfully in action" is obtained when the four poles are all effective, meaning the poles are both "available" and "coherent". "Available" means that the content of a pole is defined and actually exists for the subject to act. "Coherent" means that any part of a pole does not counteract another part of the same pole. In the present study, psychosocial risk assessment at work was undertaken by work analysts in a French company. After a preliminary informative meeting, a representative collective of participants was constituted for each profession on a volunteer basis, met twice, first to undertake a collective analysis of the profession, second to share and validate the conclusions. Between the two meetings, the work analysts categorized the collected raw material per family, gathered and eventually added recommendations. The SPEAC model was used to detect difficulties related to skill discretion, identifying which criteria (availability, coherence, adequacy), which poles could describe this difficulty and which kind of interpolar conflict was concerned (if any) through this difficulty. This approach helped the analysts to objectify one or several areas for improvement consisting in restoring availability, coherence, adequacy. **RESULTS AND DISCUSSION:** In the company, 35 professions and more than 140 subjects were met, producing Ncases =213 cases associated to skill discretion. Correlations were calculated to assess the strength of the relationships between the poles and the criteria possibly leading to interpolar conflicts. Having to act showed being few concerned by a lack of availability ($r = -0.76$, $p<0.0001$) and often concerned by a problem of adequacy ($r=0.67$, $p<0.0001$). A refined analysis showed that this inadequacy could relate to other poles: Being able to act (62%), Wanting to act (42%) and Knowing to act (22%). Being able to act appeared to be few concerned by problems of coherence ($r=-0.314$, $p<0.002$). Wanting to act appeared to be few concerned by problems of availability ($r=-0.37$, $p<0.002$) and concerned by problems of adequacy ($r=0.50$, $p<0.0001$). Knowing to act appeared to be concerned by problems of availability ($r=0.23$, $p<0.02$). The other correlations were not significant. The fact that Having to act showed being few concerned by a lack of availability was not surprising as most of the time the content of the task is perceived defined, both because the order-giver (most of the time the management) specified it and/or because the organization provides documents and contexts for it. Conversely, Having to act was highly concerned by a lack of adequacy

with other poles, mainly with Being able to act with 14.5% of Ncases and 77.1% of the professions concerned. This was related to feeling of overwhelmed, of incompetency associated with a lack of recognition and a frustration not to reach the goal, features characteristics of burnout (Farber, 2000; Montero-Marín & García-Campayo, 2010). Having to act was also concerned by a problem of adequacy associated to Wanting to act, representing 7.5% of Ncases and including 65.7% of the professions. This was mainly related to feeling of ethical suffering concerning almost one profession over two. To a lesser extend compared with the previous interpolar conflicts, Having to act showed a problem of adequacy associated to Knowing to act with 4.6% of Ncases and 28.5% of the professions. This was related to feeling of incompetency and frustration, to a feeling of lack of training and to ethical suffering. Such feeling of incompetence and frustration could generate a progressive devaluation of subjects' academic and occupational qualifications usually painfully perceived as reported and described for other cases (see Jeudy-Ballini, 2002; Mamarbachi, 2007). As any methods involving categories or criteria, applying the SPEAC model for psychosocial risk assessment facilitated the objectification of the results, adding a quantitative dimension to the usual qualitative dimension of psychosocial material. It also helped the analysts to evaluate the appropriateness of the remedial measures (e.g. reducing/increasing an interpolar conflict). The main limit lies in the protocol itself rather than in applying the SPEAC-based method. This limit concerns the time left by the order-giver for the assessment, a sizing factor of quality. **RESEARCH SUPPORT:** This work was supported by Electricité de France.

SYMPOSIUM 5: THE RUSSIAN SOCIETY OF PSYCHIATRISTS' SYMPOSIUM: PERSONALIZED PSYCHIATRY - THE POINT OF VIEW OF EARLY CAREER RESEARCHERS

Chairs: NN Petrova, I Fedotov (Russia)

INTRODUCTION. NN Petrova and I Fedotov, Department of Psychiatry and Addictions, St. Petersburg State University, Committee for Working with Young Psychiatrists and Researchers, Psychiatry Department, Ryazan State Medical University, Early Career Psychiatrists' Council, the Russian Society of Psychiatrists, Ryazan, Russia

PERSONALIZED PSYCHIATRY. NN Petrova, School of Medicine, St. Petersburg State University, St. Petersburg, Russia

In this introductory talk, I will discuss current state of personalized psychiatry, and how advances in biochemistry, genetics and neurobiology improve our understanding of human mental disorders. How the tools may be used to help psychiatrists understand the components of their patients' unique endophenotypic profiles, and how psychiatrists can leverage neuroimaging, biomarkers and genetics to personalize their patients' care, will be discussed. The talk will also emphasize the integration of new data on biological, social and environmental factors that influence mental illness into clinical and diagnostic infrastructure, to advance a truly pre-emptive psychiatry. I will further illustrate the growing application of such personalized medicine approaches using schizophrenia and depression as selected examples. An individual's unique characteristics, critical for tailoring CNS therapies, include genetic profiles, epigenetic modifications, observable biomarker changes, and environmental factors. Discussing some new approaches currently used in the field, we also note that defining the illnesses can also influence tailoring of individualized therapies. Although personalized medicine in psychiatry has progressed rapidly in the past decade, most of these findings are not yet ready for clinical application. Thus, the greatest progress towards this goal can be expected at the intersections of multiple categories (e.g., genes, environment and biomarkers), collectively enabling psychiatry to make biological systems-based evaluations.

BEHAVIORAL RISK FACTORS FOR HIV INFECTION. EM Chumakov, NN Petrova, Department of Psychiatry and Addictions, St. Petersburg State University, Kaschenko First St. Petersburg Psychiatric Hospital, Section on Web-resources, the Early Career Psychiatrists' Council of the Russian Society of Psychiatrists, St. Petersburg, Russia

INTRODUCTION: Mental disorders significantly increase the risk of HIV infection. The relationship between the severity of psychotic symptoms and abnormal behavior was noted, and the successful treatment of psychotic symptoms leads to a reduction in risky behavior. **METHODS:** 1430 case histories of patients with mental disorders were studied. **RESULTS:** HIV was diagnosed in 2.3% of patients (significantly more frequently than in the population in Russia). The majority of HIV-infected patients (84.8%) had experience of active consumption of illegal drugs: opioids (84.8%), psychostimulants (27.3%), cannabinoids (39.4%). Alcohol abuse was found in 84.8% of cases. Patients were hospitalized for exacerbation of schizophrenia (F20, 39.4%), mental disorders due to organic brain damage (F06, 33.3%) and mental disorders due to psychoactive substance use (30.3%).

All patients with schizophrenia had an abnormal behavior with delinquent and antisocial behavior during adolescence including prostitution and criminal activity. All patients had comorbid polydrug use. The HIV infection in all patients with schizophrenia occurred prior to the manifestation of psychosis due to abnormal behavior. Patients with mental disorders due to organic brain damage were also characterised by an abnormal behavior. The age of the onset of risky behavior (18.5±4.7 and 31.2±7.9, respectively, $p<0.05$) and onset of psychosis (21.9±4.1 and 25.8±7.7, respectively, $p<0.05$) was higher in them compared with patients with schizophrenia. Patients with organic brain damage were characterized by long-term illegal drug and alcohol use, they remained sexually active during the disease progression (in contrast to patients with schizophrenia). HIV-infected patients with drug addictions (F10; F11; F19) were characterized by long-term addiction (polydrug abuse, alcoholism) prior to the first hospitalization in psychiatric hospital due to psychotic symptoms, behavioral disorders and suicidal behavior on the background of consumption and withdrawal of substance. **DISCUSSION:** The prevalence of HIV-infection in patients with mental disorders is higher than in general population in Russia. We found the high incidence of addictive disorders and abnormal behavior in HIV-infected patients with schizophrenia and mental disorders due to organic brain damage. Patients with schizophrenia could be infected by HIV in consequence of abnormal behavior which can start prior to the manifestation of psychosis which indicates the advisability of psychosocial interventions at the prodromal stage of the disease. Abnormal behabior is linked with various types of risky behavior and is a characteristic of patients with schizophrenia and mental disorders due to organic brain damage with comorbid HIV infection.

GENETIC PREDICTORS OF TREATMENT-RESISTANT SCHIZOPHRENIA. DN Sosin, MG Yanushko, MV Shamanina, MV Ivanov, St. Petersburg Bekhterev Psychoneurological Research Institute, Section on Scientific projects, the Early Career Psychiatrists' Council of the Russian Society of Psychiatrists, St. Petersburg, Russia

INTRODUCTION: Schizophrenia is highly heterogeneous disease and there is need to progress research of aetiology, mechanisms and treatment. While the majority of patients with schizophrenia respond to typical or atypical non-clozapine antipsychotics, roughly a third of patients do not respond well and are considered as treatment- resistant schizophrenia (TRS). Among mental illness, TRS is associated with the highest levels of impaired functioning, rates of hospitalisation, and costs to society - TRS leads to an additional $34 billion in direct healthcare costs in the United States alone. Evidence suggests that treatment-resistance is a stable trait, as an early lack of response to treatment has been consistently shown to predict poor treatment outcome and diagnosis of TRS. There is a dufficulty with absence of common criteria of TRS. Criteria provided by Kane J.M. et al (1988) are widely used. **METHODS:** The dopamine hypothesis is arguably the most well-known and well-supported neurochemical model of schizophrenia, but has been unable to explain the occurrence of TRS. While clinical response to antipsychotics is strongly correlated with dopamine receptor D2 occupancy for most patients, TRS patients do not show clinical response even when their D2 receptor occupancy is above of therapeutic threshold. **RESULTS AND DISCUSSION:** According to above, it matters to research reasons of TRS and to find biomarkers. Investigations of genetic predictors of TRS are very perspective. But results of genetic studies in this field are heterogenous, especially for vary ethnical groups. Predictive role for TRS was strongly shown for BDNF, HTR2A, TPH1, RELN, DRD3, HLA. However, before results would be implemented into clinical practice, there is need to replicate them on own ethnical group.

BLOOD-BASED BIOMARKERS, COGNITIVE IMPAIRMENT AND THE COURSE OF SCHIZOPHRENIA. M Dorofeikova, St. Petersburg Bekhterev Psychoneurological Research Institute, the Early Career Psychiatrists' Council of the Russian Society of Psychiatrists, St. Petersburg, Russia

INTRODUCTION: Schizophrenia is associated with increased inflammation, including abnormal blood levels of C-reactive protein (CRP). Neuron-specific enolase (NSE) is used to investigate damage to neuronal structures. Glial protein S100B, a neuro- and gliotrophin inducing plasticity, is thought to be involved in pathogenesis of psychiatric diseases including schizophrenia and also to be a marker of therapeutic response. Our aim was to evaluate the value of serum biomarkers relevant for neuropsychiatric research and investigate their possible associations with clinical and cognitive features in patients with schizophrenia. **METHODS:** 91 patients with paranoid schizophrenia (56,0% men, mean age 34.6±9.9 years) were assessed using PANSS and MADRS. Blood levels of neuron-specific enolase (NSE), protein S100B, C-reactive protein (CRP), brain-derived neurotrophic factor were determined. **RESULTS AND DISCUSSION:** The severity of condition indicating poor therapeutic response (number of hospitalizations, several positive symptoms, treatment resistance) was correlated with laboratory parameters, though there was no significant increase in NSE or S100B concentrations. Patients with more impaired visuospatial short-term memory were characterized by higher levels of CRP. Our findings suggest that the activation of inflammatory response might be a pathogenic factor

for the development of schizophrenia in some cases. **RESEARCH SUPPORT:** The survey was supported by a grant from the Russian Science Foundation (Project No 14-50-00069).

TOWARDS THE ZEBRAFISH-BASED MODELS FOR PERSONALIZED PSYCHIATRY - INSIGHTS FROM INDIVIDUAL, STRAIN AND GENDER DIFFERENCES, AND MODELING GENE X ENVIRONMENT INTERACTIONS. AD Volgin, OV Yakovlev, KA Demin, MS de Abreu, PA Alekseeva, AJ Friend, TG Amstislavskaya and AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Almazov National Medical Research Center, Military Medical Academy, St Petersburg, Ural Federal University, Ekaterinburg, Russian Center for Radiology and Surgical Technologies, Pesochny, Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia; Bioscience Institute, University of Passo Fundo (UPF), Passo Fundo, Postgraduate Program in Pharmacology, Federal University of Santa Maria, Santa Maria, Brazil; Tulane University School of Science and Engineering, New Orleans, LA, USA; School of Pharmacy, Southwest University, Chongqing, China; The International Zebrafish Neuroscience Research Consortium (ZNRC), ZENEREI Research Center, Slidell, LA, USA

Currently becoming widely recognized, personalized psychiatry focuses on patients' unique physiological and genetic profiles to best tailor their therapy. However, the role of individual differences, as well as genetic and environmental factors, in human psychiatric disorders remain poorly understood. Animal experimental models are a valuable tool to improve our understanding of disease pathophysiology and its molecular mechanisms. Due to high reproduction capability, fully sequenced genome, easy gene editing and high physiological homology with humans, zebrafish (Danio rerio) are emerging as a novel powerful model in biomedicine. Mounting evidence support zebrafish as a useful model organism in CNS research. Robustly expressed in these fish, individual, strain and sex differences shape their CNS responses to genetic, environmental and pharmacological manipulations. Here, we discuss zebrafish as a promising translational tool to further advance patient-centered personalized psychiatry.

ALTERED DEVELOPMENTAL MRNA EXPRESSION OF SHORT AND LONG D2 DOPAMINE RECEPTOR WITHIN PREFRONTAL CORTEX AND WORKING MEMORY DEFICIT IN THE RAT MODEL OF CHRONIC EARLY LIFE INFLAMMATION. AP Schwarz, AYu Rotov, OI Chuprina, AN Trofimov, AM Ischenko, OE Zubareva and VM Klimenko, Institute of Experimental Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Research Institute of Highly Pure Biopreparations, St. Petersburg, Russia

Long (D2L) and Short (D2S) isoforms of D2 dopamine receptor (DR) differ by biochemical and physiological properties. However contribution of distinct D2DR isoforms to cognitive dysfunctions is not clearly understood. In the present study we evaluated developmental mRNA expression of D2S/D2LDR within rat medial prefrontal cortex (mPFC) and working memory (WM) performance in the rat model of neurodevelopmental cognitive dysfunction induced by chronic early life treatment with pro-inflammatory cytokine IL-1β (1 μg/kg, P15-21 daily). WM performance (Y-maze test) and D2S/D2L mRNA expression (qRT-PCR) within mPFC were evaluated in juvenile (P27), adolescent (P42-47) and adult (P75-90) rats. IL-1β elevation during the 3rd week of life led to working memory deficit originating in juvenile animals and persisting into adulthood. D2S mRNA expression was downregulated during adolescence, and such decrease was exaggerated in IL-1β-treated rats. D2S/D2l mRNA ratio was increased during adolescence in control (intact and vehicle-treated) animals, while in IL-1β-treated ones increase in D2S/D2L ratio was observed only in adult compared to adolescent/juvenile rats. Thus, IL-1β-evoked developmental dysregulation of D2DR splice variants expression within mPFC may underlie long-lasting cognitive deficit associated with neonatal pathology.

SYMPOSIUM 6: NEURONUTRITIOLOGY

Chairs: SA Apryatin, VA Rozanov (Russia)

EATING DISORDERS, STRESS AND SUICIDE. VA Rozanov, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: Eating disorders (anorexia nervosa, bulimia nervosa, binge eating and some others, like night eating syndrome) seem to become more prevalent in modern adolescents and young adults, which may be explained by growing stress and social pressure. From the psychodynamic point of view they are often perceived as signs of self-hate, loss of instinct of self-preservation and refusal of childbirth. **METHODS:** We would like to evaluate studies and viewpoints regarding existence of common roots of dysfunctional and life-threatening eating behaviors and suicidal behaviors in young

adults in relation to stress experienced by them. **RESULTS AND DISCUSSION:** Eating disorders and dysfunctional eating habits are more varied and variable than current psychiatric diagnostic criteria trying to categorize them in certain diagnoses suggest. They are associated with such non-psychiatric health issues like distorted nutritional status, many comorbid physical health problems and forceful practices like laxative and diuretics use, purging, vomiting and obsessive exercising, all the above mentioned associated with stress. Multiple studies find high rates of suicide in patients with anorexia nervosa, whereas suicide rates do not appear to be elevated in bulimia nervosa. In contrast, suicide attempts occur in approximately 3-20% of patients with anorexia nervosa and in 25-35% of patients with bulimia nervosa. Factors that may underlie such associations are numerous and may be multilevel and multifaceted. It may be speculated that among deepest unconscious factors there are loss of the self-preservation and reproduction instinct. On the other hand, eating disorders can be understood as a mixed form of addiction combining both psychological and chemical (food) components, thus implicating hedonic impulses. In comparison to many other mental health problems eating disorders are especially strongly influenced by psycho-social factors (information pressure of socially promoted standards of body images) and are generally associated with higher educational level of their victims. It suggests much stronger influence of psychic factors (consciousness, cognitive ideas and social conformism). On the other hand such behaviors are evidently influenced by genes and are known to be associated with early development, which implies possible role of epigenetic phenomena and stressful life experiences. Eating disorders may have a link to suicidal behavior through different mechanisms, for instance through lowered cholesterol level (known to be a risk factor of suicide). On the other hand higher prevalence of anorexia and bulimia in women is partly explaining “suicide paradox” (lower suicide rates in women while depression rate in them is higher) by extending potentially fatal behavior into alternative behavioral domains. Our analysis shows that eating disorders belong to most complex psychosocial phenomena, their pathogenesis combines vast variety of biological and psychological risk factors and is strongly influenced by psychosocial context, including perceived stress and deep existential sufferings associated with existing mental health problems like depression and social anxiety.

COMPARATIVE ANALYSES OF THE EFFECTS OF HIGH-FAT AND HIGH-CARBOHYDRATE DIET ON THE LEVEL OF ANXIETY, NEUROMOTOR AND COGNITIVE FUNCTION OF THE DOPAMINE TRANSPORTER KNOCKOUT RATS IN DIET-INDUCED OBESITY. SA Apryatin, VA Shipelin, KV Mzhel'skaya, VS Evstratova, NV Trusov, NV Kirbaeva, RR Gainetdinov and IV Gmoshinski, Federal Research Centre of Nutrition and Biotechnology, Moscow, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: Behavioral responses are the most informative among the indicators that reflect the development of alimentary obesity on in vivo models in laboratory animals. The aim of the work was a comparative analysis of the level of anxiety, neuromotor and cognitive function of rats with obesity, induced by consumption of a diet with increased quota of fats and fructose, depending on various allelic variants of the dopamine transporter gene(DAT)mutants. **METHODS:** Studies were conducted in male rats (10-12 weeks old) of the outbred wild type Wistar (+/+),heterozygotes (+/-) and DAT knockout (DAT-/-) rats. The animals were divided into 6 groups. Animals of 1st (-/--, n = 4), 3rd (+/--, n = 12) and 5th (+/+ n = 8) groups received a control balanced diet according to AIN93M, and the 2nd (-/-, n = 6), the 4th (+/-, n = 9) and the 6th (+/+, n = 8) groups - high fat (30% fat) diet with 20% fructose instead of water (HFCR). Assessment of the neuromotoric (muscle tone) state of rats was carried out on the 25th day by determining the grip strength of the front paws. Indices of short-term and long-term memory of animals were studied in the test of the "Conditional Reflex of Passive Avoidance" (CRPA) on the 37th, 38th and 59th days. The level of anxiety and motor activity in experimental animals was evaluated in the test "Elevated Plus Maze" (EPM) on the 7th and 50th days of the experiment. **RESULTS AND DISCUSSION:** The study of the neuromotor function showed that DAT -/-rats are characterized by a higher specific muscular force of compression (per unit body weight) compared to both DAT+/--and DAT+/+ rats. The indicator of short-term memory, expressed in the degree of fixation of the CRPA in DAT+/-rats was significantly higher in comparison with DAT+/- rats under conditions of HFCR consumption, but not in the control diet. The level of anxiety, determined in view of the key indicators in the EPM test, was lowering the DAT+/-- and, in particular, in the DAT-/-rats compared to wild type controls who consumed the control diet. Heterozygous rats were less disturbed at the background of the HFCR consumption in comparison with DAT-/- rats. HFCR reduced anxiety in wild type and, to a lesser extent, in heterozygous rats in the second test versus the control diet, but has no effect, in DAT-/- rats Thus, the knockout of the DAT gene in rats affects the neuromotor state, formation of a short memory trace and level of anxiety, and consumption of HFCR significantly modifies the severity and direction of these effects, which is suggested to be related to the effect of this diet on the processes related to altered dopamine transmission in the brain. **RESEARCH SUPPORT:** The work was supported by the grant of the Russian Scientific Foundation No. 17-16-01043 “Search for effector units of metabolism regulated by alimentary factors in obesity for the development of innovative specialized food”.

EFFECTS OF QUERCETIN ON NEUROMOTOR FUNCTION AND BEHAVIORAL RESPONSES OF THE ZUCKER RATS ON A HIGH-FAT AND HIGH-CARBOHYDRATE DIET. KV Mzhel'skaya, VA Shipelin, AA Shumakova, AD Evstratova, DM Rezaeva, NV Trusov, NV Kirbaeva, SA Apryatin and IV Gmoshinski, Federal Research Centre of Nutrition and Biotechnology, Moscow, Russia

Introduction. An actual scientific and medical problem is at present the search for new mechanisms for the regulation of metabolic processes and the development on their basis of dietary methods for the prevention and treatment of obesity, metabolic syndrome and other alimentary-dependent pathologies. The study of biologically active substances (polyphenols, vitamins, antioxidants, amino acids, etc.) action on the neuromotor and behavioral indices of laboratory animals on diet-induced in vivo models of obesity is a promising direction in neuronutritiology - a science that studies the neuroregulation of various metabolic processes mediated by a biological action of exonutrients.
The aim of the study was to study the effect of quercetin on behavioral responses in the Zucker rats with diet-induced obesity on a diet with a high quota of fats and fructose.
Methods. Studies were conducted on 24 male rats (8-10 weeks old) of the Zucker strain predisposed to obesity which were obtained from the Charles River cattery, Italy. The animals were divided into 4 groups of equal numbers (N=6). For 65 days, the animals of the 1st group (control) received a control balanced diet according to AIN93M, the 2nd - control diet + quercetin in the dosage of 50 mg/kg of body weight, the 3rd - a high-fat (30% fat) diet with 20% fructose instead of water (HFCR), 4th - HFCR + 50 mg quercetin/kg of a body weight. Evaluation of the neuromotor (muscle tone) state of the rats was carried out by determining the grip strength of the front paws on the 28th day. The level of anxiety and motor activity of the experimental animals was evaluated in the test "Elevated plus maze" (EPL) on the 9th and 50th days of the experiment. A short-term and long-term memory of animals was evaluated using the "Conditional Reflex of Passive Avoidance" test (CRPA) on the 37th, 38th and 59th day of the experiment.
Results and discussion. The studies conducted did not reveal significant differences in the neuromotor function between groups of rats that received experimental rations and quercetin. A comparative analysis of the time spent by animals in open and closed maze arms during the first test showed that the effects of experimental rations on the level of anxiety were not observed also. The rats of all experimental groups became significantly less anxious in the second EPL test, which was reflected in a significant decrease in the number of visits to the closed arms of the maze. The motor activity indexed by the total distance traveled in the maze significantly decreased with age in all rats with the exception of the rats on the control diet which received quercetin. In the same animals, motor activity was the largest among the remaining groups and significantly increased in comparison with the 1st group receiving a control diet. In the CRPA test, the parameters of fastening of the reflex (short-term memory) did not differ significantly in rats, who received or not quercetin on both types of diets. However, it was shown that when compared to rats of a control group those, receiving quercetin with HFCR, synergistically reduced the degree of the short memory trace fixation (83% in the 1st and 17% in the 4th group). abnormally elevated levels (more than 15 times in comparison with the control) of blood plasma leptin were observed simultaneously in Group 4 (HFCR + quercetin). Thus, the consumption of quercetin by the Zucker rats promotes an increase in their motor activity, and together with a high-calorie diet significantly decreases the short-term memory values.
Research Support. The work was supported by the grant of the Russian Scientific Foundation No. 17-16-01043 "Search for effector units of metabolism regulated by alimentary factors in obesity for the development of innovative specialized food".

CHANGES IN THE COMPOSITION OF INTESTINAL MICROBIOTA IN PATIENTS WITH MULTIPLE SCLEROSIS BY VARIOUS DISEASE-MODIFYING THERAPIES. IN Abdurasulova, EA Tarasova, IV Kudryavtsev, AV Matsulevich, MK Serebryakova, EI Ermolenko, IG Nikiforova, AG Il'ves, EV Ivashkova, ID Stolyarov and VM Klimenko, Institute of Experimental Medicine, Institute of Human Brain RAS, St. Petersburg, Russia

INTRODUCTION: For many decades, the opinion was formed that the triggers of multiple sclerosis (MS) and its exacerbations are infections of various genesis. Recently, a number of evidence has emerged about the effect of intestinal microbiota (dysbiosis) disorders in the pathogenesis of MS, since patients have been diagnosed with dysbiotic conditions. However, it is still not clear whether changes in the microbiota can be one of the causes of MS development / progression or are due to disease-modifying therapies (DMTs). The aim of the study was to reveal the peculiarities of intestinal microbiota in patients with MS receiving Glatiramer Acetate (GA) or Fingolimod (FG) therapy. **METHODS:** 34 patients with MS were examined, 17 patients (14 women, 3 men) received GA (Copaxone, Teva, Israel) 20 mg subcutaneously daily, the average duration of admission was 3.3 g; EDSS = 3.1 ± 0.3. 17 patients (12 women, 5 men) received FG (Gilenia, Novartis) 0.5 mg orally 1 per day, the average duration of admission was 6.1 g; EDSS = 4.0 ± 0.4. The intestinal microbiota was

determined by the culture method and by real-time PCR (PCR-RT). **RESULTS AND DISCUSSION:** In a bacteriological study, 71% of patients treated with GA showed a decrease in the level of lactobacilli, whereas in the FG group the population of these bacteria decreased only in 17% of patients. But against the background of FG treatment, the proportion of patients who did not have an Escherichia coli with normal enzyme activity and detected atypical forms of these bacteria was greater than in the treatment of GA (65% and 23.5%, respectively). In addition, 71% of patients receiving FG were seeded with other pathogenic enterobacteria (Enterobacter spp., Citrobacter spp.). Fungi of the genus Candida were isolated in both groups in 35-40% of patients. In the study of microbiota by PCR-RT method, 29% of patients receiving FG showed an increased level of total bacterial mass (> 12.6 lg), 65% of signs of anaerobic imbalance (high value, 150-1000, the coefficient reflecting the proportion of representatives of births Bacteroides / Faecalibacterium), 82% of patients had Enterobacter spp. significantly exceeded the threshold values (6-9 lg CFU / g). In the GA group were detected Proteus spp. (in 47% of patients), Parvimonas micra (in 35% of patients). Among the patients receiving GA therapy were patients with relatively effective treatment and did not respond. It turned out that it was in the second subgroup of the microbiota that Parvimonas micra was detected. Changes in the intestinal microbiocenosis were accompanied by specific qualitative and quantitative changes in various populations of immune cells in the blood, both Th cells and cytotoxic T cells. In particular, in patients with effective therapy, the percentage of central memory Th cells and Tc cells decreased, and the percentage of naïve Th and Tc increased. **CONCLUSION:** In all patients with MS, the effects of different DMTs and the effectiveness of therapy on the microbiocenosis of the intestine were revealed. Further research in this area will reveal the status of human microbiota that can be used as biomarkers for predicting the effectiveness of DMTs, as well as the direction of correction of the state of intestinal flora for increasing the effectiveness of treatment of MS.

SYMPOSIUM 7: THE ROLE OF NEUROINFLAMMATION AND MITOCHONDRIAL DYSFUNCTION IN THE PATHOPHYSIOLOGY OF NEUROPATHOLOGICAL CONDITIONS: PREVENTIVE AND THERAPEUTIC IMPLICATIONS

Chairs: T Strekalova (Netherlands, Russia), W Lim (Taiwan), D Anthony (UK)

RESILIENCE VERSUS SUSCEPTIBILITY TO THE DEPRESSIVE-LIKE SYNDROME IN ANIMAL MODELS OF DEPRESSION: METHODOLOGICAL AND CONCEPTUAL ASPECTS.

T Strekalova, Department of Neuroscience, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands; Laboratory of Psychiatric Neurobiology, Sechenov 1st Moscow Medical State University, Moscow, Russia

INTRODUCTION: Major depression is a serious, epidemiologically spread disorder that claims more lives per year than road-traffic accidents and currently projected to become the second most common cause of disability worldwide by 2020. At the same time, depression is regarded to be a neuropsychiatric condition that can be precipitated by environmental factors, and substantial inter-individual variability in the susceptibility to this disease is well documented. This aspect is not always taken into account while modelling major depression in rodents. **METHODS:** In our studies, we addressed potential neurobiological mechanisms that are associated with individual resilience / susceptibility to a development of the depressive-like syndrome using two mouse paradigms, a model of chronic stress-induced anhedonia and a model of enhanced learning of aversive context. **RESULTS AND DISCUSSION:** We found that distinct molecular pathways are involved in the mechanisms of resilience vs. susceptibility in a model of stress-induced anhedonia. Our studies suggest importance of mitochondrial functions and central insulin receptor-mediated signalling In the mechanisms to individual resilience to stress-induced depressive-like syndrome. In the model of modified swim test, increased acquisition of context of aversive experience was related to enhanced exhibition of behavioral despair. We found that individual susceptibility to this state is associated with heightened brain expression of GSK3-related molecules and pro-inflammatory cytokines. Together, the use of both mouse paradigms of depression, highlights the importance of the phenomenon of inter-individual variability in susceptibility to experimentally induced depressive-like state. In general perspective, targeting mechanisms of resilience to depression may open new perspectives in therapeutic management of this disorder. **RESEARCH SUPPORT:** This research was supported by “500-100 Russian Excellence Program”, Russian Federation, Deutsche Forschungsgemeinschaft, Germany and NARSAD Brain and Behavior Research Foundation, USA.

MITOCHONDRIAL CONTROL OF INSULIN RECEPTOR ACTIVATION IN NEURONS.

IA Pomytkin, VG Pinelis, NA Semenova, ZI Storozheva, Laboratory of Psychiatric Neurobiology, Sechenov 1st Moscow Medical State University; Scientific Center of Children's Health; Emergency Children's Surgery and Traumatology Research Institute, Moscow, Russia

INTRODUCTION: Insulin receptors, predominantly short isoform A (IR-A), are widely distributed in neurons of the central nervous system (CNS), where insulin/IR-A signaling plays diverse roles including regulation of synaptic plasticity, adult neurogenesis, and hypothalamic-pituitary-adrenal axis response to psychosocial stress. Here we demonstrate that mitochondria-to-insulin receptor interactions control activation of insulin receptors in neurons. **METHODS:** Tyrosine phosphorylation of insulin receptors was studied in primary culture of cerebellar granule neurons (CGNs) by ELISA. Behavioral tests and whole-brain ATP measurements with 31P NMR in vivo were performed in rats. **RESULTS AND DISCUSSION:** We found that mitochondrial signaling controls insulin receptor autophosphorylation (i.e. activation) in response to insulin in a "all-or-nothing" manner. If magnitude of insuin-induced mitochondrial H2O2 signal exceeds a certain threshold, the receptor becomes activated. If the H2O2 signal below the threshold, the receptor cannot be activated by even highest insulin dose. Targeting of the mitochondrial signal with the neuronal insulin receptor sensitizer makes the receptor sensitive to low suboptimal insulin doses and ameliorates brain energy metabolism and behavir in animal models of CNS disorders. **RESEARCH SUPPORT:** This research was supported by research grant 5-04-07885 RFBR and Biosignal (Moscow).

INCREASED IMPULSIVITY AND MICROGLIA ACTIVATION IN THE PREFRONTAL CORTEX IN MICE HOUSED ON THE WESTERN DIET ARE ASSOCIATED WITH MULTIPLE BEHAVIORAL ABNORMALITIES. E Veniaminova, M Oplatchikova, A Gorlova, D Pavlov, N Bazhenova, I Pomytkin, K-P Lesch, DC Anthony and T Strekalova, Laboratory of Psychiatric Neurobiology, Institute of Molecular Medicine, Sechenov University, Moscow, Russia; Department of Neuroscience, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands; Faculty of Biology, Lomonosov Moscow State University, Moscow, Russia; Department of Advanced Cell Technologies, Institute of Regenerative Medicine, Sechenov University, Moscow, Russia; Division of Molecular Psychiatry, Laboratory of Translational Neuroscience, Department of Psychiatry, Psychosomatics and Psychotherapy, University of Wuerzburg, Wuerzburg, Germany; Department of Pharmacology, Oxford University, Oxford, UK

INTRODUCTION: The "Western diet", which is enriched with saturated fat, simple carbohydrates and cholesterol, is associated with metabolic abnormalities and an increased risk of neuro-psychiatric conditions. However, the cause of the neurobiological effects remain poorly understood. We sought to investigate the effects of an insulin sensitizer on the behavior and underlying molecular changes and in female C57Bl6J mice after the consumption of a western diet for three weeks. **METHODS:** Tests for locomotion, social exploration, impulsivity, motor coordination, cognition and emotionality were employed. In addition, we studied mitochondrial and inflammatory markers by RT-qPCR, Western blot, and immunohistochemistry (iba-1) in the prefrontal cortex, and the effect of the insulin receptor sensitizer dicholine succinate on outcome. **RESULTS AND DISCUSSION:** Exposure to Western diet induced signs of impulsivity, reduced exploration, and aberrant social interactions that are reminiscent of autistic-like syndrome. Mice housed on Western diet displayed motor deficits, increased measures of anxiety and depressive-like changes, deficits hippocampus-dependent performance, liver dystrophy and lowered glucose tolerance. Increased central and peripheral expression of inflammatory marker, Toll-like receptor4 (TLR4), and decrease in expression of mitochondrial activity markers PPARGC1a and b were also observed. Western diet mice had elevated number of iba1-positive cells in prefrontal cortex, but not in hippocampus. Dosing with insulin receptor sensitizer dicholine succinate during dietary challenge attenuated many of these changes. The aberrant behaviors induced a Western diet in mice induces behavioral changes that appear to be associated with decreased glucose tolerance as they can be reversed with an insulin sensitizer. Most surprising among the behavioral findings was that the diet induced autism-like behaviors, which suggests that this type of diet may be exacerbating autism in populations where there is high consumption of the "Western diet". **RESEARCH SUPPORT:** This research was supported by Russian Research Excellence project "5-100" and the European Community (EC: AGGRESSOTYPE FP7/no. 602805 and Eat2beNICE Horizon 2020/no. 677302).

BEHAVIORAL ALTERATIONS AND RESPONSE TO SYSTEMIC INFLAMMATION IN MICE WITH THE *FUS* GENE MUTATION, A NEW MODEL OF AMYOTROPHIC LATERAL SCLEROSIS. A Trofimov, J de Munter, E Lysikova, E Veniaminova, A Gorlova, E Wolters, VM Klimenko, K-P Lesch and T Strekalova. Department of Neuroscience, School for Mental Health and Neuroscience, Maastricht University, Maastricht, Netherlands; Laboratory of Psychiatric Neurobiology, Sechenov 1st Moscow Medical State University, Moscow, Institute of Experimental Medicine, St. Petersburg, Russia; Department of Psychiatry, University of Wurzburg, Wurzburg, Germany

INTRODUCTION: amyotrophic lateral sclerosis (ALS) is a devastating lethal disease which is currently incurable. Systemic inflammation is known to plan important pathogenetic role with neurodevelopmental conditions including ALS, however these mechanisms remain poorly investigated. **METHODS:** a novel line of transgene mice, which express mutated FUS protein, one of the

determined causes of ALS, was recently generated and validated as a new paradigm of the ALS. Using this model, we studied the role of systemic inflammation in behavioral aberrations of FUS-transgenic (FUS-tg) mice at their pre-symptomatic stage after the LPS challenge. First, we studied behavioral features of FUS-tg strain. Male and female FUS-tg were compared against wildtype littermates for their motor performance in the wire test, cat walk, Pole test, grip, novel cage test and rotarod. Mice were also tested for parameters of emotionality in the forced swim test, tail suspension, sucrose preference test, O-maze and dark-light box, and for their cognitive abilities in the new object recognition test and tube test of food pellet displacement paradigm. Second, a cohort of female mice was challenges with a bolus intraperitoneal injection of low dose of lipopolysaccharide (0.1 mg/kg) and studied for novelty exploration, sucrose preference test, food pellet displacement and elevated O-maze. **RESULTS AND DISCUSSION:** Our study revealed numerous behavioral deviations of FUS-tg animals at their pre-symptomatic stage, as well as altered response to systemic inflammation. Based on our findings we suggest that neurodegenerative processes in brain areas, which regulate emotionality and cognition may occur prior the development of main symptoms of amyotrophic lateral sclerosis and are independent from this syndrome. In addition, FUS-tg mice display altered response to pro-inflammatory challenge that may play a role in the mechanisms of genetically induced pathology in this model and thus, be of clinical importance. Further studies are required to address neurobiological mechanisms of these changes during ALS.

EFFECTS OF INTRACEREBROVENTRICULAR ADMINISTRATION OF NEURO-CELLS ON MOTOR HALLMARKS OF AMYOTROPHIC LATERAL SCLEROSIS IN THE *FUS*-TRANSGENIC MICE. A Gorlova, J de Munter, E Walters, D Pavlov, N Bazhenova, E Veniaminova, DC Anthony and T Strekalova, Sechenov First Moscow State Medical University, Moscow, Russia; Lomonosov Moscow State University, Moscow, Russia; Maastricht University, Maastricht, Netherlands; Neuroplast Ltd, Maastricht, Netherlands; Oxford University, Oxford, United Kingdom

INTRODUCTION: We used a novel transgenic mouse line, which development was based on the mutation of Fused in sarcoma protein (FUS), DNA/RNA-binding factor, a cause of 5-7% of clinical cases of amyotrophic lateral sclerosis (ALS). Current study was aimed at the investigation of possible protective effects of “Neuro-cells”, human stem cells, on motor hallmarks of the ALS syndrome in FUS-transgenic (FUS-tg) mice. **MATERIAL AND METHODS:** FUS-tg male mice bred on CD1 background and their wild type littermates were divided in 6 groups: wild type, vehicle-treated (WT-Veh), wild type, Riluzole-treated (WT-Ril), wild type, Neuro-cell-treated (WT-NC), FUS-tg, vehicle-treated (FUS-Veh), FUS-tg, Riluzole-treated (FUS-Ril), FUS-tg, Neuro-cell-treated (FUS-NC). Riluzole was administrated at the dose 8 mg/kg/day via drinking water. “Neuro-cells”, a mixture of 500.000 of hemopoetic stem cells and 500.000 of mesenchymal stem cells suspended in 10 µl of buffer or vehicle were injected intra-cerebro-ventricular. All groups were weekly monitored for and motor functions in the wire test, rotarod, pole test and novel cage test for Weeks 1-6 post-surgery/onset of dosing with Riluzole. On seventh week, mice were sacrificed, their brain, muscles and spinal cord were dissected for subsequent study. **RESULTS AND DISCUSSION:** On Week 6, FUS-Veh group displayed profound motor deficits, significantly reduced body weight, food and water intake, suggesting the onset of ALS-like pathology. In the FUS-Ril group, lesser number of these parameters were affected significantly, that was even less in the FUS-NC mice. Weight of muscles, body weight, food and water intake, motor functions in the wire test, were significantly ameliorated in the FUS-NC mice in comparison to the FUS-Veh group. No changes in WT-Ril and WT-NC groups in comparison to the WT-Veh control were found, suggesting that treatment procedure and treatments applied do not affect per se measured parameters in this study. **RESEARCH SUPPORT:** This research was supported by Russian Research Excellence project “5-100” and the Neuroplast Ltd.

ISBS SPECIAL PLENARY LECTURE: DEEP BRAIN STIMULATION IN EXPERIMENTAL STRESS ANIMAL MODEL OF DEPRESSION. LW Lim, Li Ka Shing Faculty of Medicine, the University of Hong Kong, Hong Kong

INTRODUCTION: Deep brain stimulation has been proposed as a potential therapy for patients with treatment-resistant depression. In this study, we investigated the effects of high-frequency stimulation (HFS) in specific brain regions on various depressive-like behaviors using the stress resilience and vulnerable rat depression models. **METHODS:** Animals were exposed to chronic unpredictable stress procedures (CUS) and tested for depressive-like behaviors after receiving HFS in the lateral habenula, ventromedial prefrontal cortex (vmPFC), and nucleus accumbens. Vulnerable and resilience animals were characterized based on their sucrose consumption levels during CUS procedures. The investigation on changes of midbrain dopaminergic and serotonergic neurons, and hippocampal neuroplasticity were performed using both molecular and immunohistological labeling methods. **RESULTS AND DISCUSSION:** Our results demonstrated that electrical stimulation targeting specifically the vmPFC, most effectively treats symptoms of mood-related behaviors, as compared to

several potential antidepressant stimulated-brain regions. Further, our results have shown that it could also be used to enhance the growth of brain cells in the hippocampus, which mitigates the harmful effects of dementia-related conditions and improve the learning and memory functions in object recognition and Morris water maze tests. Our data showed a remarkable increase of hippocampal neural progenitors, surviving BrdU-positive cells, and dendritic arborization after vmPFC stimulation as compared to the sham. Interestingly, vmPFC HFS also rescued the stress-induced midbrain dopamine neuron degeneration, as well as evoked a specific brain circuitry modulation of the serotonergic pathway, which linked to the dorsal raphe nucleus in regulation of mood-related and hippocampal-dependent memory behaviors. Overall, our results suggest that vmPFC HFS effectively restores depressive-like behaviors by mechanisms of hippocampal neuroplasticity, serotonergic neurotransmission, and dopaminergic neurons restoration in the vulnerable CUS-induced model. Further studies are needed to understand the underlying mechanisms of HFS on the resilience and vulnerable group of CUS-induced depression models. **RESEARCH SUPPORT:** This research was supported by the Hong Kong Research Grant Council (RGC-ECS Grant 27104616).

THE EFFECTS OF CAFFEINE AND STRESS ON PSYCHOSIS-LIKE EXPERIENCE. C Ágoston, Z Demetrovics, Doctoral School of Psychology, Institute of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary

INTRODUCTION: There is some evidence from epidemiological, cross-sectional and case studies that psychosocial stress and acute caffeine use may increase the occurrence of psychosis-like experiences (e. g. hallucinations, persecutory ideations) in people with schizophrenia and also in the non-psychiatric population. The current study is aimed to obtain experimental evidence for the effects of caffeine, stress, and their interaction on features of perception, namely on auditory changes in perception and threat-related associations, in a safe laboratory setting. The study is aimed as well to examine the possible differences between medium/high caffeine consumers (> 50 mg/day) and non/low consumers. **METHODS:** Medium/high caffeine consumer participants (N = 88) and non/low consumer participants (N = 79) were randomly assigned into caffeine (100 mg) (C) or placebo (P) groups and stress (S) or non-stress (N) groups. Stress was induced by using the Montreal Imaging Stress Task while the N group watched a documentary on railways. We used the White Christmas Paradigm (WCP) to assess hallucination-like experiences and a recall task with threat-related, depression-related, and emotionally neutral words to measure bias towards threat-related associations. **RESULTS AND DISCUSSION:** The S group had significantly more false alarms in the WCP [$F(1) = 8.077$, $p = 0.005$, $\eta 2 = 0.048$] and recalled more depressive words [$F(1) = 4.227$, $p = 0.041$, $\eta 2 = 0.026$] than the N group. There were no main effects or interactions of caffeine, stress or consumer status on the number of recalled threat-related or neutral words. Our results indicate that experiencing psychosocial stress can induce hallucination-like experiences but not threat-related biases in cognition. The acute ingestion of an ordinary dose of caffeinedoes not seem to affect hallucination-like experiences nor result in recall bias towards threat-related thoughts in participants from the general population. Future studies should further examine the relationship of stress and cognitive biases related to depression. **RESEARCH SUPPORT:** The study was supported by the Hungarian National Research, Development and Innovation Office.

IMPACT OF SEVERE PEDIATRIC EPILEPSY (DRAVET SYNDROME) ON PARENTAL STRESS AND ANXIETY. T Leonova, S Auvin, S Caharel, N Coqué, Nabbout, M Robert, A de Saint Martin and A Piquard-Kipffer, Université de Lorraine, Hôpital Robert-Debré, Agro-Paris-Tech, Hôpital Necker, Université de Strasbourg, France; Université du Québec en Outaouais, Canada

INTRODUCTION: Dravet syndrome (DS) is a severe form of epilepsy that usually emerges in the first year of life. DS is relatively rare, with early estimates of the incidence ranging from 1 in 20,000 to 1 in 40,000. On the one hand, pediatric epilepsy has a significant impact on a child's life, the extent to which is based on four factors: epilepsy, cognition, behavioral, and physical/neurologic function. On the other, caring for a child with DS is associated with significant humanistic burden and direct costs. The purpose of this study was to compare parenting stress and anxiety patterns in parents of children with DS, with autism and controls. **METHODS:** Parents of children whith DS (n = 29), parents of children with autism (n = 19) and parents of healthy children (controls, n = 56) completed the demographic questionnaire, parenting stress measures (Indice de Stress Parental, Bigras, LaFreniere, & Abidin, 1996) and anxiety measures (Inventaire d'anxiété état trait-Forme Y, Spielberger et al., 1983; version française: Bruchon- Schweizer & Paulhan, 1993). **RESULTS AND DISCUSSION:** No statistically significant differences were found in anxiety level in parents of children with disability vs healthy children (p ns). Results indicated that parents of children with disability (DS + autism) experienced the level of parental stress significantly higher compared with parents of controls (healthy children). Parenting stress was also significantly higher in parents of children with DS compared with parents of children with autism ($p < 0.05$). Severe pediatric epilepsy affects the parental stress more

than autism disorder. **RESEARCH SUPPORT:** Research reported in this communication was supported by the grant Défi S2C3 from the Mission pour l'interdisciplinarité at the The National Center for Scientific Research (CNRS, France).

Day 4. Sat, May 19, 2018

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

ISBS PRESIDENTIAL LECTURE: ZEBRAFISH NEUROBEHAVIORAL MODELS, STRESS AND ENVIRONMENTAL ENRICHMENT. KA Demin, AD Volgin, OV Yakovlev, MS de Abreu, PA Alekseeva, AJ Friend, TG Amstislavskaya and AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Almazov National Medical Research Center, Military Medical Academy, St Petersburg, Ural Federal University, Ekaterinburg, Russian Center for Radiology and Surgical Technologies, Pesochny, Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia; Bioscience Institute, University of Passo Fundo (UPF), Passo Fundo, Postgraduate Program in Pharmacology, Federal University of Santa Maria, Santa Maria, Brazil; Tulane University School of Science and Engineering, New Orleans, LA, USA; The International Zebrafish Neuroscience Research Consortium (ZNRC), ZENEREI Research Center, Slidell, LA, USA; School of Pharmacy, Southwest University, Chongqing, China

Environmental stimuli are critical in preclinical research that utilizes laboratory animals to model human brain disorders. The main goal of environmental enrichment (EE) is to provide laboratory animals with better choice of activity and greater control over social and spatial stressors. Thus, in addition to being a useful experimental tool, EE becomes an important strategy for increasing the validity and reproducibility of preclinical data. Although zebrafish (Danio rerio) is rapidly becoming a promising new organism for neuroscience research, the role of EE in zebrafish CNS models remains poorly understood. Here, we discuss EE in preclinical studies using zebrafish and its influence on brain physiology and behavior. Improving our understanding of EE effects in this organism may enhance zebrafish data validity and reliability. Paralleling rodent EE data, mounting evidence suggests the growing importance of EE in zebrafish models of brain disorders.

SYMPOSIUM 8: LAPIN SYMPOSIUM ON TRANSLATIONAL BIOLOGICAL PSYCHIATRY

Chair: AV Kalueff (Russia, China)

INTRODUCTION: PROFESSOR IZYASLAV LAPIN

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

LONG-TERM EFFECTS OF PRENATAL HYPOXIA ON EMBRYONIC DAYS E14 OR PROLONGED PRENATAL HYPERHOMOCYSTEINEMIA ON THE NUMBER AND LOCALIZATION OF CORTICAL NEURONS AND GLIA DEPEND ON THE TIME PATTERN OF PRENATAL STRESS. DS Vasilev, NL Tumanova and AD Shcherbitskaia, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg State Pediatric Medical University, St. Petersburg, Russia

INTRODUCTION: The action of different stressors during pregnancy leads to various complications both in the maternal organism and developing fetus increasing risk of abnormal brain development and functioning in later life, however, little is known about the mechanisms of long-term consequences of such developmental impairment. The negative effects of prenatal hyperhomocysteinemia (HHC) or hypoxia (Hpx) resulted in disruption of short-term, long-term and working memory in adult offspring were described earlier. In this study we examined the effects of maternal Hpx or HHC on structural abnormalities in brain tissue. **METHODS:** HHC was induced in pregnant female rats by administration of methionine (0.6mg/kg) in drinking water in the period of days 4-21 of pregnancy. Other pregnant females were subjected to Hpx (7% O2, 3h) on the 14th day of pregnancy. 5′ethynyl-2′deoxyuridine (EdU) was used to label neurons generated on E14 in the fetuses. Their distribution was analyzed in cortical tissue of pups on P5. The elimination of cells during the first month was analyzed by morphometry and immunohistochemistry of marker proteins. **RESULTS AND DISCUSSION:** In both groups of rat pups subjected to Hpx or to HHC, the total number of EdU-labeled cells in the parietal cortex was decreased (in HHC it was 57.7% of the number in naïve control, 44.0% in Hpx) while the number of labeled neurons scattered within the superficial cortical layers was increased (19.1% in naïve control, 73.4% in HHC, 42.0% in Hpx). It can be suggested that both Hpx and HHC cause a disruption in neuroblast generation and migration with similar outcome after birth. In the first month after birth the reduction in the total number of cortical neurons was observed in both groups of pups. The analysis of cell morphology (chromotolysis, hyperchromotosis), the distribution of proapoptotic marker proteins (p53, caspase-3, APAF) and the neuronal marker NeuN suggested death of pyramidal cortical neurons. It was shown that the neurodegenerative processes in parietal cortex of pups subjected to HHC were more developed, as beside of neuronal death the number of glial elements in parietal cortex was shown to be increased 3.8 folds, suggesting the activation of glia in the period of cell elimination. The data obtained suggest that both HHC and hypoxic action affects formation of cortical cytoarchitecture in postnatal ontogenesis leading to cortical dysfunction. The intensity of neuronal death in postnatal period depends on the failure of neuroblast migration in the embryonic period. **RESEARCH SUPPORT:** RFBR 16-04-00694 and 18-015-00099. It was carried out within the state assignment of FASO of Russia (AAAA-A18-118012290373-7).

PHARMACOLOGICAL SCREENING OF MAFEDINE, A NOVEL ALPHA2 ADRENORECEPTOR AGONIST, IN ZEBRAFISH. YI Sysoev, DA Meshalkina, SV Okovitiy, PE Musienko and AV Kalueff, St. Petersburg State Chemical Pharmaceutical University, Institute of Translational Biomedicine (ITBM), St. Petersburg State University, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China

INTRODUCTION: The aim of this investigation was a of 6-oxo-1-phenyl-2- (phenylamino)-1,6-dihydropyrimidine-4-sodium olate (mafedine), alpha-2 adrenergic receptor agonist, in the zebrafish model in the Novel tank test. The effects of doses of 15 mg/L, 30 mg/L and 60 mg/L were studied under the condition of acute exposure (20 min). Madedine at 60 mg/L had a moderate psychostimulating action, with elements of anxiogenic effect. **METHODS:** The study was performed in adult zebrafish. Behavioral testing was performed using the novel tank test. Before the testing, the fish were kept for 20 min in smaller opaque plastic containers in 0.5 L water or a solution of mafedine at several concentrations. Animals were randomly divided on 4 experimental groups, 15 fish in each of them: control, mafedine 15, 30 mg/L (Experiment 1) and control and mafedine 60 mg/L (Experiment 2). Trials were recorded for 5 min by web-camera for further analyses. For each animal, the distance travelled (cm), the mean and maximum velocity (cm/s) and turn angle (deg) were estimated. Also the frequency and duration (s) of immobile state (no movements, except eyes and fins > 2 s) and not moving state (no changes of location), the time spent in the top and in the bottom zones (s), the frequency of transition from bottom to top and latency time of the first bottom-top transition (s), as described earlier. The statistical significance of differences between groups in Experiment 1 was assessed using the Kruskal-Wallis test followed by Dunn´s post-hoc test and in Experiment 2 Mann-Whitney U-test was used. The level of confidence was set as 95%. **RESULTS AND DISCUSSION:** In Experiment 1 tested groups did not show significant differences from controls, although there were some changes of fish behavior. Acute mafedine exposure at dose of 60 mg/L in Experiment 2 led to 1.3-fold significant increase of traveled distance in comparison with control group. The turn angle was significantly lower (in 1.7 times) in treated group than in controls. Also the mafedine group spent significantly more time in bottom zone than control fish. Compared to control the 60 mg/L group had a 1.4-fold increase of immobile state frequency and a 2.3-fold decrease of not moving state cumulative duration. Overall, these findings suggest that mafedine has a moderate psychostimulant action in

zebrafish, as evidenced by longer distance traveled and mild acceleration. However, the drug also caused longer time spent in bottom zone of the tank, as well as the frequent immobility episodes, which may suggest the anxiogenic action of mafedine. The presence of stimulant action of mafedine raises possibility of its clinical applications. For example, such moderate psychostimulant action can be beneficial for correcting asthenia which often occurs in various CNS pathologies, such as traumatic brain injury and stroke. **ACKNOWLEDGEMENTS:** The research was supported by the Russian Foundation for Basic Research (RFBR) grant 16-04-00851 to AVK. The funders had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. The authors declare no conflicts of interest.

INTRANASAL EXPOSURE TO MANGANESE INDUCES ACTIVATION OF CALPAINS IN RAT BRAIN. IS Oblamskaya, VA Maistrenko, EA Skomorohova, MN Karpenko and VM Klimenko, Institute of Experimental Medicine, St. Petersburg, Russia

INTRODUCTION: Manganese (Mn) is an essential trace element. However, chronic exposure to Mn causes a variety of psychiatric and motor disturbances, termed manganism. In the present study we have evaluated Mn neurotoxicity in rats after MnCl2 intranasal administration. The participation of the calcium-dependent protease calpain-1 and calpain-2 was monitored in the striatum and hippocampus. Mn induced an increase of the activity and production of calpain-2 in the striatum, while the activity of calpain-1 also increases but not its mRNA. In the hippocampus in turn only calpain-1 activity was increased. We have also shown that Mn like calcium directly activates calpain-1 but not calpain-2 in vitro. **METHODS:** Adult male Wistar rats, 220–250 g, were used in this study. Mn-exposed rats received intranasal injections 20 µl/rat in total 1mg MnCl2 once per day, for 10 consecutive weeks. Control animals received the same volume of sterile saline. Mn levels were measured in the olfactory bulb, hippocampus and striatum by atomic absorption spectrometry. The mRNA protein levels, concentration and activity of calpain-1 and calpain-2 were measured. **RESULTS AND DISCUSSION:** In this study, we showed that Mn was significantly elevated in Mn-exposed rats than in controls (2-fold for olfactory bulb, 1.5-fold for hippocampus and 5-fold for striatum). Levels of manganese in circulating blood were not changed. We were able to show that as a result of intranasal administration of MnCl2 manganese accumulates in the striatum at a very high level and to lesser extent in the hippocampus. That causes increase of the activity and production of calpain-2, while activity of calpain-1 also increases but not its mRNA. In the hippocampus in turn only calpain-1 activity is increased. We demonstration by zymography in gel that Mn, accumulated by the cells of the hippocampus and striatum, directly activated calpain-1.

WHEN FISH TAKE A BATH-2: EXAMINING THE EFFECTS OF ACUTE AND CHRONIC TREATMENT OF ALPHA-PYRROLIDINOPENTIOPHENONE (ALPHA-PVP), A BATH SALT "FLAKKA", IN ADULT ZEBRAFISH. TO Kolesnikova, SL Khatsko, OS Eltsov, VA Shevyrin and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

INTRODUCTION: Alpha-pyrrolidinopentiophenone (α-PVP) is a synthetic cathinone and a 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 as "flakka", "bath salts" or "gravel", α-PVP (currently a Schedule 1 agent in US) is strictly controlled 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 neuropsychopharmacological research. Here, we further characterize the effects of α-PVP in-vivo by assessing its acute and chronic behavioral effects in adult zebrafish. **METHODS:** A total of 240 wild type short-fin zebrafish (50:50 male:female ratio) were used for this study. All fish were experimentally naïve and housed in groups of 40 per 40-L tank, filled with filtered water maintained at 22-24 □C. The novel tank test was used to assess zebrafish behavior for 5 min. We evaluated the latency (s) and

number of top entries, time spent in the upper part of tank (top), duration and frequency of freezing behavior, the number of anxiety-like erratic movements, velocity, distance travelled, frequency and duration mobility and immobility states. In Experiment 1, we were evaluated acute effect of 10 mg/L (n=20), 30 mg/L (n=20) and 60 mg/L (n=20) of α-PVP in adult zebrafish compared with control (n=20) after standard 20-min pre-treatment. In Experiment 2, we were measured behavioral effects of chronic 1-week α-PVP treatment in doses of 0 mg/L (control, n=20), 1 mg/L (n=20), 5 mg/L (n=20) and 10 mg/L (n=20) and zebrafish behavior 2 days after the withdrawal of flakka in same doses. In Experiment 3, we were estimated effect of flakka after 1-week repeated 5-hour withdrawal of 1 mg/L (n=20), 5 mg/L (n=20) and 10 mg/L (n=20) of α-PVP vs control group (n=20). **RESULTS:** In Experiment 1, flakka in all doses significantly reduced number of erratic movements compared with control group. In 10 mg/L and 30 mg/L α-PVP increased freezing duration. Frequency and duration of top entries were significantly decreased in 30 mg/L as well as latency of entries in the upper part of tank was significantly longer than in control group. The maximal movement velocity and distance travelled significant fell in the 10 mg/L, 30 mg/L and 60 mg/L. In addition, frequency and duration of immobility state was significantly higher in all groups than in control. Also, minimum and maximum acceleration was lower in all concentrations, similar to tendency to decreased of mean and total meandering. In Experiment 2, similar to Experiment 1, we found decreasing of number of erratic movement in all studied doses and increasing of freezing duration, but average freezing duration was high only at 5 mg/L and 10 mg/L. Freezing frequency was significantly lower only in dose 10 mg/L. Also, flakka reduced total distance traveled and total velocity in all experimental groups. A-PVP at 1,5 and 10 mg/L did not change key novel tank endpoints after 2 days withdrawal. However, frequency and cumulative duration of high mobility state was increased in 10 mg/L. In Experiment 3, α-PVP significantly increased total and average freezing duration in 1, 5 and 10 mg/L, but increased freezing frequency only in 1 mg/L. Also, number of erratic movements was decreased in all experimental groups. We did not found any differences in latency, frequency and duration of top entries in groups, which were exposed in flakka. Total velocity and distance travelled were significantly decreased in 1. 5 and 10 mg/L compared with control as well as frequency and duration of mobility state. Acceleration minimum and maximum were lower in 5 mg/L and 10 mg/L. Taken together, our results suggest that chronic treatment of flakka may induce suppression of locomotor activity and modulate zebrafish behavior and possibly cause similar effects in rodent. It is known that the effects of withdrawal of flakka include depression and increased fatiguability in human. Thus, these 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. **RESEARCH SUPPORT:** Ural Federal University, Ekaterinburg, Russia.

BEHAVIORAL EFFECT OF 2-(4-FLUOROPHENYL)-4H,5H,6H,7H-8Λ^5--[1,2,3]TRIAZOLO[1,5-A]PYRIDIN-8-YLIUM-3-OLATE (C-66) IN MICE IN THE OPEN FIELD AND ELEVATED PLUS-MAZE TESTS. TO Kolesnikova, AS Kraeva, VG Borygina, SL Khatsko, TV Gluhareva, Y Nein, IA Kotov and AV Kalueff, Ural Federal University, Ekaterinburg, Institute of Translational Biomedicine, St. Petersburg, Russia; School of Pharmacy, Southwest University, Chongqing, China; ZENEREI Research Center, Slidell, LA, USA

INTRODUCTION: Stress-like states are one of the most important problems in the modern world, which makes it necessary to look for new medications that do not cause side effects. 1,2,3-triazoles and its fused analogues are poorly studied class, because their biological properties are not described. However, these compounds are promising because of high stability even under strong oxidation and reduction conditions. Also, the propensity to form hydrogen bonds increases the solubility of 1,2,3-triazoles, which makes it possible to effectively binding towards biomolecular targets. The aim of our experiment was to study the behavioral effects of 2-(4-fluorophenyl)-4H,5H,6H,7H-8λ□-[1,2,3]triazolo[1,5-a]pyridin-8-ylium-3-olate (C-66) in adult mice in the Open field (OF) test and Elevated plus-maze (EPM) test. **METHODS:** A total of 45 white 10-month-old mice females were used for this study. All mice were experimentally naïve, had free access to water and food and were divided in five groups: control (n=9), 5 mg/kg (n=9), 25 mg/kg (n=9), 50 mg/kg (n=9) and 75 mg/kg (n=9). The substance dissolved in a 1% solution of starch mucus was injected intraperitoneally. The Of test and EPM test were utilized to assess mouse behavior for 5-min in each test following 30-min pre-treatment with C 66. In Open field test we were calculated locomotor activity, frequency, latency and duration of freezing, grooming, rearing and hole-poking behavior. In Elevated plus-maze test we were scored the time spent in closed and open arms; the number of squares crossed and entrance in closed and open arms, locomotor activity, the latency, frequency and duration of freezing and rearing behavior. **RESULTS AND DISCUSSION:** Overall, C 66 in dose 5 mg/kg and 25 mg/kg did not change any parameters in OF test and EPM test compared with control group. Tested substance in doses of 50 mg/kg and 75 mg/kg ($p<0.05$) was significantly decreased the number of squares crossed, also C-66 reduced the exploratory activity at the 50 mg/kg dose ($p<0.05$). Increased of freezing duration was noted for 75 mg/kg ($p<0.05$), and conversely the hole-poking behavior was decreased in 50 mg/kg ($p<0.05$). At 75 mg/kg and 50 mg/kg doses, C 66 in EPM test significantly

reduced the total and average duration of rearing behavior ($p<0.05$), and increased the average duration of rearing behavior in 50 mg/kg ($p<0.05$), and 75 mg/kg ($p<0.01$). Also, the number of grooming patterns ($p<0.01$) and grooming duration ($p<0.05$) were increased in 75 mg/kg. Based on the data obtained, we can conclude that the substance C-66 in certain doses is likely to have anxiogenic-like properties. Thus, triazoles and their analogues can be excellent base for medicines to treatment of stress-like states.

THE STUDY OF EMOTIONAL INTELLIGENCE OF A PRIMARY SCHOOL TEACHER IN THE CONTEXT OF PROFESSIONAL CHOICE PROBLEM. MN Anderson, Pushkin Leningrad State University, St. Petersburg, Russia

OBJECTIVES: Research is devoted to studying the problem of emotional intelligence of the students of different training areas: the students of the profile "Primary education" of the faculty of psychology and students of the faculty of mathematics as a control group, each group consisted of 16 people. We have set a priority to prove that the students of pedagogical profile have been characterized by a high level, either of the total value of emotional intelligence or of the value of its leading component – interpersonal emotional intelligence. **METHODS:** Methodical apparatus of the study included the questionnaire of emotional intelligence by D. V. Lucin, where we gave preference to the three scales, the total scale of emotional intelligence and interpersonal emotional intelligence; Mann-Whitney test verified the accuracy of the pairwise differences. **RESULTS AND DISCUSSION:** Study of overall emotional intelligence in the experimental group of students showed high level data (91,3), which can be explained from different sides. First, group emotional properties related to professionally significant properties of the personality of the teacher, which involves the personal basis of choice of profession: we can assume that the profession of a teacher, especially elementary school teachers, have more reason to choose people with more pronounced emotional personality characteristics. On the other hand, the mastery of theoretical and practical knowledge in the field of education of students is accompanied by significant professional and personal development, since, as already mentioned, vocational training is the dominant activity of student's age. Identified terms of interpersonal emotional intelligence allows us to refine the previously obtained results: the group average is within a high level (48,4). As mentioned above, the choice of the procession of the teacher has every reason to be caused by emotional characteristics of the individual student. Accordingly, a high level of interpersonal emotional intelligence of student's teachers allow us to determine the specificity of these characteristics. So, D. V. Lucin under interpersonal emotional intelligence understand the ability to understand and identify the emotions of others and managing. We believe that significantly more expressed characteristics of interpersonal emotional intelligence in student teachers are quite natural result, because the main content of the teaching profession are the relationships with people - children, their parents, colleagues. In these relationships often occur situations for which the teacher should possess not only a high level of stress tolerance, but also a sufficient level of ability to identify and understand the emotions of others [Anderson, 2012]. In addition, a significantly higher level on this scale of future teachers indirectly due to the presence in the curriculum, among other things, a considerable number of disciplines of applied nature, aimed at the development of communicative skills (for example, "the training of partner communication"). **CONCLUSIONS:** The study identified general data of emotional intelligence among the group of pedagogical profile students, that had proved our assumption regarding the high level, either of the total value of emotional intelligence or of the value of its leading component –interpersonal emotional intelligence. Accordingly, we have reason to believe that the specificity of professional orientation determines the specificity of personal development.

THE ASSOCIATION BETWEEN THE BRAIN-DERIVED NEUROTROPHIC FACTOR GENE POLYMORPHISMS AND AGITATION OR EARLY TRAUMATIC EXPERIENCE IN PATIENTS WITH POST-TRAUMATIC STRESS DISORDER. N Pivac, M Konjevod, L Tudor, M Nikolac Perkovic, D Svob Strac, G Nedic Erjavec, S Uzun and O Kozumplik, Division of Molecular Medicine, Rudjer Boskovic Institute, Clinic for Psychiatry Vrapce, Zagreb, Croatia

INTRODUCTION: Posttraumatic stress disorder (PTSD) is a trauma and stressor related disorder where the full remission is achieved in only one third of patients. Besides traumatic event's exposure(s), vulnerability to develop PTSD and different symptoms depend on the numerous risk factors such as various risk genotypes (among others, variants for the brain derived neurotrophic factor (BDNF) gene), gender and exposure to early traumatic experience. BDNF has neurotrophic and functional roles in the brain, but it also modulates stress response and therapeutic response to antidepressants. Reduced BDNF levels were reported in stress exposed subjects and in PTSD. Therefore, validated, specific and sensitive biomarkers of the vulnerability to PTSD, development of serious symptoms but also of treatment response are needed. The aim of the study was to assess the association of BDNF (rs6265 [G196A or Val55Met] and rs56164415 [C270T]) gene polymorphisms

with various symptoms or exposure to the early life stress in PTSD. **METHODS:** The diagnosis of PTSD (N=692) in male patients was made with SCID according to the DSM-5 criteria. Various symptoms or exposure to the early life stress were evaluated using the Clinician Administered PTSD scale (CAPS), the Positive and Negative Syndrome Scale (PANSS) and the Childhood Trauma Questionnaire (CTQ). Genotyping was done with the real time PCR. Statistical evaluation of the results was done using Kruskal-Wallis ANOVA, Mann Whitney test and $\chi 2$ test. **RESULTS AND DISCUSSION:** Significantly increased positive, psychotic, excitement and depressive symptoms were detected in A/G (Met/Val) compared to GG (Val/Val) carriers of the BDNF rs6265, while significantly higher psychotic, positive and cognitive symptoms, and emotional and physical abuse scores of the CTQ were found in T compared to CC carriers of the BDNF rs56164415. The severity of the traumatic symptoms evaluated using the CAPS was not associated with BDNF rs6265 and rs56164415 genotypes. The significant association between BDNF variants, related to reduced BDNF function, and particular early traumatic experience and/or more severe positive, psychotic, agitated, cognitive or depressed symptoms was found in male patients with PTSD. These data suggest that genetic markers might be used to predict development of worse symptoms that contribute to the more complicated and more severe clinical features of PTSD. **RESEARCH SUPPORT:** This research was supported in part by the Croatian Science Foundation, project No. IP-2014-09-4289.

BLASTOCYSTS INVASION IN PATIENTS WITH MULTIPLE SCLEROSIS IN ST PETERSBURG. EA Tarasova, IN Abdurasulova, AV Matsulevich, EI Ermolenko, IG Nikiforova, AG Il'ves, EV Ivashkova, ID Stolyarov and VM Klimenko, Institute of Experimental Medicine, Institute of Human Brain RAS, St. Petersburg, Russia

INTRODUCTION: In the last years, there has been an increasing interest in the role of the gut microbiota in autoimmune disorders and especially, in the pathogenesis of multiple sclerosis (MS). It was shown that almost 70% of MS patients have different gastrointestinal problems, which may be the result of intestinal microbiota dysbiosis. Intestinal microbiota can produce antimicrobial factors and inhibiting the growth of some pathogenic bacteria. Currently, the gastrointestinal microbiota is not only a community of various bacteria and fungi, but also various parasitic and non-parasitic protozoa. Blastocystis is one of the enteric parasites that can be found in patients with or without gastrointestinal symptoms. When studying the composition of microbiota in patients with blastocyst infection, in 90% of cases describe the state of gastrointestinal dysbiosis, which allows us to consider them as one of the characteristics of dysbiosis. Epidemiological studies have identified different Blastocystis subtypes but no one subtype has been strongly correlated with any disease. Earlier we have detected Blastocystis sp. more often in group of children with allergic disorders and in group of patients with chronic viral hepatitis (CVH) than in group without any gastrointestinal symptoms. The aim of the present study was to analyze Blastocystis among the isolates from patients with MS in Saint Petersburg and identify the typical subtypes for that group of patients. **METHODS:** 49 stool samples were collected from patients with MS and 2360 from healthy people. We identify Blastocysts at first by light microscopy and by PCR method with specific primers for 18S RNA gene. Samples were genotyped using seven subtype-specific sequence tagged site (STS) primer by PCR. **RESULTS:** Blastocysts were found in 42,8% of samples from MS patients (21 isolates). In control group only 17,8 % consist Blastocystis. Also in control group we mainly detect subtypes 3 (65,4%), that now described as not pathogenic. Analysis of the level of Blastocystis colonization showed that subtypes 2 (47,6 %) were the most common subtype in group with MS. Subtype 3 were detected only in 19,4% of all isolates in that group and subtype 1 in 14,2 %. Previously we have shown prevalence of subtypes 2 in group of children with allergic disorders. **CONCLUSION:** Nowadays remains unknown, the dysbiosis of intestinal microbiota contributes to the development of MS or it develops against the background of autoimmune pathology of the central nervous system. Present study demonstrate that Blastocystis detected in 2,4 times more often in group of patients with MS than in control group. Subtyping of Blastocystis allowed showing that patients with MS mainly colonized by subtype 2 of Blastocystis infection. The data obtained allow to consider the blastocyst, as one of the essential characteristics of the intestinal microbiota composition in MS.

STRESS AND ANXIETY IN PETS: ADOPTION OF THE HUMANE THERAPEUTIC APPROACH. KK Ganina, EA Karelina, SA Tarasov, Research and Production Company "Materia Medica Holding", Institute of General Pathology and Pathophysiology, Moscow, Russia

INTRODUCTION: Psycho-emotional disorders have long been recognized as a serious problem in human patients, but in animal healthcare the branch of behavioral medicine is still fully acknowledged. Hence, the shortage of safe and efficient anti-anxiety and stress-protecting medicines for pets is evident. **METHODS:** The released-active anti1bodies to the S100 protein (active pharmaceutical ingredient of Tenoten and Tenoten for children for human use) or placebo were used in a shelter for a 14-days course of a blind placebo-controlled treatment trial on cats (n=16 in each group) and dogs

(n=10 in each group) that experienced high levels of stress. The drug in the specifically designed form of a water-soluble powder for animal use was delivered per os. Clinical and emotional state of the animals was recorded daily using modified RASS (Richmond Agitation Sedation Scale) for dogs and CSS (Cat Stress Scale) for cats. **RESULTS AND DISCUSSION:** The results of the trial showed the statistically significant improvement of the dogs' emotional state beginning from the day 7 of treatment. By the end of the course the difference of RASS scores between the drug and placebo groups reached 30%. Dynamics of the cats' behavior was no less prominent, with significant differences of CSS scores by the day 13 of the study. Both in cats and dogs additional personal grading of each animal's progress was made by the veterinarian based on their interaction with humans and other animals. In both species the percentage of animals with the A grade (improved sociability, lack of tenseness, fear and aggression towards humans) was more common in the groups of the testing drug (30% vs 0% in the placebo group for dogs and 37% vs 25% in the placebo group for cats). Based on the results of the previous preclinical studies and clinical trials in animals a novel drug for veterinary use Anoten has been registered. The experience of the released-active antibodies to the S100 protein usage in human healthcare further supports the promising therapeutic approach for the veterinary behavioral medicine. RASS and CSS used in this study can also be introduced into veterinary clinical routine. **RESEARCH SUPPORT:** All the described studies have been performed under the sponsorship of Research and Production Company "Materia Medica Holding".

INFLUENCE OF SHORT-TERM PHYSICAL EXERCISES ON THE STRENGTH OF VISUAL ILLUSIONS. VA Lyakhovetskii, VJu Karpinskaia, II Shoshina, Pavlov Institute of Physiology RAS, Russian Scientific Center for Radiology and Surgical Technologies, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: The influence of stress or physical tiredness onto the perception of visual illusions is rarely studied leading to contradictory results. The mechanism of influence of such factors can be based on the changes in attentional processes. The physical arousal influences the attentional processes by narrowing of attention to the central components of the task, and the changes in attentional pattern, in turn, may change the illusion's strength. The aim of the present study was to check the dependence of the illusion's strength on the short-term physical exercise, Harvard step test, using as verbal as sensorimotor responses. **METHODS:** The control and experimental groups have a three-stage testing twice, before and after 5-min rest or Harvard step test respectively. These testing consists of measurement of the heart rate with the help of pulsometer, "verbal response" and "sensorimotor response" stages. At "verbal response" stage the participants had to tell on how many percent differs the length of the central shafts of the stimuli. At "sensorimotor response" stage the participant moved his right hand across the touch screen monitor; then the stimulus disappeared and the participant repeated such movements over the empty touch screen. The relative strengths of the illusions and the mean movements speed were calculated. The same 15 stimuli were used at "verbal response" and at "sensorimotor response" stages. At first, we present to participants five neutral stimuli consisting of two shafts without any flanks, then five stimuli eliciting Müller-Lyer illusion (upper shaft looks longer), then five stimuli eliciting classical Ponzo illusion. **RESULTS AND DISCUSSION:** We failed to find the influence of fatigue elicited by short-term physical exercise onto the illusion's strength. The similar results were obtained in (Lybrand et al., 1954) with the help of Müller-Lyer illusion though the physical load of their participants was much higher. We should underline that even the researches of sensory deprivation performed approximately in the one experimental design with the help of the one Müller-Lyer illusion lead to very different results. E.g., Freedman et al. (1961) claimed that the variability of the individual alignments was significantly greater for the control subjects while the mean strength of the illusion stayed unchanged. In contrast, Ueno and Tada (1965) obtained an increase in average magnitude of the illusion, and Suzuki et al. (1965) had received its decrease. **RESEARCH SUPPORT:** This research supported by Russian Humanitarian Scientific Fund 16-36-01008.

DAILY HASSLES, STRESS AND PSYCHOLOGICAL WELL-BEING: GENDER DIFFERENCES. S Savenysheva, St. Petersburg State University, St. Petersburg, Russia

Contemporary studies of psychological stress showed that the high level of perceived stress, accumulation of daily hassles have a strong negative impact on the physical health and well-being. The gender analysis indicated a higher level of both general stress and everyday stress in women. However, gender differences in relationship structure of daily hassles, perceived stress and psychological well-being less studied. **THE AIM** of our study was to investigate and compare level and relations of daily hassles, perceived stress, life event and psychological well-being in women and men. Sample: 190 women and 108 men aged 20-60 years with different marital and educational status lived in Russia. **METHODS:** Questionnaire of everyday hassles, The Life events scale, The Scale of perceived stress-10, The Scales of psychological well-being, Satisfaction with Life Scale. **RESULTS:** A comparative analysis of the level of well-being in men and women revealed no differences in overall

index of psychological well-being and satisfaction with life, but analysis of separate components showed that the level of autonomy and competence is higher in men (p<0,01). A comparative analysis of the level of perceived stress and general indicators of daily hassles demonstrated higher level of perceived stress (p<0,001), intensity (p<0,01) and frequency of daily stressors (p<0,01) in women, especially personal daily stressors (p<0,001) and daily stressors associated with the household (p<0,001).
Regression analysis of the relation between psychological well-being, satisfaction with life and everyday stressors in women has shown that only personal daily hassles predict satisfaction with life (p<0,001), whereas predictors of psychological well-being were daily hassles associated with the household (p<0,01) and relationship with friend and relatives (p<0,05). Regression analysis of the relation between psychological well-being, satisfaction with life and perceived stress in women indicated that it depends both on stress experience (p<0,01) and resistance to stress (p<0,01). Analysis of the relation between psychological well-being, satisfaction with life and overall stress indicators in men didn't reveal any links, only with separate ones. **CONCLUSION:** Results of our study is consistent with previous results about higher level of perceived stress and daily stressors in women compared to men. Our research showed that daily hassles and perceived stress play a key role in psychological well-being, satisfaction with life in women, but not in men. **RESEARCH SUPPORT:** This research was supported by grant of RSF №16-18-10088.

MODERATING ROLE OF SELF-ACCEPTANCE FOR PERCEIVED STRESS AND LOCUS OF CONTROL IN ADULTS. O Strizhitskaya, L Golovey, St. Petersburg State University, St. Petersburg, Russia

Modern life of adults implies a variety of situations that can cause overload allostatic load, daily and overall stress. Stress can be associated with a variety of factors and predictors, including physiological, psychological, social and economic variables. Solid body of psychological research uncovered a significant role of various psychological and subjective factors that can be associated with experiences of stress. The questions for stress mechanisms would be if stress can affect relatively stable psychological characteristics or those stable characteristics determined stress resistance and severity of stress experiences. The aim of the study was to investigate associations between perceived stress (PS) (Perceived stress scale), self-acceptance (SA) (psychological well-being scale) and locus of control (LC) (Rotter's Internal-External Locus of Control Scale). We controlled for education and material satisfaction. We tested 4 alternative models: (1) SA predicts both PS stress and LC that are intercorrelated; (2) SA is affected by both PS and LC that are intercorrelated; (3) LC affects SA that in turn affects PS; (4) PS affects SA that in turn affects LC. These models were based on two major beliefs that stress, LC and SA are affecting each other (models 1 and 2), or there is a pathway between those three characteristics (models 3 and 4). Participants were 336 adults aged 20 – 60 (119 males, 227 females). Correlation analysis showed that PS, LC and SA were correlated. Thus we tried structural analysis to test our models. We added education as an additional variable to fix the models with an objective nonreversible parameter and material satisfaction as it could affect well-being scale (SA). Structural analysis showed that models 1 had good model fit (Chi-square=4.933, df=5, p=.424, RMSEA=.000, PCLOSE=.785) but the association between LC and PS was not significant. Model 2 showed low data fit (Chi-square=11.717, df=5, p=.039, RMSEA=.063, PCLOSE=.268) and the association between LC and PS was not significant. Thus models 1 and 2 were rejected. Model 3 also showed bad model fit (Chi-square=11.808, df=6, p=.066, RMSEA=.054, PCLOSE=.386). Model 4 showed acceptable fit indexes (Chi-square=8.322, df=6, p=.215, RMSEA=.034, PCLOSE=.638). Education and material satisfaction were significant predictors of SA. With material satisfaction excluded significance of the effect for education decreased. Our results add to the field new data on the associations between PS, SA and LC. We showed that stress can affect relatively stable personality characteristics such as SA and LC. These data broadens understanding of psychological component of stress and proves the destructive role of stress for personality. Research was supported by RSF grant 16-18-10088.

EVALUATION OF DENTAL ISSUES IN ADMITTED PATIENTS IN PSYCHIATRIC EMERGENCY: ALBANIAN EXPERIENCE. F Elezi, S Tomori, A Braho, E Sotiri, E Myslymi, Emergency Unit, Psychiatric Service, Neuroscience Pole, Neuropediatry Service, University Hospital Center "Mother Teresa", Tirana, Albania

BACKGROUND: most of people suffering from psychiatric disorders fail to take care for personal hygiene and especially in relation to oral hygiene. For these reasons is very important to help and incourage them for the prevention and ongoing dental monitoring during the follow up. **OBJECTIVE:** assessing and understanding the oral issues that affect psychiatric patients admitted to Psychiatric Emergency Unit in Psychiatric Service of University Center of Tirana "Mother Teresa", during September 2017. Methodology: Are included all patients admitted during the September 2017. The

DMFT index was used for evaluation of dental caries and the CPI index for periodontal evaluation. The statistical analyzes were performed with SPSS (Statistical Package for the Social Sciences), using a descriptive statistics to determine averages, standard deviations and frequencies. Result: patients had contact with dentist very rarely, 45% performed their own oral hygiene and 65% did not use dental floss. Some patients had great problems and needed of restorations of one surface and some of them needed dental prosthesis. Conclusion: in our study most of patients have a high risk of developing oral disorders, however, few carriers visite a dental professional regularly. In addition, the delay to seek treatment and lack of staff training, lead to solutions often crippling. **Key words:** psychiatric disorders; self care; oral hygiene; oral health; professional training; health education

RELATIONS BETWEEN HAIR CORTISOL AND SELF-REPORTED CHRONIC STRESS AND HEALTH IN YOUNG AND AGE WOMEN. OM Razumnikova, AE Ilinykh, AA Yashanina and NV Asanova, Department of Psychology and Pedagogic of Novosibirsk State Technical University, Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia

Understanding mechanisms of illnesses under stress has received considerable research attention, but the relations between biologically measured and self-reported chronic stress are characterized by heterogeneous results. It seems that chronic stress leads to a higher sensitivity for negative experiences and more negative assessment of different health states. Hair cortisol is a stable measure of chronic HPA axis activity that can provide a retrospective biomarker of accumulated stress effect. So, the aim of this pilot study was to investigate associations between concentrations of cortisol in hair and self-assessments of perceived stress, emotional intelligence components, and health status in young and age women. The groups of healthy older (66±4 years, n=13) (OW) and young (22±1 years, n=12) women (YW) were involved in the study. The Russian versions of the Trier Inventory for the Assessment of Chronic Stress (TICS) during the last three months, the Emotional Intelligence trait measures (EI-IPIP), and the 36-Item Health Survey (SF-36) (QoL) were used. The hair samples were collected in order to quantify determine an accumulation of the cortisol using a commercially available immunoassay with chemiluminescence detection in the biochemical laboratory of the University of Dresden (Germany). Mean cortisol level was not significantly differed between OW and YW. Whereas YW compared with OW had higher level of the integral index of physical health but lower score of the social functioning scale of the QoL; higher indices of both EI-IPIP and TICS components. Cortisol concentrations tended to negatively correlate with the QoL scale: role limitations caused by emotional problems, and EI scale: empathic concern in OW. Whereas in YW cortisol concentrations significantly and negatively related with vitality and integral index of mental health ($Rs < -0.61$, $p<0.05$). Moreover, in YW cortisol in hair positively related with integral score of EI and a scale of “social isolation” as TICS component ($0.70<Rs<0.52$, $0.03<p<0.09$). The groups of OW and YW differed with regard to varied patterns of the EI, QoL, and TICS components. YW is characterized by more multitudinous associations between self-reported stress and emotional intelligence, whereas in OW associations were found between stress and health status components. In summary, results of pilot study show that in different age groups cortisol in hair is specifically related with different self-reported stressors and has specific associations with their emotional regulation and quality of life. This research was funded by the Russian Foundation for Basic Research, grant number 17-06-00166.

OBJECTIVE TOTAL SLEEP TIME IS LONGER THAN SUBJECTIVE TOTAL SLEEP TIME IN PATIENTS WITH SLEEP DISORDERS. J-S Lee, Pusan National University Yangsan Hospital, Yangsan, South Korea

INTRODUCTION: It is assumed that there is a discrepancy between subjective and objective total sleep time in patients with sleep disorders. This study aimed to confirm the common belief by assessing the difference between the objective total sleep time (TST) and the subjective TST obtained from nocturnal polysomnography (NPSG) and sleep questionnaires in patients diagnosed with primary insomnia or obstructive sleep apnea syndrome (OSA). **METHODS:** The subjects were 311 consecutive patients who were referred to the sleep clinic and were finally diagnosed with NPSG as primary insomnia or OSA. They were also asked to complete two questionnaires: Pittsburgh Sleep Quality Index (PSQI) including TST of recent 1 month (TST_PSQI) and a Morning Questionnaire administered on the morning right after NPSG about the subjective TST during NPSG (TST_MQ). ANOVA (with post hoc Tukey B test) and Pearson correlation (each with significance level of $p<0.05$) were used for analyses. **RESULTS AND DISCUSSION:** Among the 311 subjects, 77 were diagnosed with primary insomnia (40 males, 37 females, and mean age 55.1+13.1) and 234 were diagnosed with OSA (198 males, 36 females, and mean age 49.0+6.7). In both diagnostic groups, TST_NPSG, TST_PSQI and TST_MQ significantly differed (primary insomnia: 388.6+68.8 min vs. 297.1+101.9 min vs. 272.0+113.0 min, $F=31.3$, $df=2$, $p<0.01$) (OSA: 411.8+56.4 min vs. 374.0+83.3 min vs. 369.0+107.4 min, $F=18.0$, $df=2$, $p<0.01$). Tukey B test revealed that TST_NPSG differed significantly either from TST_PSQI or from TST_MQ in both diagnostic groups ($p<0.05$, respectively). Differences

of TST_NPSG and TST_PSQI between primary insomnia and OSA (91.5±117.3 min vs. 37.8±99.5 min, respectfully) and of TST_NPSG and TST_MQ between primary insomnia and OSA (116.7±117.5 min vs. 43.2±100.1 min, respectfully) were all significant ($t=3.9$, $p<0.01$; $t=5.3$, $p<0.01$, respectfully). Differences between TST_NPSG and TST_PSQI and between TST_NPSG and TST_MQ were positively correlated with PSQI total scores in both diagnostic groups (primary insomnia: $r=0.62$, $p<0.01$ and $r=0.29$, $p<0.01$, respectfully) (OSA: $r=0.42$, $p<0.01$ and $r=0.25$, $p<0.01$, respectfully).
The subjective TST was shorter than the objective TST not only in patients with primary insomnia but also in patients with OSA. The differences were significantly higher in primary insomnia than in OSA, probably reflecting additional psychological factor involved in the pathophysiology of primary insomnia vs. OSA. We also noted that the difference between the objective and the subjective TSTs increases, as the subjective sleep quality measured with PSQI gets poorer. **Key words:** total sleep time, objective, subjective, polysomnography, sleep questionnaire

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

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