COBRAIN Center for Fundamental Brain Research
Yerevan State Medical University named after M. Heratsi
The International Stress and Behavior Society (ISBS)
L.A. Orbeli Institute of Physiology NAS RA
Institute of Molecular Biology NAS RA
Armenian IBRO Association and Armenian Neuroscience Society
School of Science, Xi'an Jiaotong-Liverpool University (XJTLU)

NEUROSCIENCE WEEK 2024
MAY 16-19, 2024

Joint Conference Final Program and Abstract Book

May 16-19, 2024, Yerevan, Armenia

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Joint Conference

NEUROSCIENCE WEEK 2024
MAY 16-19, 2024

Joint conference of COBRAIN Armenia and 30th International Jubilee ISBS "Stress and Behavior" Conference - in partnership with, and support from, Orbeli Institute of Physiology, Institute of Molecular Biology NAS RA (Armenia) and the School of Science of Xi'an Jiaotong-Liverpool University (XJTLU, China)

Conference Program

VENUES:

May 16-18, 2024 – COBRAIN Center, Heratsi Yerevan State Medical University
1 Heratsi Str., Yerevan 0025, Armenia

May 19, 2024 - Orbeli Institute of Physiology of the National Academy of Sciences
22 Orbeli Brothers Str., Yerevan 0028, Armenia

Day 1, May 16, 2024

Venue – Yerevan State Medical University

09.00-17.00 **REGISTRATION**

09.30-10.00 **OPENING AND WELCOMING ADDRESSESS**
AA Muradyan, YSMU Rector
AV Kalueff, ISBS President and Conference Chair
KB Yenkoyan, YSMU Vice-Rector for Science, COBRAIN Center Director and Conference Co-Chair

10.00-10.30 OPENING PLENARY LECTURE – MIKHAIL AGHAJANOV MEMORIAL LECTURE: THE INVOLVEMENT OF BONE MARROW IN MECHANISMS OF NEURONAL SURVIVAL IN ALZHEIMER'S TYPE NEURODEGENERATION. KB Yenkoyan, MI Aghajanov, Neuroscience Laboratory, COBRAIN Center, Department of Biochemistry, Mkhitar Heratsi Yerevan State Medical University, Yerevan, Armenia.

10.30-10.55 ISBS PLENARY LECTURE: INTERSECTING PATHWAYS OF RESILIENCE AND VULNERABILITY: A BIOMARKER APPROACH TO PREDICTING MENTAL HEALTH OUTCOMES. DC Anthony, Department of Pharmacology, University of Oxford, Oxford, UK.

10.55-11.20 COBRAIN PLENARY TALK: GENES UNDERLYING THE MORPHOLOGY OF MATURE NEURONS AND THEIR RELATIONSHIP TO STRESS AND DEPRESSION. J Jaworski, J Zeng, R Pagano, I Majewski, D Komorowski, P Boguszewski, M Urbanska, International Institute of Molecular and Cell Biology, Nencki Institute, Warsaw, Poland; COBRAIN Center, M Heratsi Yerevan Medical State University, Yerevan, Armenia.

11.20-11.50 ISBS PLENARY TALK: DISSOCIATION BETWEEN NEURONAL AND ASTROCYTIC RESPONSE TO LOCOMOTION IN MICE. AV Semyanov, Neuroscience Center, Jiaxing University College of Medicine, Jiaxing, China.

11.50-12.10 **Coffee Break**

12.10-12.35 ISBS PLENARY TALK: UNVEILING THE NEUROBIOLOGICAL BASIS OF ENVIRONMENTAL BURDEN OF DISEASE IN A CONTEXT OF ISOTOPE CONTENT OF DRINKING WATER: INSIGHTS FROM ANIMAL MODELS. T Strekalova, Maastricht University, Maastricht, Netherlands.

12.35-12.55 ISBS TALK: STRESS, EPIGENETICS AND SUICIDES IN ADOLESCENTS (AN EVOLUTIONARY APPROACH). VA Rozanov**,** St. Petersburg State University, VM Bekhterev National Medical Research Center for Psychiatry and Neurology, St. Petersburg, Russia.

12.55-13.20 COBRAIN TALK: PAIN PERCEPTION AT ADULT AGE IS DEPENDENT ON NEONATAL CONDITIONING. BW Kramer, M Daly, Poznan University of Medical Sciences, Poznan, Poland; Irish Neonatal Health Alliance, Wicklow, Ireland.

13.20-13.30 GENERAL DISCUSSION AND CONFERENCE ANNOUNCEMENTS

13.30-14.30 Lunch Break

14.30-16.00 COBRAIN SYMPOSIUM – MIKHAIL AGHAJANOV MEMORIAL SYMPOSIUM (Chairs: KB Yenkoyan, J Jaworski)

14.30-14.40 INTRODUCTION: IN MEMORIAM: PROFESSOR MIKHAIL I. AGHAJANOV (1939-2024)

14.40-14.55 THE INFLUENCE OF ELECTRIC FIELD ON OXIDATIVE STRESS MARKERS IN RATS. HA Harutyunyan, KB Yenkoyan, Neuroscience Laboratory, COBRAIN Center, Heratsi Yerevan State Medical University, Yerevan, Armenia.

14.55-15.10 THE PREVALENCE AND PECULIARITIES OF AUTISM SPECTRUM DISORDER IN URBAN CITIES IN ARMENIA. NZ Khachikyan, SH Mkrtchyan, AA Hayrapetyan, MA Mkhitaryan, A Mkrtchyan, GH Sakanyan, LR Avetisyan, KB Yenkoyan, Department of Hygiene and Ecology, Neuroscience Laboratory, COBRAIN Center, Heratsi Yerevan State Medical University, Yerevan, Armenia.

15.10-15.25 COMPARATIVE STUDY OF PRE- AND POSTNATAL VALPROIC ACID (VPA) MODELS OF AUTISM SPECTRUM DISORDER: IDENTIFYING BRAIN VULNERABILITY TO VPA-EVOKED DEFICITS ACROSS THE TIMELINE. KS Fereshetyan, M Danielyan, KB Yenkoyan, Neuroscience Laboratory, COBRAIN Center, Department of Biochemistry, Heratsi Yerevan State Medical University, Laboratory of Histochemistry and Electromicroscopy, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

15.25-15.40 INCREASING BIOACTIVE LEPTIN LEVELS TO ENHANCE COGNITIVE FUNCTION IN AMYLOID BETA 1-42-INDUCED NEURODEGENERATION. H Harutyunyan, R Minasyan, G Vardanyan, KB Yenkoyan, Neuroscience Laboratory, COBRAIN Center, Department of Biochemistry, Heratsi Yerevan State Medical University, Yerevan, Armenia.

15.40-16.00 IGNITING IDEAS IN NEUROSCIENCE – STUDENTS BLITZ-SESSION

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16.00-16.15 EPIGENETIC REGULATION DISTURBANSES IN MULTIPLE SCLEROSIS AND THEIR RELATIONSHIP WITH CHANGES IN FOLATE METABOLISM. VI Lioudyno, EA Tsymbalova, EA Chernyavskaya, GN Bisaga, IN Abdurasulova, Institute of Experimental Medicine, Almazov National Medical Research Center, St. Petersburg, Russia.

16.15-16.25 Coffee Break

16.25-16.45 PRETERM BIRTH IS STRESS FOR LIFE – BEHAVIORAL PATTERNS IN FORMER PRETERM INFANTS. M Daly, Irish Neonatal Health Alliance, Wicklow, Ireland.

16.45-17.05 UNRAVELLING CORTICAL EXCITABILITY DURING SPIKE AND WAVES AND ITS CONSEQUENCES FOR SEIZURE INTERRUPTION IN A GENETIC EPILEPSY MODEL. G van Luijtelaar, B de Ruiter, Donders Centre for Cognition, Radboud University, Nijmegen, Netherlands.

17.05-17.25 AGE-RELATED FEATURES OF THE FUNCTION OF NEUROENDOCRINE SYSTEMS UNDER CONSTANT LIGHTING. ND Goncharova, AM Ermolaeva, OA Chigarova, TE Oganyan, NV Timoshenko, National Research Centre "Kurchatov institute", Sochi, Russia.

17.25-17.40 CLUSTERING TECHNIQUE TO STUDY NEURAL ACTIVITY IN GENETIC AND NON-GENETIC PATIENTS WITH PARKINSON'S DISEASE. EM Belova, PN Pavlovskiy, UN Semenova, NN Semenov Federal Research Center for Chemical Physics RAS, Moscow, Russia.

17.40-18.00 ISBS ONLINE TALK: PSYCHOSOCIAL RISK ASSESSMENT IN SMALL GROUPS. Ph. Fauquet-Alekhine, JAK Erskine, Group INTRA robotics, France; SEBE-Lab-Behavioural and Psychological Science, St George's University of London, London, UK.

18.00-18.20 ISBS TALK: REGULATED EXOCYTOSIS IN HUMAN GLIOBLASTOMAS. V Parpura, V Montana, International Translational Neuroscience Research Institute, Zhejiang Chinese Medical University, Hangzhou, China.

18.20-18.40 VESICULAR GLUTAMATE RELEASE MODULATION BY PRESENILIN FROM ASTROCYTES. V Montana, V Parpura, International Translational Neuroscience Research Institute, Zhejiang Chinese Medical University, Hangzhou, China.

18.40-19.30 COBRAIN ARMENIA Welcoming Reception

DAY 1 EVENING CITY BUS TOUR (tickets required)
TOUR DEPARTS FROM COBRAIN CENTER MAIN ENTRANCE

Day 2, May 17, 2024

Venue – Yerevan State Medical University

09.00-17.00 REGISTRATION

09.00-09.20. NEUTRAL SPHINGOMYELINASE DETERMINES THE COMORBIDITY TRIAS OF ALCOHOL ABUSE, MAJOR DEPRESSION AND BONE DEFECTS. LS Kalinichenko, Department of Psychiatry and Psychotherapy, University Clinic, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany.

09.20-11.20. SYMPOSIUM 2: NEUROMOLECULAR BASIS OF NORMAL AND PATHOLOGICAL BEHAVIOR (Chair: VN Naumenko)

09.20-09.40 INTERACTIONS OF SEROTONIN RECEPTORS IN THE REGULATION OF BEHAVIOR AND CENTRAL NERVOUS SYSTEM FUNCTION. VS Naumenko, EM Kondaurova, TV Ilchibaeva, AS Tsybko, AYa Rodnyy, Institute of Cytology and Genetics, SB RAS, Novosibirsk, Russia.

09.40-09.55 EFFECT OF PHD INHIBITION ON BIOELECTRICAL NEURAL NETWORK ACTIVITY DURING IN VITRO HYPOXIA MODELING. MV Vedunova, TA Mishchenko, EV Mitroshina, Lobachevsky State University Nizhny Novgorod, Russia.

09.55-10.10 IMPACT OF 5-HT4R ACTIVATION ON CA^{2+} NETWORK ACTIVITY AND INTERCELLULAR SIGNALING IN VITRO. EV Mitroshina, EA Marasanova, MV Vedunova, Lobachevsky State University, Nizhny Novgorod, Russia.

10.10-10.35 THE 5-HT1A RECEPTOR IN BTBR MICE AUTISM. EM Kondaurova, TV Ilchibaeva, AS Tsybko, VS Naumenko, NK Popova, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia.

10.35-10.50 BDNF IS IMPLICATED IN THE MECHANISMS OF AUTISTIC-LIKE BEHAVIOR IN BTBR MICE. AS Tsybko, TV Ilchibaeva, AI Sherbakova, YP Kaminskaya, DV Eremin, VS Naumenko, Institute of Cytology and Genetics SB RAS; Novosibirsk State University, Novosibirsk, Russia.

10.50-11.05 SEROTONIN 5-HT$_4$ RECEPTOR AFFECTS AGGREGATION AND PHOSPHORYLATION OF TAU PROTEIN. TV Ilchibaeva, VS Snisar, NA Shved, VV Kumeiko, VS Naumenko, Institute of Cytology and Genetics SB RAS, Novosibirsk State University, Novosibirsk, Far Eastern Federal University, Vladivostok, Russia.

11.05-11.20 EFFECT OF THE 5-HT7 RECEPTOR GENE OVEREXPRESSION IN THE MIDBRAIN ON BEHAVIOR AND NEUROPLASTICITY IN MICE DURING LONG-TERM ETHANOL CONSUMPTION. DV Bazovkina, AS Oreshko, AYa Rodnyy, VS Naumenko, Federal Research Center Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia.

11.20-11.40 Coffee Break

11.40-13.30 SYMPOSIUM 3: ZUKOVSKA-PASTUKHOV SYMPOSIUM ON TRANSLATIONAL NEUROSCIENCE (Chairs: AV Kalueff, AV Semyanov, IV Ekimova)

11.20-11.40 BEHAVIORAL TESTS OF THE MOUSE VISUAL FUNCTION UNDER OPTOGENETIC THERAPY USING TRANSFORMER MAZE. VI Ni, EV Filatova, IY Morina, ML Firsov, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia.

11.40-12.00 EFFECT OF INTRAVENOUS ADMINISTRATION OF CAFFEINE MODULATED SPLENOCYTES IN THE DEVELOPMENT OF NEUROINFLAMMATORY PROCESSES IN THE MODEL OF LASER-INDUCED TRAUMATIC BRAIN INJURY IN ZEBRAFISH. TG Amstislavskaya, EV Markova, EV Nehoroshev, WS Hao, MA Kleshchev, AA Akopyan, MA Tikhonova, IV Savkin, EV Serenko, AV Kalueff, Novosibirsk State University, Scientific Research Institute of Neurosciences and Medicine, Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia; School of Science, XJTLU, Suzhou, China.

12.00-12.20 ADAPTIVE AND PATHOLOGICAL RESPONSES TO STRESS: REEVALUATING PTSD PATHOPHYSIOLOGY. AP Sarapultsev, MV Komelkova, EY Gusev, South Ural State University, Chelyabinsk, Russia.

12.20-12.40 CHRONIC SLEEP RESTRICTION: CONSEQUENCES FOR THE BRAIN AND ENDOCRINE FUNCTIONS. IV Ekimova, MB Pazi, KV Lapshina, KV Derkach, AO Shpakov, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

12.40-12.55 THE ROLE OF WATER CHANNEL AQP4 IN THE NEUROPROTECTIVE MECHANISMS IN A RAT MODEL OF PARKINSON'S DISEASE. KV Lapshina, MV Khanina, MA Guzeev, MP Kaismanova, IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

13.30-14.30 Lunch Break

14.30-14.50 ISBS TALK: HIPPOCAMPUS AND AMYGDALOID NUCLEI - THE BRAIN STRUCTURES MOST RESISTANT TO VOLUME DECREASE IN PHYSIOLOGICAL AGING: MR VOLUMETRIC STUDY. D Kozic, S Stojanoski, J Boban, University of Novi Sad Faculty of Medicine, Novi Sad, Serbia.

14.50-15.10 ISBS TALK: INNOVATIVE APPROACHES TO NEUROMODULATION AFTER SPINAL CORD INJURY. PE Musienko, Laboratory of Neuroprostheses, St. Petersburg State University, Pavlov Institute of Physiology RAS, St. Petersburg, Neurobiology Department, Sirius University of Science and Technology, Sirius, Neurorehabilitation Technologies Laboratory, LIFT (Life Improvement by Future Technologies) Center, Moscow, Russia.

15.10-17.50 SYMPOSIUM 4: EXECUTIVE FUNCTION IN ONTOGENESIS (Chairs: EI Nikolaeva, KI Kunnikova, Discussant: M Lebedev)

15.10-15.25 THE ROLE OF EXECUTIVE CONTROL IN THE EFFECTIVENESS OF COGNITIVE TRAINING. OM Razumnikova, Novosibirsk State Technical University, Novosibirsk, Russia.

15.25-15.40 THE INFLUENCE OF SCREEN TIME ON THE QUALITY OF EXECUTIVE FUNCTIONS OF PRESCHOOL CHILDREN. Nikolaeva EI, Kalabina IA, Sutormina NV, Isachenkova MV, Herzen State Pedagogical University, St. Petersburg, Russia.

15.40-15.55 FORMATION OF EXECUTIVE FUNCTIONS IN CHILDREN WITH EXPERIENCE OF INSTITUTIONALIZATION. E Dydenkova, G Portnova, K Minin, Nizhny Novgorod State Pedagogical University, Nizhny Novgorod, Institute of Higher Nervous Activity and Neurophysiology, Moscow, Russia.

15.55-16.10 THE SPECIFICS OF EXECUTIVE FUCTIONS IN YONGER CHILDREN WITH INTELLECTUALL DISABILITIES. E Dunaevskaya, Herzen State Pedagogical University of Russia, St. Petersburg, Russia.

16.10-16.25 PSYCHOPHYSIOLOGICAL FACTORS OF RESISTANCE TO SUBSTANCE DEPENDENCE. P Ivashina, Herzen State Pedagogical University of Russia, St. Petersburg, Russia.

16.25-16.40 PRECURSORS OF FEATURES OF COGNITIVE DEVELOPMENT OF PREMATURE CHILDREN IN PRESCHOOL AGE. OA Ivanova, Voronezh State University, Voronezh, Russia.

16.40-17.00 Coffee Break

17.00-17.15 PSYCHOPHYSIOLOGICAL MECHANISMS OF COGNITIVE DEVELOPMENT IN CHILDREN WITH ARTERIAL ISCHEMIC STROKE: RESEARCH DESIGN. KI Kunnikova, Ural Federal University, Ekaterinburg, Russia.

17.15-17.35 RELATIONSHIP OF ONLINE INFORMATION SEARCH AND EXECUTIVE FUNCTIONS IN CHILDREN. N Sutormina, Herzen State Pedagogical University of Russia, St. Petersburg, Russia.

17.35-17.50 A COMPARATIVE ANALYSIS OF CORRELATION BETWEEN THE DEVELOPMENT OF EXECUTIVE FUNCTIONS AND INTERNAL HEALTH IN PRIMARY SCHOOLCHILDREN AND ADOLESCENTS. VS Merenkova, SA Burkova, Bunin Yelets State University, Yelets, Herzen State Pedagogical University of Russia, St. Petersburg, Russia.

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17.50-18.10 ISBS TALK: DYSFUNCTION OF THE HIPPOCAMPAL ASTROCYTES OF KRUSHINSKY-MOLODKINA RATS DURING EPILEPSY DEVELOPMENT. MV Glazova, YS Grigorieva, AA Naumova, SD Nikolaeva, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

18.10-19.00 COBRAIN GLOBAL EDUCATIONAL INITIATIVE: ROUND TABLE ON CAREERS IN NEUROSCIENCES. Moderator: M Movsisyan, Discussants: KB Yenkoyan, TV Strekalova, J Jaworski, AV Kalueff, AV Semyanov, TG Amstislavskaya.

19.00-20.00 COBRAIN YOUNG SCIENTIST PROJECT EXPERT REVIEW PANEL MEETING. Moderator: M Movsisyan.

18.10-20.30 MODERATED POSTER SESSION 1

THE ROLE OF TRANSCRIPTION FACTOR NEUROD1 IN MOUSE CORTICOGENESIS. MS Gavrish, AD Okhalnikov, AO Motorina, VS Tarabykin, Research Institute of Neurosciences, Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia; Institute of Cell Biology and Neurobiology, Charité Medical University, Berlin, Germany.

BEHAVIORAL CHARACTERISTICS OF DIFFERENT LINES OF ZEBRAFISH. DS Galstyan, TO Kolesnikova, AN Ikrin, AM Moskalenko, AV Kalueff. Institute of Translational Biomedicine, St. Petersburg State University, Institute of Experimental Medicine, Almazov National Medical Research Centre, St. Petersburg, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

ANXIETY AND DEPRESSION-LIKE BEHAVIOR OF ZEBRAFISH IN A MODEL OF UNPREDICTABLE CHRONIC STRESS. MM Kotova, SV Amikishiev, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

INVESTIGATION OF THE EFFECT OF DRUGS ON ZEBRAFISH BEHAVIORAL PATTERNS USING MACHINE LEARNING. DA Lukovikov, TO Kolesnikova, AA Korotaev, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, St. Petersburg State University, Almazov National Medical Research Centre, St. Petersburg, Russia; School of Science, XJTLU, Suzhou, China.

EXTRACT OF *AMANITA MUSCARIA* INDUCES ANXIETY-LIKE BEHAVIOR IN ZEBRAFISH. AE Makhortykh, VD Riga, NO Prokhorenko, TO Kolesnikova, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

USING EEG BIOMARKERS FOR PHENOTYPING SOCIAL DEFICITS IN RATS. VD Riga, AA Rebik, IS Midzyanovskaya, Sirius University of Science and Technology, Sirius Federal Territory, Institute of Higher Nervous Activity and Neurophysiology RAS, Moscow, Russia.

CRISPR/CAS9 MEDIATED INACTIVATION OF THE KCNQ3 GENE CAUSES MALFORMATION OF THE CORPUS CALLOSUM. AA Babaev, MS Gavrish, SA Tutukova, AD Okhalnikov, VS Tarabykin, Research Institute of Neurosciences, Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia; Institute of Cell Biology and Neurobiology, Charité Medical University, Berlin, Germany.

BEHAVIORAL CONSEQUENCES OF GENETICALLY DETERMINED DYSFUNCTION OF STRIATAL-ENRICHED PROTEIN TYROSINE PHOSPHATASE STEP IN MICE. VS Moskaliuk, PD Komleva, NV Khotskin, DV Bazovkina, EA Kulikova, Institute of cytology and genetics SB RAS, Novosibirsk, Russia.

ACUTE AND CHRONIC EFFECTS OF GBR 12909, FLUOXETINE AND THEIR COMBINATION ON ADULT ZEBRAFISH (*DANIO RERIO*). AN Ikrin, AM Moskalenko, AD Shevlyakov, SV Amikishiev, TO Kolesnikova, DS Galstyan, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia; School of Science, XJTLU, Suzhou, China.

A NEW SENSOR FOR NON-INVASIVE ASSESSMENT OF STRESSOR CONDITIONS OF THE ORGANISM. LG Simonyan, GG Karamyan, AM Manukyan, VR Sargsyan, HL Kostanyan, LH Misakyan, RSh Sargsyan, Laboratory of Integrative Biology, LA Orbeli Institute of Physiology NAS RA, Armenia.

THE ROLE OF EVOLUTIONARY NEW ENHANCERS ON NEOCORTEX DEVELOPMENT. AO Kustova, A Newman, JCC Suescún, VS Tarabykin, Research Institute of Neurosciences, Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia; Institute of Cell Biology and Neurobiology, Charité Hospital, Berlin, Germany.

THE CHEMOGENETIC MODULATION OF DAT-KO RATS BEHAVIOR IN HEBB-WILLIAMS MAZE. AA Gromova, TS Shemyakova, AD Belskaya, NP Kurzina, RR Gainetdinov, AB Volnona, Institute of Translational Biomedicine, St. Petersburg State University Faculty of Biology and University Hospital, St. Petersburg, Russia.

ASSESSMENT OF AGE-RELATED BEHAVIORAL EFFECTS OF CHRONIC STRESS IN LABORATORY RATS *(RATTUS NORVEGICUS)*. TO Kolesnikova, AM Moskalenko, AN Ikrin, NO Prokhorenko, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia; School of Science, XJTLU, Suzhou, China.

EFFECTS OF LOW-DOSE 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN EXPOSURE ON THE DEVELOPMENT OF RAT OFFSPRING. KV Pakhomov, DS Vasilev, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

PERSEVERATION IN ADHD SYNDROME: MODEL EXPERIMENTS ON DOPAMINE KNOCKOUT RATS. AB Volnona, AD Belskaya, AA Gromova, RR Gainetdinov, NP Kurzina, Institute of Translational Biomedicine, St. Petersburg State University Faculty of Biology and University Hospital, St. Petersburg, Russia.

EMOTIONAL-PAINFUL STRESS IN RATS WITH CONTRAST EXCITABILITY AFFECTS THE CELL GENOME STABILITY OF CENTRAL NERVOUS SYSTEM DIFFERENTLY. VD Shcherbinina, MB Pavlova, NA Dyuzhikova, EV Daev, Pavlov Institute of Physiology RAS, St. Petersburg State University, Saint Petersburg, Russia.

ACUTE BEHAVIORAL EFFECTS OF RACLOPRIDE, A SELECTIVE D2 ANTAGONIST ON ADULT ZEBRAFISH. KV Apukhtin, VS Nikitin, AV Kalueff, Sirius University of Science and Technology, Russia.

THE EFFECTS OF NEUROLIPINS ON LIPOPOLYSACCHARIDE-INDUCED NEUROINFLAMMATION IN VITRO. KA Arsentiev, SP Konovalova, MYu Bobrov, VV Bezuglov, PE Musienko, Sirius University of Science and Technology, Sirius, Russia.

RELATIONSHIP BETWEEN SPEECH AND READING IN CHILDREN WHO SURVIVED POSTERIOR FOSSA TUMORS. S Mironets, M Shurupova, A Karelin, Neurocognitive Laboratory, Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, RAE Data Center, Federal Center of Brain and Neurotechnologies, Moscow, Russia.

MOUSE REPEATED AGRESSION PARADIGM: DEPRIVATION FROM FIGHTING RESULTS IN HIGHTENED ANXIETY AND AGRESSION IN MALE CD1 MICE. AS Mutovina, KA Ayriyants, AA Sapronova, PE Kisaretova, NP Bondar, Novosibirsk State University, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia.

INTENSITY DEPENDENCE OF AUDITORY-EVOKED POTENTIALS AS AN INDICATOR OF DEPRESSION SYMPTOMS SEVERITY. S Prasad, DG Mitiureva, OV Sysoeva, Institute of Higher Nervous Activity and Neurophysiology RAS, National Research University Higher School of Economics, Moscow, Russia.

MODELING OF PTSD IN SEXUALLY MATURE MALE RATS BORN TO MOTHERS STRESSED DURING PREGNANSY CAUSES MEMORY IMPAIRMENT AND HORMONAL DYSFUNCTION OF THEIR OFFSPRING. ED Shigalugova, GI Kholova, NE Ordyan, Pavlov Institute of Physiology RAS, St. Petersburg, Russia.

EEG FACE ODDBALL PARADIGM AS THE TEST FOR EMOTIONAL REACTION. A Popyvanova, E Pomelova, D Bredikhin, M Koriakina, AN Shestakova, E Blagovechtchenski, Centre for Cognition and Decision Making, Institute for Cognitive Neuroscience, HSE University, Moscow, Russia.

ANTIMICROBIAL, ANTIPROLIFERATIVE, AND POTENTIAL ANTISEIZURE PROPERTIES OF *ARTEMISIA VULGARIS* AND *ARTEMISIA GLAUCA* FROM KAZAKHSTAN. O Karapina, A Trofimov, B Sailike, Y Yermagambetov, G Mamytbekova, D Birimzhanova, Y Suleimen, B Akbay, T Tokay, Nazarbayev University, Kazakh University of Technology and Business, Astana, Kazakhstan.

PECULIARITIES OF DEVELOPMENT IN CHILDREN WITH MOTOR DISORDERS: THE EEG ASPECT. MM Koriakina, DO Bredikhin, OE Agranovich, AN Shestakova, ED Blagoveshchensky, National Research University HSE, Moscow, Turner Scientific Research Institute for Children's Orthopedics, St Petersburg, Russia.

C.R.A.B.: THE PARADIGM TO STUDY READINESS POTENTIAL. E Pomelova, D Bredikhin, A Popyvanova, K Bartseva, A Kuznetsova, A Kirsanov, M Koriakina, E Blagovechtchenski, Centre for Cognition and Decision Making, Institute for Cognitive Neuroscience, HSE University, Moscow, Laboratory of Behavioural Neurodynamics, St. Petersburg State University, St. Petersburg, Russia.

FACILITATORY EFFECTS OF COLD PRESSOR TASK ON CORTICOSPINAL EXCITABILITY: A PILOT STUDY. KV Bartseva, UR Nikishina, MM Koriakina, MU Lukov, AS Kirsanov, DA Fomicheva, DA Andreeva, EA Levchenko, AS Dasaeva, ED Blagovechtchenski, St. Petersburg State University, St Petersburg, HSE University, Moscow, Russia.

mTOR, AUTOPHAGY AND SIRT-1 IN BRAIN DURING PRENATAL HYPERHOMOCYSTEINEMIA. AV Mikhel, IV Zalozniaia, AD Shcherbitskaia, SK Bochkovskii, YP Milyutina, DS Vasilev, AV Arutjunyan, Ott Research Institute of Obstetrics, Gynecology and Reproductive Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

STRESS AND ELECTRICAL INJURIES IN LARGE FARM ANIMALS. NS Orlyansky, ON Eremenko, Trubilin Kuban State Agrarian University, Krasnodar, Russia.

DYNAMICS OF BRAIN ELECTRICAL ACTIVITY DURING PROLONGED AUDIOVISUAL STIMULATION. NE Tadevosyan, BB Forghan, AA Tumanian, LV Vahradyan, AS Khachunts, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

EVALUATION OF SIMPLE VISUAL-MOTOR REACTION TIME IN DIFFERENT AGE GROUPS DURING MENTAL LOAD. AA Tumanian, AS Khachunts, AR Sargsyan, NE Tadevosyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

COMPARATIVE STUDY PARAMETERS OF HEART RATE VARIABILITY AND OF PSYCHOLOGICAL STATE OF THE ARTSAKH WAR PARTICIPANTS. AA Sahakyan, HG Galstyan, AV Sargsyan, LV Vahradyan, NE Tadevosyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

STUDY OF THE QUALITY OF LIFE AND ANXIETY OF THE POPULATION OF ARTSAKH IN THE POST-WAR PERIOD USING THE SF-36 QUESTIONNAIRE. HG Galstyan, AA Tumanian, GH Sakanyan, MA Mardiyan, LA Orbeli Institute of Physiology NAS RA, M Heratsi Yerevan State Medical University, Yerevan, Armenia.

APPLICATION OF THE "WHO SHORT QUESTIONNAIRE" METHOD IN THE ANALYSIS OF HEALTH-RELATED QUALITY OF LIFE IN INDIVIDUALS DURING POST-WAR TIME ON THE EXAMPLE OF THE POPULATION OF ARTSAKH. AV Sargsyan, AA Sahakyan, NE Tadevosyan, HG Galstyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

REFINEMENT OF DECELLULARIZED GRAFTS FOR PERIPHERAL NERVE TISSUE ENGINEERING. VS Grigoryan, GP Sevoyan, SS Gasparyan, PV AnjanKumar, SV Karapetyan, ZI Karabekian, LA Orbeli Institute of Physiology NAS RA, University of Traditional Medicine, M Heratsi Yerevan State Medical University, Yerevan, Armenia; George Washington University, Washington DC, USA.

USING TEMPORAL EEG SIGNAL DECOMPOSITION TO IDENTIFY NEUROPHYSIOLOGICAL MARKERS AMONG STROKE PATIENTS. DG Muhammad, N Syrov, A Medvedeva, Y Alieva, L Yakovlev, D. Petrova, GE Ivanova, AY Kaplan, MA Lebedev, Vladimir Zelman Center for Neurobiology and Brain Rehabilitation, Skolkovo Institute of Science and Technology, Federal Center of Brain Research and Neurotechnologies, FMBA, Laboratory for Neurophysiology and Neuro-Computer interfaces, Faculty of Biology, Faculty of Mechanics and Mathematics, Lomonosov Moscow State University, Moscow, Russia.

NEURAL CORRELATES OF INDIVIDUAL DIFFERENCES IN TIME PERCEPTION. DG Mitiureva, OV Sysoeva, Institute of Higher Nervous Activity and Neurophysiology of RAS, Moscow, Russia.

MOTOR LEARNING AND BELIEF UPDATING IN BIPOLAR DISORDER. M Ivanova, K Germanova, G Kopytin, A Ragymova, D Petelin, M Herrojo Ruiz, National Research University Higher School of

Economics (HSE), First Moscow State Medical University, Moscow, Russia; Goldsmiths, University of London, London, UK.

THE VULNERABILITY OF DOPAMINERGIC NEURONS IN MICE WITH CONDITIONAL INACTIVATION OF THE ALPHA-SYNUCLEIN GENE AND CONSTITUTION BETA-SYNUCLEIN KNOCK-OUT. R Karpov, A Krayushkina, O Morozova, T Ivanova, E Lysikova, K Chaprov, Institute of Physiologically Active Compounds at Federal Research Center of Problems of Chemical Physics and Medicinal Chemistry RAS, Chernogolovka, Russia.

EFFECTS OF AGING ON THE DEVELOPMENT OF EPILEPSY IN THE KRUSHINSKY-MOLODKINA (KM) RATS. EP Aleksandrova, AA Kulikov, AP Ivlev, EV Chernigovskaya, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

ALTERATIONS IN SELF-GROOMING MICROSTRUCTURE AND EXPLORATION-RELATED BEHAVIOR IN TPH2-KO MICE. NA Krotova, IS Zhukov, PD Shabanov, N Alenina, AV Kalueff, KA Demin, RR Gainetdinov, Institute of Translational Biomedicine, St. Petersburg University Hospital, St. Petersburg State University, Institute of Experimental Medicine, Almazov National Medical Research Centre, St. Petersburg, Higher School of Economics, Moscow, Neurobiology Program, Sirius University of Science and Technology, Sirius, Russia; Cardiovascular and Metabolic Diseases, Max-Delbrück-Center for Molecular Medicine (MDC), Berlin, Germany.

THE FUNCTIONAL STATE OF ASTROGLIA IN THE HIPPOCAMPUS OF NORMAL AND EPILEPTIC RATS: ANALYSIS OF GENETICALLY DETERMINED DIFFERENCES AND THE EFFECT OF PIRACETAM. AA Naumova, YS Grigorieva, SD Nikolaeva, KA Ivanova, MV Glazova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

EARLY SIGNS OF AUTISM SPECTRUM DISORDER. O Frolovskaia, Herzen State Pedagogical University of Russia, St. Petersburg, Russia.

MOUSE MODELS OF NEURODEGENERATIVE DISEASES. EI Leonova, II Akhmarov, OA Kirillov, AV Chirinskaite, JV Sopova, Center of Transgenesis and Genome Editing, St. Petersburg State University, St. Petersburg, Russia.

Day 3, May 18, 2024

Venue – Yerevan State Medical University

09.00-17.00 REGISTRATION

09.30-09.45 ISBS TALK: A LONG HISTORY OF ISBS CONFERENCES – PROMOTING TRANSLATIONAL NEUROSCIENCE STRESS RESEARCH AND EDUCATION. AV Kalueff, ISBS Office, New Orleans, USA; School of Science, XJTLU, Suzhou, China.

09.45-10.00 ISBS TALK: INDUCTION OF INFLAMMATION IN EARLY POSTNATAL PERIOD: EFFECT ON ACTIVATION OF ASTROCYTES AND MICROGLIA IN BTBR MALE MICE. MM Kolesnikova, Novosibirsk State University, Novosibirsk, Russia.

10.00-11.30 SYMPOSIUM 5: ZEBRAFISH NEUROSCIENCE SYMPOSIUM (Chair: TG Amstislavskaya)

10.00-10.15 ACUTE AND CHRONIC EFFECTS OF NITROGLYCERIN IN ADULT ZEBRAFISH (*DANIO RERIO*). TO Kolesnikova, AN Ikrin, AM Moskalenko, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

10.15-10.30 COMPARATIVE STUDY OF THREE NAVIGATION STRATEGY OF ZEBRAFISH IN THE TRANSFORMER MAZE. EV Filatova, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia.

10.30-10.45 INTRANASAL METHOD OF DRUG DELIVERY IN ADULT ZEBRAFISH USING NICOTINE TARTRATE. DS Galstyan, TO Kolesnikova, AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Institute of Experimental Medicine, Almazov National Medical Research Centre, Sirius University of Science and Technology, Sirius Federal Territory, Russia; School of Science, XJTLU, Suzhou, China.

10.45-11.00 BIOCHEMICAL AND BEHAVIORAL EFFECTS OF PREDNISOLONE IN ADULT ZEBRAFISH. EV Nikiforova, AV Zhdanov, SL Khatsko, AV Kalueff, Ural Federal University, Yekaterinburg, Russia; School of Science, XJTLU, Suzhou, China.

11.00-11.15 LOCOMOTION ACTIVITY OF THE ZEBRAFISH *DANIO RERIO* REGISTERED BY SFCO HYDROPHONE. AS Khachunts, SG Gevorgyan, AA Tumanian, AR Sargsyan, NE Tadevosyan, GS Gevorgyan, LA Orbeli Institute of Physiology NAS RA, Yerevan State University, Yerevan, Armenia.

11.15-11.30 ISRIB-INDUCED BRAIN TRANSCRIPTOMIC AND BEHAVIORAL EFFECTS IN TRAUMATIC BRAIN INJURY-EXPOSED AND CONTROL ZEBRAFISH. NP Ilyin, AD Shevlyakov, GA Boyko, AM Moskalenko, AN Ikrin, DS Galstyan, TO Kolesnikova, NV Katolikova, SA Chekrygin, AV Kalueff, KA Demin, Almazov National Medical Research Centre, Institute of Translational Biomedicine, Core facility "Center Bio-Bank", St. Petersburg State University, St. Petersburg, Neurobiology Program, Sirius University of Science and Technology, Sirius, Scientific Research Institute of Neurosciences and Medicine, Novosibirsk, Russia; School of Science, XJTLU, Suzhou, China.

11.30-11.50 Coffee Break

11.50-13.50 ISBS SYMPOSIUM 6: LAPIN BIOLOGICAL PSYCHIATRY SYMPOSIUM (Chair: A Kalueff)

11.50-11.55 GENERAL INTRODUCTION

11.55-12.10 WHAT ARE THE EXPERIENCES AND CONSEQUENCES OF STRESS DUE TO EMOTIONAL ABUSE ON MARRIED WOMEN? HN Shilubane, R Mulaudzi, ET Nkhwashu, University of Venda, Thohoyandou, South Africa.

12.10-12.25 THE ORBITOFRONTAL CORTEX DETERMINES THE SPECIFICITY OF MODEL-BASED LEARNING. KM Costa, R Scholz, K Lloyd, P Moreno-Castilla, MPH Gardner, P Dayan, G Schoenbaum, National Institute on Drug Abuse Intramural Research Program, National Institute on Aging Intramural Research Program, Baltimore; University of Alabama at Birmingham, Birmingham, USA; Max Planck Institute for Biological Cybernetics, Tübingen, Germany; Concordia University, Montreal, Quebec, Canada.

12.25-12.40 CAREGIVER BURDEN AND FAMILY SUPPORT ON CLINICAL RECOVERY IN PATIENTS WITH SCHIZOPHRENIA: A LONGITUDINAL STUDY. A Caqueo-Urízar, Universidad de Tarapacá, Arica, Chile.

12.40-12.55 VOLUNTARY PHYSICAL ACTIVITY DECREASES DEPRESSION-LIKE SYMPTOMS VIA INTERLEUKINE-1β RECEPTORS IN STRESSED MICE. Z Sudani, HA Mahdirejei, Ali-Akbar Salari, Salari Institute of Cognitive and Behavioral Disorders (SICBD), Karaj, Alborz, Iran.

12.55-13.10 EFFECT OF PRENATAL HYPERHOMOCYSTEINEMIA ON THE STRUCTURE AND FUNCTIONING OF THE CIRCULAR SYSTEM OF THE RAT PLACENTA. DS Vasilev, NL Tumanova, AN Kadenov, AV Mikhel, IV Zalozniaia, YP Milyutina, AV Arutjunyan, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Ott Research Institute of Obstetrics, Gynecology and Reproductive Medicine, St. Petersburg, Russia.

13.10-13.25 DYNAMIC CHANGES IN NEUROVASCULAR CONNECTIVITY IN PATIENTS WITH CHRONIC CEREBRAL CIRCULATORY DISORDERS: A STUDY OF RESTING-STATE FMRI AND CEREBRAL PERFUSION. VD Abramova, International Tomography Center SB RAS, Novosibirsk State University, Novosibirsk, Russia.

13.25-13.40 NEW TRANSCRIPTOMIC BRAIN PATTERNS FOR AUTISM SPECTRUM DISORDERS PATIENTS. AD Shevlyakov, AN Ikrin, TO Kolesnikova, LG Danilov, KA Demin, AV Kalueff, Sirius University of Science and Technology, Sochi, St. Petersburg State University, Almazov National Medical Research Centre, St. Petersburg, Russia; School of Science, XJTLU, Suzhou, China.

13.40-13.55 EEG ASSOCIATION WITH BLOOD INDICES IN HEALTHY AGING. I Mikheev, I Polikanova, O Martynova, School of Psychology, HSE University, Federal Scientific Center for Psychological and Interdisciplinary Research, Institute of Higher Nervous Activity and Neurophysiology RAS, Moscow, Russia.

13.55-15.00 Lunch Break

15.00-16.20 MOLECULAR NEUROSCIENCE SYMPOSIUM OF THE INSTITUTE OF MOLECULAR BIOLOGY NAS RA (Chair: AA Arekelyan)

15.00-15.30 TEMPORAL CHANGES OF GENE EXPRESSION IN HEALTH AND MENTAL DISORDERS. AA Arakelyan, S Avagyan, A Kurnosov, T Mkrtchyan, G Mkrtchyan, R Zakharyan, KR Mayilyan, H Binder, Institute of Molecular Biology NAS RA, Armenian Bioinformatics Institute, Yerevan, Armenia; Interdisciplinary Center for Bioinformatics, Leipzig University, Leipzig, Germany.

15.30-15.50 CAVITY CONSTRICTION OF KCNQ CHANNELS IMPEDES K+ CONDUCTION. V Vardanyan, Institute of Molecular Biology NAS RA, Yerevan, Armenia.

15.50-16.20 THE COMPLEMENT SYSTEM: A CNS AND IMMUNITY WAYPOINT IN THE PATHOGENESIS OF PSYCHIATRIC ILLNESSES. KR Mayilyan, AF Soghoyan, RB Sim, Institute of Molecular Biology NAS RA, Yerevan, Armenia; MRC Immunochemistry Unit, Department of Biochemistry, Oxford University, Oxford, UK; Department of Therapeutics, Faculty of General Medicine, University of Traditional Medicine, Department of Psychiatry, Yerevan State Medical University, Health Ministry of Armenia, Psychosocial Recovery Center, Yerevan, Armenia.

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16.20-16.40 ISBS TALK: PROSPECTS FOR PREVENTION OF POST-STRESS DISORDERS BASED ON RESTORING THE INTEGRITY OF THE INTESTINAL BARRIER. IN Abdurasulova, AV Matsulevich, VA Nikitina, NN Matsulevich, NM Grefner, Institute of Experimental Medicine, St. Petersburg, Russia.

16.40-17.00 ISBS PLENARY LECTURE: ZEBRAFISH MODELS OF COMPLEX BRAIN DISORDERS. AV Kaluev, AD Volgin, Department of Biological Sciences, Suzhou Key Laboratory of Neurobiology and Cell Signaling, School of Science, Xi'an Jiaotong-Liverpool University, Suzhou, China; International Zebrafish Neuroscience Research Consortium (ZNRC), Global HQ, Slidell, USA.

17.00-17.20 Coffee Break

17.20-17.35 COGNITIVE FUNCTIONING, PSYCHOLOGICAL WELL-BEING, AND PROFESSIONAL MOTIVATION IN OLDER ACADEMIC WORKERS. EN Romanova, PA Manukyan, Research Institute for Brain Development and Peak Performance, RUDN, Moscow, Russia.

17.35-17.50 EFFECTS OF DYNAMIC ENVIRONMENTAL STRUCTURE ON HUMAN SPATIAL NAVIGATION IN A VIRTUAL MAZE. PA Manukyan, VV Tolchennikova, EN Romanova, Research Institute for Brain Development and Peak Performance, RUDN University, Biological Faculty, Lomonosov Moscow State University, Moscow, Russia.

17.50-18.05 IMMUNE FUNCTION, GUT ULTRASTRUCTURE, AND MICROBIOTA COMPOSITION MODULATION BY *ENTEROCOCCUS FAECIUM* L-3 ADMINISTRATION REDUCES DISEASE SEVERITY IN EAE MODEL IN RATS. AN Trofimov, EA Tarasova, AV Matsulevich, NM Grefner, MK Serebryakova, IV Kudryavtsev, EI Ermolenko, IN Abdurasulova, Institute of Experimental Medicine, St. Petersburg, Russia.

18.05-19.00 COBRAIN GLOBAL EDUCATIONAL INITIATIVE: SESSION FOR YOUNG SCIENTISTS – KEYS TO SUCCESS. Moderators: M Movsisyan, KB Yenkoyan

Day 4, May 19, 2024

Venue – LA Orbeli Institute of Physiology NAS RA

09.00-17.00 **REGISTRATION**

09.30-09.40 **OPENING AND WELCOMING ADDRESSESS**
NM Ayvazyan, Institute of Physiology Director and Conference Co-Chair
AV Kalueff, ISBS President and Conference Chair

09.40-10.00 ISBS TALK: NEUROBIOLOGY AND THERAPEUTIC UTILITY OF NATURAL NEUROTOXINS TARGETING PRE- AND POSTSYNAPTIC MECHANISMS OF NEUROMUSCULAR TRANSMISSION. NM Ayvazyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

10.00-14.15 **ORBELI SYMPOSIUM ON PHYSIOLOGY** (Chairs: NM Ayvazyan, LM Firsov)

10.00-10.15 CORRELATION OF SYNAPTIC PROCESSES IN THE PERIAQUEDUCTAL GRAY MATTER OF THE BRAIN IN A MODEL OF PARKINSON'S DISEASE WITH HYDROCORTISONE PROTECTION. MV Poghosyan, ME Hovsepyan, MH Danielyan, AL Minasian, HY Stepanyan, KV Karapetyan, RSh Sargsyan, JS Sarkissian, LA Orbeli Institute of Physiology NAS RA, M Heratsi Yerevan State Medical University, University of Traditional Medicine, Yerevan, Armenia.

10.15-10.30 DIABETIC STRESS AND SPINAL CORD INJURY: BEHAVIORAL, MORPHOLOGICAL, AND ELECTROPHYSIOLOGICAL CORRELATES. KV Simonyan, MH Danielyan, AS Isoyan, RA Avetisyan, LG Avetisyan, KA Nebogova, VA Chavushyan, Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

10.30-10.45 CHANGES IN CENTRAL BLOOD FLOW UNDER THE INFLUENCE OF SPELEOCLIMATE AND RHEOGRAM PARAMETERS. VA Semiletova, Department of Normal Physiology, Voronezh State Medical University, Voronezh, Russia.

10.45-11.00 THE NEUROIMMUNE-INFLAMMATORY MODEL OF CHRONIC STRESS, DISTRESS, AND DEPRESSION. MV Komelkova, AP Sarapultsev, EY Gusev, South Ural State University, Chelyabinsk, Russia.

11.00-11.15. PSYCHONEUROIMMUNOMODULATORY EFFECTS OF IMMUNE CELLS IN DEPRESSION-LIKE STATE. EV Markova, MA Knyazheva. Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia.

11.15-11.30 A SPIKE IS A SPIKE: ON THE UNIVERSALITY OF ITS FREQUENCY CHARACTERISTICS IN FIVE EPILEPSY MODELS. A Sargsyan, PM Casillas-Espinosa, D Melkonian, TJ O'Brien, G van Luijtelaar, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia; Department of Neuroscience, Central Clinical School, Monash University, Melbourne, Victoria,

Kaoskey Pty Ltd, Sydney, New South Wales, Australia; Donders Centre for Cognition, Radboud University, Nijmegen, Netherlands.

11.30-11.45 EMOTIONAL ABNORMALITIES AS EARLY BEHAVIORAL SYMPTOMS OF ALZHEIMER'S DISEASE IN APP/PS1 MUTANT MICE TO CORRELATE WITH PLAQUE FORMATION. K Sitdikova, A Gorlova, S Morozov, Z Nefedova, K Chaprov, T Strekalova, Institute of General Pathology and Pathophysiology, Sechenov First Moscow State Medical University, Moscow, Institute of Physiologically Active Compounds RAS, Chernogolovka, Belgorod State National Research University, Belgorod, Russia.

11.45-12.15 Coffee Break

12.15-12.30 THE EFFECTS OF COMPETITIVE STRESS ON THE COMPONENTS OF EVENT RELATED POTENTIALS DURING JOINT VERBAL PROBLEM SOLVING. NV Shemyakina, ZhV Nagornova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia.

12.30-12.45 MOTOR EVOKED POTENTIALS CHANGE UNDER CONDITIONS OF VARIOUS DOPAMINERGIC CONTROL IN THE DAT-KO RAT MODEL. DS Kalinina, OV Gorsky, RR Gainetdinov, PE Musienko, Department of Neuroscience, Sirius University of Science and Technology, Sirius, Institute of Translational Biomedicine, St. Petersburg State University, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Pavlov Institute of Physiology RAS, St. Petersburg, Life Improvement by Future Technologies Center "LIFT", Moscow, Russia.

12.45-13.00 ISBS ONLINE TALK. AN INTERDISCIPLINARY BIOLOGICAL MODEL OF PSYCHOPHARMAPHYSIOLOGICAL FUNCTION QUANTITATIVELY VISUALIZED BY MOLECULAR AND BODY TEMPERATURE INDICATORS IN THE ELDERLY. M Koshiba, Yamaguchi University, Yamaguchi, Tohoku University, Tohoku, Saitama Medical University, Saitama, Japan.

13.00-13.15 ANALYSIS OF THE EEG RHYTHMS POWER DURING VIEWING AN EMOTIONAL VIDEO AS A BIOMARKER OF A PERSON'S PSYCHO-EMOTIONAL STATE. ED Blagovechtchenski, MM Koriakina, KV Bartseva, UR Nikishina, MU Lukov, DA Fomicheva, VV Moiseeva, AN Shestakova, National Research University HSE, Moscow, St Petersburg State University, St Petersburg, Yaroslav-the-Wise Novgorod State University, Novgorod, Russia.

13.15-13.30 CONTINUOUS MEASURMENT OF ELRCTRODERMAL ACTIVITY AS AN INDICATOR OF STRESS LEVELS EXCITABILITY: A PILOT STUDY. MY Lukov, ES Zemnukhov, St. Petersburg State University, St. Petersburg, Novgorod State University, Velikiy Novgorod, Russia.

13.30-13.45 PAIN AND BEHAVIOR. AV Voskanyan, AV Moghrovyan, LM Parseghyan, SS Poghosyan, AA Darbinyan, LA Orbeli Institute of Physiology NAS RA, M Heratsi Yerevan State Medical University, Armenia, Yerevan.

13.45-14.00 THE RELATIONSHIP OF EXCITATORY AND DEPRESSOR SYNAPTIC PROCESSES IN ANTINOCICEPTIVE RAPHE MAGNUS NUCLEUS ON THE MODEL OF PARKINSON'S DISEASE UNDER CONDITIONS OF PROTECTION WITH *NAJA NAJA OXIANA* (NNO) VENOM POISONING. HY Stepanyan, AL Minasyan, MV Poghosyan, TK Harutyunyan, KV Tsakanyan, HG Vahradyan, ZA Avetisyan, JS Sarkissian, LA Orbeli Institute of Physiology NAS RA, University of Traditional Medicine, Yerevan Haybusak University, Yerevan, Armenia.

14.00-14.15 SLEEP DISTURBANCES IN PATIENTS AS A RESULT OF STRESS FACTOR DUE TO HEADACHE ATTACKS. IV Fokin, Moscow Central House of Sciences, Moscow, Russia.

14.15-15.30 Lunch Break

15.30-18.00 MODERATED POSTER SESSION 2

ERP AMPLITUDES TO "EDIBLE" VS "INEDIBLE" NOUNS CHANGE DEPENDING ON GLUCOSE LEVEL IN HUMAN BLOOD (A PILOT STUDY). El Galperina, VA Ivanov, YA Chiligina, OV Kruchinina, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Herzen Russian State Pedagogical University, St. Petersburg, Russia.

1-DEAMINO-8-D-ARGININE-VASOPRESSIN IMPLEMENTS ITS ANALGESIC EFFECTS IN ELECTROCUTANEOUS PAW STIMULATION TEST IN RATS BY MODULATING THE ACTIVITY OF MONOAMINES IN THE BRAIN. AA Nikitina, SG Belokoskova, SG Tsikunov, Institute of Experimental Medicine, St. Petersburg, Russia.

THETA OSCILLATIONS MAY INTERFERE WITH ALPHA AND BETA DESYNCHRONISATION OF SUBTHALAMIC NEURONS DURING MOVEMENTS IN PARKINSON'S DISEASE PATIENTS. AA Nezvinskiy, EM Belova, AA Gamaleya, AA Tomskiy, AS Sedov, Semenov Research Center for Chemical Physics RAS, NN Burdenko National Medical Research Center of Neurosurgery, Moscow, Russia.

THE ROLE OF DIET AND DRINKING WATER IN EMOTIONAL RESPONSES: AN INSIGHT FROM ANIMAL MODELS. A Burova, A Gorlova, G Somlyai, K Chaprov, K Sitdikova, A Litavrin, E Svirin, J de Munter, T Strekalova, Neuroplast BV, Department of Psychiatry and Neuropsychology, Maastricht University, Maastricht, Netherlands; Institute of General Pathology and Pathophysiology, Sechenov First Moscow State Medical University, Moscow, Russia; HYD Pharma Inc., Budapest, Hungary.

AGING-RELATED IMPAIRMENT OF GLUCOSE TOLERANCE: THE EFFECTS OF THE WESTERN DIET AND DRINKING WATER WITH ALTERED DEUTERIUM CONTENT. Z Nefedova, A Burova, E Svirin, J de Munter, E Kochina, A Gorlova, G Somlyai, T Strekalova, A Umriukhin, Neuroplast BV, Maastricht, Netherlands; RUDN University, Department of Normal Physiology, Sechenov Moscow State Medical University, Institute of General Pathology and Pathophysiology, Moscow, Russia; HYD Pharma Inc., Budapest, Hungary.

THE ZEBRAFISH VERTICAL 100-500-ML CYLINDER TEST AS A SIMPLE AND FAST METHOD FOR MEASURING FISH STRESS AND ANXIETY. L Yang, Y Zhang, Y Lin, J Cui, Y Qin, C Zhao, AV Kaluev, Department of Biological Sciences, Suzhou Key Laboratory of Neurobiology and Cell Signaling, School of Science, Xi'an Jiaotong-Liverpool University, Suzhou, China

ANTIDEPRESSANT AND ANXIOLYTIC EFFECTS OF SMALL DOSES OF ANTIPSYCHOTIC DRUG SULPIRIDE IN ZEBRAFISH. AS Lebedev, DS Galstyan, TO Kolesnikova, MS Papulova, DK Saklakova, AV Kalueff, St. Petersburg State University, St. Petersburg, Russia; School of Science, XJTLU, Suzhou, China.

EFFECTS OF CHRONIC NITROGLYCERINE ADMINISTRATION ON MECHANICAL SENSITIVITY OF RATS. VD Ilyushichev, AA Kochneva, NO Fokeeva, PE Musienko, EV Gerasimova, Sirius University of Science and Technology, Sochi, Russia.

EFFECT OF NITROGLYCERIN ON MAST CELL DEGRANULATION IN A MODEL OF CHRONIC MIGRAINE IN RATS. NO Fokeeva, VD Ilyushichev, AA Kochneva, PE Musienko, EV Gerasimova, Sirius University of Science and Technology, Sochi, Russia.

COMPARISON OF PAIN SENSITIVITY THRESHOLDS IN RATS WITH DIFFERENT DOPAMINE LEVELS USING THE ELECTRONIC VON FREY SYSTEM. AA Kochneva, VD Ilyushichev, NO Fokeeva, PEM Musienko, EV Gerasimova, Center for Genetics and Life Science, Sirius University of Science and Technology, Sochi, Russia.

PATTERNS OF ELECTRICAL BRAIN ACTIVITY FOLLOWING ACUTE NITROGLYCERIN EXPOSURE IN ADULT ZEBRAFISH, AND THEIR RELEVANCE TO MODELING MIGRAINE. VD Riga, TO Kolesnikova, DS Kalinina, EV Gerasimova, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

THE NARROW 5-ML VERTICAL CYLINDER TEST AS A POTENTIAL RAPID ASSAY FOR ZEBRAFISH STRESS-EVOKED 'DESPAIR'-LIKE BEHAVIOR. L Yang, Y Zhang, Y Lin, C Zhao, Y Qin, J Cui, AV Kaluev, Department of Biological Sciences, Suzhou Key Laboratory of Neurobiology and Cell Signaling, School of Science, Xi'an Jiaotong-Liverpool University, Suzhou, Jiangsu, China.

THE EFFECT OF LASER BEAMS ON BEHAVIOR OF ADULT ZEBRAFISH: TOP, SIDE OR BOTTOM LASER HAS NO EFFECT ON FISH ANXIETY. KV Apukhtin, VS Nikitin, TO Kolesnikova, AV Kalueff, Sirius University of Science and Technology, Sochi, Russia.

THE IMPACT OF DIFFERENT CONCENTRATIONS OF BACTERIAL MELANIN ON THE BEHAVIOR, MORPHO-FUNCTIONAL STATE OF THE BRAIN, AND BONE MARROW IN A RAT MODEL OF PARKINSON'S DISEASE. KV Karapetyan, KA Nebogova, AG Karapetyan, AM Dallakyan, MV Pogosyan, ZA Avetisyan, MH Danielyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

THE IMPACT OF HYDROPONIC *SUTHERLANDIA FRUTESCENS* ON HIPPOCAMPAL NEURONAL ACTIVITY IN A RAT MODEL OF PARKINSON'S DISEASE. LP Manukyan, LE Hambardzumyan, VH Sarkisian, KV Simonyan, LE Hovhannisyan, LV Darbinyan, Sensorimotor Integration Lab, Neuroendocrine Relationships Lab, Orbeli Institute of Physiology NAS RA, GS Davtyan Institute of Hydroponics Problems NAS RA, Yerevan, Armenia.

PROTECTIVE EFFECTS OF L-THYROXINE ON HIPPOCAMPAL VASCULAR MORPHOLOGY AND ELECTRICAL ACTIVITY IN THYROIDECTOMIZED RATS. LV Darbinyan, KV Simonyan, LG Avetisyan, LE Hambardzumyan, LP Manukyan, KV Karapetyan, MH Danielyan, Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

NEW THERAPIES AND THERAPEUTIC DIET PROTOTYPE: PROMISING EFFECTS IN FEMALE APP/PS1 MICE, A MODEL OF ALZHEIMER DISEASE. K Sitdikova, J de Munter, K Chaprov, A Tsoy, A Gorlova, Z Nefedova, E Svirin, A Kassenova, L Ohanyan, N Ayvazyan, K Lebedeva, M Kuznetsova, T Veremeyko, ED Ponomarev, S Askarova, T Strekalova, Institute of General Pathology and Pathophysiology, Sechenov First Moscow State Medical University, Moscow, Russia; Neuroplast BV, Maastricht, Netherlands; Astana National Laboratory, Department of Biology, School of Sciences and Humanities, Nazarbayev University, Astana, Kazakhstan; LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia; Biomedical Sciences Department, City University of Hong Kong, Hong Kong, China.

NEONATAL INFLAMMATION DOES NOT LEAD TO DELAYED EFFECTS ON THE GLUTAMATERGIC SYSTEM AND BRAIN NEUROPLASTICITY: CHARACTERISTICS OF MICE WITH AUTISM-LIKE PHENOTYPE. EV Mezhlumyan, KA Ayriyants, AS Mutovina, MM Kolesnikova, NP Bondar, Novosibirsk State University, Institute of Cytology and Genetics, Novosibirsk, Russia.

COPPER COMPLEXES Cu (L^{CF3})$_2$ AND Cu(L^{cur})$_2$$H_2O$ AS RADIOPROTECTIVE COMPOUNDS. AG Karapetyan, VS Grigoryan, AM Dallakyan, LA Orbeli Institute of Physiology NAS RA, University of Traditional Medicine of Armenia, Yerevan, Armenia.

COMPARATIVE ELECTROPHYSIOLOGICAL STUDY OF THE ACTIVITY OF VESTIBULO- AND RETICULOSPINAL NEURONS IN FROG. LR Manvelyan, DO Terzyan, ML Grigoryan, LR Ohanyan, Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

IMPLEMENTATION OF STIMULATION OF SOME LIMBIC BRAIN STRUCTURES ON IDENTIFIED VAGAL NEURONS OF THE SOLITARY TRACT NUCLEUS. EA Avetisyan, AA Petrosyan, SA Shogeryan, NA Sahakyan, VH Sarkisian, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

INVESTIGATION OF THE ROLE OF TRACE AMINE-ASSOCIATED RECEPTOR 5 (TAAR 5) IN THE RESTORATION OF SENSORIMOTOR FUNCTIONS AFTER SPINAL CORD INJURY. AD Buglinina, DS Kalinina, EA Romanyuk, PE Musienko, Department of Neuroscience, Sirius University of Science and Technology, Sirius, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Life Improvement by Future Technologies Center "LIFT", Moscow, Russia.

AUTOPHAGOLYSOSOMES FORMATION IN BRAIN TISSUE OF RAT FETUSES SUBJECTED TO PRENATAL HYPERHOMOCYSTEINEMIA. AV Alov, NL Tumanova, AV Mikhel, IV Zalozniaia, YP Milyutina, DS Vasilev, AV Arutjunyan, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Ott Research Institute of Obstetrics, Gynecology and Reproductive Medicine, St. Petersburg, Russia.

THE PRACTICAL CHALLENGES AND LIMITATIONS OF DETECTING MOTOR UNITS FROM SURFACE ELECTROMYOGRAPHY. GV Iskarevsky, AD Buglinina, AE Pozdnyakova, AA Pekonidi, DA Onishchenko, AM Beknazarova, YR Bravyy, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

IS ARTIFICIAL INTELLIGENCE AN EFFECTIVE TOOL FOR PROVIDING THERAPY ADVICE IN NEUROREHABILITATION? AM Beknazarova, NO Prokhorenko, GV Iskarevsky, AA Pekonidi, YR Braviy, DA Onishchenko, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

EFFECT OF BLOOD FLOW RESTRICTION ON RECRUITMENT THRESHOLD AND AMPLITUDE-FREQUENCY CHARACTERISTICS OF MOTOR UNITS DURING EXERCISE. AA Pekonidi, GV Iskarevsky, AE Pozdnyakova, AM Beknazarova, AS Kirsanov, DA Onishchenko, YR Bravyy, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

RAPID CORTICAL PLASTICITY: DISSOCIATING THE EFFECTS OF ACTIVE AND PASSIVE ATTENTION IN AUDITORY PROCESSING. G Kopytin, A Kondratenko, M Ivanova, A Gorin, A Shestakova, V Moiseeva, National Research University Higher School of Economics, Moscow, Russia.

REGULATION OF CHARACTERISTICS OF ELECTRICAL RHYTHMOGENESIS IN THE REPRODUCTIVE SYSTEM. AV Mkrtchyan, NG Hunanyan, RG Chibukhchyan, TA Piliposyan, HH Mkrtchyan, YY Trofimova, KV Kazaryan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.

ACUTE BEHAVIORAL EFFECTS OF NOVEL N-BENZYL-2-PHENYLETHYLAMINE DERIVATIVES IN ZEBRAFISH LARVAE. DD Martynov, DS Galstyan, NP Ilyin, NI Golushko, AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg State Pediatric Medical University, St. Petersburg, Institute of Experimental Medicine, Almazov National Medical Research Centre, Sirius University of Science and Technology, Sirius Federal Territory, Russia; School of Science, XJTLU, Suzhou, China.

BEHAVIORAL EFFECTS OF TOFIZOPAM IN ZEBRAFISH NOVEL TANK AND TAIL IMMOBILIZATION TESTS. VV Tishkina, DS Galstyan, TO Kolesnikova, MS Papulova, AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg State Pediatric Medical University, Institute of Experimental Medicine, Almazov National Medical Research Centre, St. Petersburg, Sirius University of Science and Technology, Sirius Federal Territory, Russia; School of Science, XJTLU, Suzhou, China.

RHODOPSIN G-PROTEIN SPECIFICITY ADJUSTMENT FOR RETINA OPTOGENETIC PROSTHESIS. DA Meshalkina, SD Losev, ML Firsov, Sechenov Institute of Evolutional Physiology and Biochemistry RAS, St. Petersburg State University, St. Petersburg, Russia.

THE STRUCTURE OF COURTSHIP BEHAVIOR IN DROSOPHILA MALES: BOUNDARIES OF PLASTICITY. SA Fedotov, AA Goncharova, NG Besedina, LV Danilenkova, EA Kamysheva, JV Bragina, Laboratory of Toxinology and Molecular Systematics, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia; Laboratory of Comparative Behavioral Genetics, Pavlov Institute of Physiology RAS, St. Petersburg, Russia.

EFFECTS OF REPEATED EXPERIENCE OF AGGRESSION ON GENE EXPRESSION IN HYPOTHALAMUS IN MALE MICE. AA Sapronova, AS Mutovina, PE Kisaretova, R Salman, NP Bondar, Institute of Cytology and Genetics SB RAS, Novosibirsk State Research University, Novosibirsk, Russia.

BRIDGING SELF- AND SOCIAL GROOMING: COMPUTATIONAL ANALYSES OF RODENT BEHAVIOR AND BRAIN GENES. AM Moskalenko, AN Ikrin, AV Kozlova, TO Kolesnikova, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia.

17.00-17.30 CONFERENCE CLOSING
ANNOUNCING FUTURE ISBS CONFERENCES AND EVENTS

DAY 4 TOUR: PANORAMIC TOUR OF YEREVAN (tickets required)
TOUR DEPARTS FROM ORBELI INSTITUTE MAIN ENTRANCE

CONFERENCE DINNER (tickets required)

POST-CONFERENCE DAYS
May 20-21, 2024

Research visits to laboratories:

- ***Yerevan State Medical University***
- ***YSMU COBRAIN Center***
- ***LA Orbeli Institute of Physiology NAS RA***

MAY 20, 2024

POST-CONFERENCE TOUR 1: GARNI, GERHARD, ARARAT (tickets required)
TOUR DEPARTS FROM COBRAIN MAIN ENTRANCE

ISBS WORKING RESEARCH FIELD VISIT (BY INVITATIONS ONLY)
BUS DEPARTS FROM COBRAIN MAIN ENTRANCE

MAY 21, 2024

POST-CONFERENCE TOUR 2: ETCHMIADZIN-ZVARTNOTZ (tickets required)
TOUR DEPARTS FROM COBRAIN MAIN ENTRANCE

ISBS WORKING RESEARCH FIELD VISIT (BY INVITATIONS ONLY)
BUS DEPARTS FROM COBRAIN MAIN ENTRANCE

Conference Abstracts

Day 1, May 16, 2024

Venue – Yerevan State Medical University

OPENING PLENARY LECTURE – MIKHAIL AGHAJANOV MEMORIAL LECTURE: THE INVOLVEMENT OF BONE MARROW IN MECHANISMS OF NEURONAL SURVIVAL IN ALZHEIMER'S TYPE NEURODEGENERATION. KB Yenkoyan, MI Aghajanov, Neuroscience Laboratory, COBRAIN Center, Department of Biochemistry, Mkhitar Heratsi Yerevan State Medical University, Yerevan, Armenia. Associated with increasing life expectancy and number of elderly people, the incidence of Alzheimer's disease (AD) is also increasing, posing a growing challenge to societies and health systems worldwide. Currently, there is no effective treatment for this disease, one of the reasons for which is the lack of complete understanding of the mechanisms of the development and course of PC. The main pathological hallmarks of AD are Aβ plaques, neurofibrillary tangles composed of tau protein, gliosis and neuronal loss accompanied by cerebrovascular amyloidosis, neuroinflammation, oxidative stress and synaptic changes. Over the past years our group focused on searching for new neuroprotectors that form the basis of AD treatment. From this prospective we paid specific attention on activation the adult neurogenesis at AD brain. These cells could generate directly in brain as well as migrate into the brain from main reservoirs of the organism. Such reservoir can serve bone marrow. On the other hand, a number of studies have observed the migration of bone marrow-derived monocytes to the brain during AD, their proliferation in the brain, as well as their possible differentiation into brain macrophages. Results of our group showed that bone marrow react to AD-like neurodegeneration via activation the internal proliferative processes, as well as changes of cells differentiation, transcription and growth factors release. At the same time, we followed to the changes of the same factors in AD target brain structures and those are responsible for neurogenesis. These all allow us to consider bone marrow-derived cells as possible candidates for therapeutic intervention in AD. **RESEARCH SUPPORT:** Higher Education and Science Committee, ESCS of Armenia (24YSMU-CON-I-3AN, 21T-3A327), YSMU.

PLENARY LECTURE: INTERSECTING PATHWAYS OF RESILIENCE AND VULNERABILITY: A BIOMARKER APPROACH TO PREDICTING MENTAL HEALTH OUTCOMES. DC Anthony, Department of Pharmacology, University of Oxford, Oxford, UK. The complex interplay of genetic, environmental, and psychological factors contributes significantly to the development of major depressive disorder (MDD) and anxiety disorders, two of the most prevalent mental health challenges worldwide. This talk will explore the findings from two of our recent studies leveraging the UK Biobank's vast dataset to unravel the molecular underpinnings of resilience and susceptibility to these disorders. By employing machine learning techniques, including random forests, we analyzed the role of blood and urine metabolites, alongside sociodemographic, psychosocial, and physiological factors, in predicting the onset of MDD and anxiety disorders. In the first study, we rigorously matched individuals with a history of MDD against resilient individuals without an MDD diagnosis, integrating 381 blood metabolites and clinical chemistry variables, and 4 urine metabolites. Our findings revealed that increased pyruvate levels were key biomarkers of resilience to MDD, offering potential avenues for therapeutic targeting and risk stratification. This study showcased a predictive accuracy (ROC AUC) of 0.89 for initial MDD diagnosis, with prospective resilience/susceptibility prediction accuracy decreasing over time. The second study extended these methodologies to anxiety disorders, demonstrating the predictive value of blood biochemistry, psychosocial variables, and neuroticism scores in identifying individuals at risk. Elevated neuroticism and a history of trauma emerged as significant risk factors, while blood biomarkers highlighted anemia and systemic inflammation in anxious individuals. However, in contrast to the MDD study, biomarkers alone could not predict resilience or susceptibility to anxiety disorders, emphasizing the intricate role of psychosocial and demographic factors. Collectively, these studies underscore the potential of integrating biological and psychosocial markers to enhance our understanding and prediction of mental health outcomes. They illuminate the pathways of resilience and vulnerability, highlighting the importance of a multifaceted approach in the early identification and intervention of mental health disorders. Through this lens, we

propose a comprehensive framework for mental health risk stratification, paving the way for novel preventative and therapeutic strategies.

COBRAIN TALK: GENES UNDERLYING THE MORPHOLOGY OF MATURE NEURONS AND THEIR RELATIONSHIP TO STRESS AND DEPRESSION. J Jaworski, J Zeng, R Pagano, I Majewski, D Komorowski, P Boguszewski, M Urbanska, International Institute of Molecular and Cell Biology, Nencki Institute, Warsaw, Poland; COBRAIN Center, M Heratsi Yerevan Medical State University, Yerevan, Armenia. **INTRODUCTION:** The dendrites of neurons receive information from other cells within the neuronal network, and the morphology of dendritic arbors is specific to a particular class of neurons. Because the shape of the dendritic arbor is critical for adequately integrating incoming signals, it is stable throughout its lifespan once established during development. Given that dendrites have to remain intact for more than 80% of the neuron's lifetime, surprisingly little is known about molecular mechanisms underlying this phenomenon. At the same time, clear evidence exists that the stability of mature dendritic arbors is lost in depression. Thus, the main objectives of our study were to identify genes responsible for dendritic arbor stability of mature neurons and their link with stress-related behaviors and cognitive problems. **METHODS:** To identify genes essential for the stability of dendritic arbors of neurons, we established conditions inducing dendritic arbor instability in mature hippocampal neurons cultured in vitro. Next, we used next-generation RNA sequencing to identify changes in gene expression profiles under those conditions. The role of selected 77 differentially regulated genes in regulating dendritic arbor stability was tested using shRNA screen in cultured neurons. Finally, using AAV vectors, we silenced the expression of selected genes in vivo in the hippocampi of mice and performed TST and fear conditioning tests followed by morphometric analysis. **RESULTS AND DISCUSSION:** We identified chronic treatment with gabazine and interleukine-1b to induce dendritic instability in mature neurons cultured in vitro. RNA-seq analysis revealed changes in hundreds of genes and we selected 77 genes downregulated by gabazine for the shRNA-based screen. Out of these, 14 turned out to be indispensable for proper dendritic morphology. Two of them were knockdown in hippocampi in vivo and such treatment led to behavioral changes in males in TST. Our results strongly suggest that changes in the expression of genes critical for dendritic arbor stability may also lead to behavioral changes typically linked to depressive-like behaviors when confronted with stressful conditions. **RESEARCH SUPPORT:** Foundation for Polish Science TEAM grant POIR.04.04.00-00-5CBE/17-00.

ISBS PLENARY TALK: DISSOCIATION BETWEEN NEURONAL AND ASTROCYTIC RESPONSE TO LOCOMOTION IN MICE. AV Semyanov, Neuroscience Center, Jiaxing University College of Medicine, Jiaxing, China. Orchestrated activation of different cell types and their interactions within the brain active milieu provide the cellular basis for brain functions. Locomotion triggers a coordinated response of both neurons and astrocytes in various brain regions. We performed two-photon calcium imaging of these two cell types in the somatosensory cortex in head-fixed mice moving on the airlifted platform. Calcium activity in astrocytes significantly increased during locomotion from a low baseline level during animal quiescence. Calcium signals first appeared in the distal processes and then propagated to astrocytic somata where calcium elevations amplified (calcium surge) and exhibited oscillatory behavior. In contrast to astrocytes, pronounced calcium activity was detected in neurons in quiescent periods, and it further increased during locomotion. Neuronal calcium increased almost immediately following the onset of locomotion, whereas astrocytic calcium elevations lagged by several seconds. The functional relevance of delayed and slow calcium transients in the astrocytes remains unclear. Calcium could trigger a metabolic response in the cells. To address this possibility, we performed Raman microspectrometry (label-free metabolic imaging) in awake mice running on a treadmill. Green fluorescent protein was expressed in astrocytes and near-infrared protein in neurons for cell identification. Raman spectra recorded from astrocytes and neurons were used to quantify reduced C- and B-type cytochromes. The relative amount of reduced cytochromes reversibly increased in astrocytes and decreased in neurons during episodes of locomotion. This finding suggests more electrons in the electron-transport chain in astrocytes, which can trigger the production of reactive oxygen species (ROS). We assessed the production of ROS with two-photon imaging of H_2O_2 in the mitochondria of astrocytes and neurons. Consistent with our hypothesis, locomotion led to the production of H_2O_2 in the astrocytic, but not neuronal, mitochondria. Astrocytic H_2O_2 generation possibly plays a role in communication between astrocytes and other cells in the brain active milieu.

ISBS PLENARY TALK: UNVEILING THE NEUROBIOLOGICAL BASIS OF ENVIRONMENTAL BURDEN OF DISEASE IN A CONTEXT OF ISOTOPE CONTENT OF DRINKING WATER: INSIGHTS FROM ANIMAL MODELS. T Strekalova, Maastricht University, Maastricht, Netherlands. **INTRODUCTION**: Environmental influences can affect disease prevalence and cause illness. National

Environment Agencies worldwide study how various factors, e.g., noise, vibration, concentrations of ozone and benzene in the air, indoor tobacco smoke and cadmium can affect the risk of diseases. However, the role of isotope content of drinking water as environmental burden of disease is currently not in a focus of any systematic studies of that kind. Meanwhile, the link between deuterium content of water and depression, and diabetes type 2 was previously demonstrated in epidemiological studies. The ratio of deuterium to protium in water shows substantial geographical variation, which affects a susceptibility to these diseases. **METHODS:** We employed mouse models of depression, such as chronic stress, ultrasound “emotional stress” and serotonin transporter (SERT) deficient mice, as well as a mouse model of Western diet - a paradigm of diabetes type 2, to study the effects of low and high content of deuterium in these paradigms. Potential effects of various natural concentrations of deuterium administrated with drinking water on hall-marks of pathological syndromes were investigated. **RESULTS AND DISCUSSION:** We found that deuterium-depleted water exerted beneficial effects on molecular hall-marks of stress, markers of hippocampal neurogenesis, EEG parameters of sleep, emotionality and cognition, and glucose tolerance. A mechanism, by which altered concentration of deuterium in drinking water affects these read-outs, remains to be elucidated. Water with reduced deuterium content has lower viscosity that could exert physicochemical effects, leading to increased fluidity of the cell membranes and less rigid organization of phospholipid bilayers. This can, in turn, alter the dispersion of neurotransmitter receptors and increase receptor affinity, affect passive blood brain barrier permeability. **CONCLUSIONS:** Thus, the deuterium content of water may influence the pathophysiology of depression and diabetes. While in the Western world the bar is set extremely high when it comes to drinking water quality, environmental protection can be increased even further with a control over its isotope content.

STRESS, EPIGENETICS AND SUICIDES IN ADOLESCENTS (AN EVOLUTIONARY APPROACH). VA Rozanov**,** St. Petersburg State University, VM Bekhterev National Medical Research Center for Psychiatry and Neurology, St. Petersburg, Russia. **INTRODUCTION:** Recent data show the growing prevalence of suicides in the youngest people in many places of the world, involving both high-income and low-income countries. Suicides in the youngsters have been growing especially fast for the last 30-40 years, which is a very short period of time from the point of view of human history. **METHODS:** Integrating knowledge from different fields. **RESULTS AND DISCUSSION:** Given the bio-psycho-social and multifaceted nature of suicide there may be many reasons for negative trends among adolescents. Adolescence is a vulnerable period of life characterized by mental health disturbances, behavioral problems, psychological frustrations and stressful experiences. The biological, especially genetic and epigenetic components, especially in relation to stress are attracting more and more attention among possible reasons of growth of suicides in youngsters quite recently. Stress experienced by modern young people is a psychosocial perceived stress induced mostly by interpersonal and social factors. In the meanwhile, it utilizes the same conservative biological mechanisms that are inherent to all vertebrates, which are known to trigger multiple structural and functional processes in the brain and are able to be imprinted in the transcriptional patterns of different organs and tissues via epigenetic mechanisms. There is accumulating evidence that epigenetics plays a role as an interface between the early environments (from in utero to early years of life) and the stable genome producing long-lasting vulnerabilities that may lead to mental health disorders later in life. There is a discussion about to what extent digital technologies and information overload are to blame for young generations mental health disturbances and suicide. An evolutionary approach based on epigenetic thinking, especially taking into account the possibility of transgenerational transmission of stress vulnerability, provides a logical and consistent explanation of differentiation in the adolescent population, with possible growth in the proportion of those who are not able to adapt and those who will benefit from such development. We consider that information exposure enhances the level of perceived stress experienced by the younger population in the modern unequal and modernistic world. Nevertheless, digital technologies can be used for suicide prevention as well.

PAIN PERCEPTION AT ADULT AGE IS DEPENDENT ON NEONATAL CONDITIONING. BW Kramer, M Daly, Poznan University of Medical Sciences, Poznan, Poland; Irish Neonatal Health Alliance, Wicklow, Ireland. **BACKGROUND:** The relationship between neonatal experiences and pain perception in adulthood is a complex and multifaceted topic. Stressful, early life experiences, including those in the neonatal period, can influence the development of various physiological and psychological systems that may shape an individual's pain perception later in life. Preterm babies are at risk for numerous painful procedures in early life. **AIM:** To assess whether perinatal factors, later pain experience and pain coping strategies are associated with altered pain threshold, pain tolerance and pain intensity in adolescents born preterm. **STUDY DESIGN:** Observational, longitudinal study (Project on Preterm and SGA-infants, POPS-19). **SUBJECTS:** We analyzed data of 412 adolescents

at the age of 19 years, who were born at a gestational age<32 weeks or with a birth weight<1500g. **OUTCOME MEASURES:** Participants performed a standardized cold pressor test to assess pain threshold, tolerance, and intensity. Furthermore, they completed a pain coping questionnaire. **RESULTS:** In univariate analysis, female gender and necrotizing enterocolitis (NEC) were associated with lower pain tolerance, indicated by reaching the ceiling time of 180s in ice water (females 19% vs. males 29%, NEC 7% vs. no NEC 25%). Female gender was associated with higher pain intensity (mean difference 0.58; 95%CI 0.21; 0.95) and lower pain threshold (log rank test p=0.007). In multivariate Cox regression analyses, emotion focused avoidance pain coping style was significantly associated with lower pain threshold (hazard ratio HR 1.38; 95%CI 1.02; 1.87) and pain tolerance (HR 1.72; 95%CI 1.21; 2.42). NEC was significantly associated with lower pain threshold (HR 1.47; 95%CI 1.01; 2.14) and pain tolerance (HR 1.63; 95%CI 1.09; 2.41). **CONCLUSIONS:** In adolescence, maladaptive pain coping strategy was associated with lower pain threshold, pain tolerance and higher pain intensity. NEC was associated with altered pain response in adolescents born preterm. The study results allow various interpretations. Stress and pain during early development can affect the development of the stress response system, including the hypothalamic-pituitary-adrenal (HPA) axis. However, epigenetic mechanisms, which involve changes in gene expression without alterations to the underlying DNA sequence, may play a role in how early experiences influence pain perception. Early-life experiences can lead to epigenetic modifications that affect genes involved in stress response and pain modulation (e.g., methylation of the cortisol receptor gene). The nervous system, including the brain and spinal cord, undergoes significant development during the neonatal period. Early experiences can contribute to the development of neural circuits involved in pain processing. Maladaptive changes in neuroplasticity may contribute to conditions like central sensitization, where the nervous system becomes hypersensitive to pain signals. Beyond the biological aspects, psychosocial factors such as early caregiving experiences, attachment patterns, and the social environment can also influence pain perception. In addition, the development of coping mechanisms and the ability to regulate stress may be shaped by early life experiences. However, not all individuals who experience neonatal pain or stress will necessarily exhibit long-term alterations in pain perception. Genetic factors, environmental factors, and the overall context of early experiences contribute to the variability in outcomes. More research is needed to fully understand the mechanisms involved and the specific conditions under which these effects occur. Additionally, interventions aimed at providing supportive and low-stress environments for preterm infants and those experiencing neonatal pain may contribute to positive outcomes in pain perception and overall well-being later in life.

COBRAIN SYMPOSIUM – MIKHAIL AGHAJANOV MEMORIAL SYMPOSIUM (Chairs: KB Yenkoyan, J Jaworski)

INTRODUCTION: IN MEMORIAM: PROFESSOR MIKHAIL I. AGHAJANOV (1939-2024). Professor Mikhail Aghajanov was born in 1939 in Tbilisi, Georgia. He graduated with honors from Yerevan State Medical Institute (later – University), where in 1966 completed postgraduate studies in Biochemistry. In 1967-1974, he worked as an Assistant Professor, in 1974-1984 as Associate Professor, since 1984 - as Professor and since 1986 – as Chair of the Department of Biochemistry, also serving in 1988-1891 as Vice-Rector for Science of YSMU. Throughout his long and accomplished scientific career, he also interned in the Departments of Biochemistry at Moscow State University (1967-1968), Leningrad University (1978, 1985), Kyiv State Medical University (1987), and Bach Institute of Biochemistry (1988). Member of ISBS from 2004, he was elected Fellow of ISBS in 2015. Author of more than 300 published works, including 2 textbooks, 4 teaching guides and 6 patents. Areas of scientific interests: oxidative stress in the pathogenesis of various CNS diseases, its regulation using natural and synthetic antioxidants; neurodegenerative diseases (Alzheimer's disease), and mechanisms of neuroprotection. Scientific consultant of nearly 30 doctoral dissertations. Founder and President of the Armenian Alzheimer's Disease Association (since 2002), Scientific Director of YSMU Student Scientific Society (since 2004). By decree of the President of Armenia, Professor Aghajanov was awarded the title “Honored Scientist of the Republic of Armenia” in 2010.

THE INFLUENCE OF ELECTRIC FIELD ON OXIDATIVE STRESS MARKERS IN RATS. HA Harutyunyan, KB Yenkoyan, Neuroscience Laboratory, COBRAIN Center, Heratsi Yerevan State

Medical University, Yerevan, Armenia. **INTRODUCTION:** The electrostatic field (ESF) is a common natural phenomenon that may affect multiple physiological systems. For example, increased EEG, and decreased posterior hypothalamic, activity can be seen at 10 kV/m ESF, whereas 180 kV/m and higher impacts action potentials from afferent fibers innervatingvarious sensory receptors in cat hind limbs. There are also several reported data of ESF effects on the pro- and anti-antioxidant systems, including transient inhibition of antioxidant enzymes activity in erythrocytes with subsequent adaptative stimulation, and increased levels of thiobarbituric acid reactive substances (TBARS) in plasma, liver, lung, and kidney tissues of white guinea pigs after exposure to 0.8-1.8 static electric fields. **METHODS:** Here, we investigated the role of erythrocytes (RBC) as a source of reactive oxygen species (ROS) in blood of rats exposed to 1-h acute and 6-day chronic (6 h daily) 200 kV/m ESF. Oxidative processes were assessed in RBC membranes, RBC hemolysates, and in blood plasma. **RESULTS:** Overall, our studies revealed RBC-dependent way of oxidative processes alterations in blood induced by ESF, suggesting the role of RBC as the source of ROS in response to external ESF. External ESF at 200 kV/m alters the pro-/antioxidant system of blood of experimental animals in RBC-dependent manner. Acute exposure to ESF is characterized by lower RBC content and coincided with activation of the prooxidant processes in blood plasma and RBC. In contrast, long term ESF exposure elevated RBC content and promoted antioxidant processes. RBC membrane-bound proteins were shown to be more susceptible to ROS damage in rats exposed to external ESF.

THE PREVALENCE AND PECULIARITIES OF AUTISM SPECTRUM DISORDER IN URBAN CITIES IN ARMENIA. NZ Khachikyan, SH Mkrtchyan, AA Hayrapetyan, MA Mkhitaryan, A Mkrtchyan, GH Sakanyan, LR Avetisyan, KB Yenkoyan, Department of Hygiene and Ecology, Neuroscience Laboratory, COBRAIN Center, Heratsi Yerevan State Medical University, Yerevan, Armenia. **INTRODUCTION:** The prevalence and structure of autism spectrum disorder (ASD) morbidity varies geographically, with no sufficient data for Armenia. **AIM:** To estimate ASD prevalence in children aged 0-18 in urban areas, starting from the capital city, Yerevan. **METHODS:** A cross-sectional study included 80% of Yerevan children population aged 0-18 in 2021, based on the existing administrative databases of records of outpatient medical establishments related to children/adolescents aged 0-18. The study cohort included children/adolescents aged 0-18, registered in Yerevan out-patient medical establishments in January-December 2021. ASD prevalence, as well as male/female ratio, were calculated for this cohort in Yerevan, and average age at diagnosis has also been estimated. **RESULTS:** ASD prevalence in urban city of Yerevan was 3.7/1000, with and average age of ASD confirmed diagnosis of 4.5±2.5, and 5.1 times more prevalent in males than in females. **DISCUSSION AND CONCLUSION:** Overall, ASD prevalence was lower, whereas the male/female ratio was slightly higher, than in studies conducted in other countries globally. **CONCLUSIONS:** These findings highlight the needs to continue ASD prevalence studies in Armenia to compare urban and rural areas, determine trends, reveal possible cause-effect relation, and prepare health care system. Our results may help national and regional health, education and other systems to develop/improve proper strategy and services for ASD children/adolescents and their families.

COMPARATIVE STUDY OF PRE- AND POSTNATAL VALPROIC ACID (VPA) MODELS OF AUTISM SPECTRUM DISORDER: IDENTIFYING BRAIN VULNERABILITY TO VPA-EVOKED DEFICITS ACROSS THE TIMELINE. KS Fereshetyan, M Danielyan, KB Yenkoyan, Neuroscience Laboratory, COBRAIN Center, Department of Biochemistry, Heratsi Yerevan State Medical University, Laboratory of Histochemistry and Electromicroscopy, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** Autism spectrum disorder (ASD) is a neurodevelopmental illness characterized by altered verbal and non-verbal communication, as well as repetitive stereotypic behavior. Heterogeneity of this disorder complicates studying its pathological mechanisms and possible treatment. Clinical data show increased risk of ASD following valproate (VPA) combined or monotherapy during the pregnancy. VPA treatment is also a widely used animal model of ASD. Based on spatiotemporal features of ASD development, we hypothesized different levels of brain vulnerability to VPA-evoked CNS deficits across the prenatal and early postnatal neurodevelopment, and severity of manifestations in correlation to deficits. **METHODS:** The study was performed in parallel on prenatally and postnatally VPA-treated groups with respective controls. A battery of behavioral tests was performed for the model validation. Neurodevelopmental markers were assessed in brain neurogenetic niches on postnatal developmental days 14 and 21 (PND14, 21). **RESULTS:** Overall, prenatal and postnatal administration of VPA may affect the migration of progenitor cells from subventricular zone to the olfactory bulb. Our results showed significantly decreased level of BDNF in subventricular zone of VPA-treated groups on PND 14, and decreased level of doublecortin in olfactory bulbs on PND 21. Moreover, the comprehensive reduction of all peptides detected in subventricular zone on PND 14 suggests suppressing effect of VPA on neurotrophin production, leading to their

depletion in subventricular zone. Considering such temporal dynamics, we assume their overlap. The imbalanced neuro-glial ratio in prefrontal cortex of VPA-treated rats is the second major outcome of this study, likely due to altered neuronal differentiation or reactive gliosis, similar to well-known and widely used prenatal model (postnatal VPA administration) of 'ASD' in adolescent rats, which confirms the validity of the model. Various structural changes in brain target regions of VPA-treated rats indicate different severity of VPA-induced deficits across different stages of brain development. Nonetheless, this study confirms that VPA postnatal administration has substantial effects on neurogenesis that may mimic autism-related behavior.

INCREASING BIOACTIVE LEPTIN LEVELS TO ENHANCE COGNITIVE FUNCTION IN AMYLOID BETA 1-42-INDUCED NEURODEGENERATION. H Harutyunyan, R Minasyan, G Vardanyan, KB Yenkoyan, Neuroscience Laboratory, COBRAIN Center, Department of Biochemistry, Heratsi Yerevan State Medical University, Yerevan, Armenia. **INTRODUCTION:** Alzheimer's disease is a progressive neurodegenerative disorder characterized by cognitive decline and dementia. The irreversible nature of the disease is associated with neuronal death, loss of synapses, and neuroinflammation, caused by accumulation of abnormal proteins. No effective prevention or treatment strategy for Alzheimer's disease is suggested yet. Leptin is a proinflammatory adipokine, known as a satiety hormone. The circulating levels of leptin are directly associated with the fat stored. Leptin receptors (ObR) are primarily expressed in the hypothalamic arcuate nucleus, suppressing food intake. Recent studies indicate neuroprotective properties of leptin, manifested through activation of the JAK-STAT signaling mechanism. Metalloproteases catalyze transmembrane shedding of leptin receptors, attenuating leptin effects. Applying metalloprotease inhibitors may contribute to increased levels of bioactive leptin signaling. We hypothesized that increasing levels of bioactive leptin can exert a neuroprotective effect and enhance cognitive status in Alzheimer's disease-induced neurodegeneration. **METHODS:** Following acclimation, 80 male albino rats underwent initial behavioral testing (Open Field, Elevated Plus Maze, and Y Maze) and then randomly divided into two groups (n=40): receiving a ventricular injection of amyloid-beta 1-42, and saline injection controls, each further subdivided into two groups (n=20), receiving palatable or regular diets. Thirty days after the injections, behavioral tests were repeated to reveal a decline in cognitive status. All the amyloid-injected groups showed worsened performance in behavioral tests, suggesting neurodegeneration. Following behavioral assessment, each group was further subdivided into two groups (n=10), to receive a single injection of GM6001 Metalloprotease inhibitor, or saline. Thirty days later, behavioral analyses will be repeated. Sample collection and analysis: Blood samples will be collected to determine circulating leptin levels (ELISA). Amyloid-beta will be determined in cerebrospinal fluid (ELISA). Two samples from each group will be preserved for Congo red staining. The hippocampus, prefrontal cortex, and hypothalamus samples will be collected to determine IL-6 and TNF-α (ELISA) to assess neuroinflammation. It is expected that the group receiving palatable food + metalloprotease inhibitor will manifest the lowest level of neuroinflammation and the highest cognitive status among amyloid-injected groups. We expect that the combination of palatable food and metalloprotease inhibitors may serve as a combined tool to slow down neurodegeneration and improve cognition in Alzheimer's disease.

EPIGENETIC REGULATION DISTURBANSES IN MULTIPLE SCLEROSIS AND THEIR RELATIONSHIP WITH CHANGES IN FOLATE METABOLISM. VI Lioudyno, EA Tsymbalova, EA Chernyavskaya, GN Bisaga, IN Abdurasulova, Institute of Experimental Medicine, Almazov National Medical Research Center, St. Petersburg, Russia. **INTRODUCTION:** Multiple sclerosis (MS) is a chronic progressive disease of the central nervous system, characterized by inflammation, demyelination and neuroaxonal damage. Dysregulation of gene expression due to epigenetic control impairment plays an important role in the pathogenesis of MS. In particular, in MS patients there is a decrease of DNA methyltransferases activity, as well as an increase of the *PAD2* gene expression due to promoter hypomethylation, which leads to an increase in the proportion of citrullinated forms of myelin basic protein and makes its structure less stable and vulnerable to destruction. It is known that expression of DNMT1, an enzyme controls the maintenance of DNA methylation patterns, may depend on the state of folate metabolism, the efficiency of homocysteine to methionine conversion, and the availability of methyl donors. Considering this, it seemed relevant to assess the level of DNMT1 expression, characterize the PAD2 promoter methylation in patients at the MS onset, and compare these indicators with the presence of polymorphisms in folate cycle genes. **METHODS:** Peripheral mononuclear cells isolated by a gradient method from the whole blood of MS patients and control subjects were used as the object. The level of DNMT1 mRNA was assessed by RT-PCR, and fluorescent PCR with methyl-sensitive high-resolution melting curve analysis (MS-HRM analysis) was used to analyze site-specific methylation. Genotypes for folate cycle gene polymorphisms were determined by PCR with allele-specific fluorescent probes. **RESULTS AND DISCUSSION:** The

influence of the combination of genotypes for polymorphisms C677T of the MTHFR gene and A2756G of the MTR gene to the level of *DNMT1* expression was revealed. Homozygous carriers of the C allele for the C677T, who have also a G-allele of A2756G, have the highest level of DNMT1 mRNA. However, this particular combination of genotypes was significantly less common in patients with MS than in healthy subjects ($\chi 2=7.136$; $p=0.008$). At the same time, the level of DNMT1 expression in patients with MS was reduced by more than 2 times (ANOVA, $F=17.59$; $p=0.0003$). It is important that a decrease in DNMT1 expression is observed already at the onset of the disease. According to HRM analysis, the degree of methylation of the promoter region of the PAD2 gene is in the range from 0% to 2%, both in patients and healthy subjects, which do not allow detecting significant quantitative differences between groups. However, there is trend towards to a decrease in the methylation level in the presence of T-allele for the C677T polymorphism. Based on the data obtained, we suggest that the combination of genotypes for polymorphisms of key genes of the folate cycle, C677T of the *MTHFR* and A2756G of the *MTR,* may influence the risk of epigenetic disturbances that contribute to the MS onset. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-25-00312.

PRETERM BIRTH IS STRESS FOR LIFE – BEHAVIORAL PATTERNS IN FORMER PRETERM INFANTS. M Daly, Irish Neonatal Health Alliance, Wicklow, Ireland. **BACKGROUND:** Preterm birth (born before 37 weeks of pregnancy) can have a range of effects on a child's development. The brain development after birth is very different than in utero. The impact of preterm birth on behavioral patterns in later life can vary widely, as it depends on various factors such as the degree of prematurity, the presence of medical complications, and the quality of postnatal care. **MATERIAL AND METHODS:** Systematic Review. **RESULTS:** The following functions were identified. Cognitive and academic challenges have been associated with preterm birth. This may manifest as difficulties in learning, attention deficits, mathematics, and lower academic achievement compared to full-term peers. Emotional and Behavioral Regulation which some preterm infants may experience as a challenge. They might be more prone to anxiety, depression, and difficulties in managing stress. Impulsivity and hyperactivity can also be observed. Social skills and relationships may be impacted. Some individuals who were born preterm may face challenges in forming and maintaining friendships, and they might be at a higher risk for social difficulties. In addition, executive functions, such as working memory, cognitive flexibility, and inhibitory control, can be affected by preterm birth. This may result in difficulties in planning, organizing, and completing tasks. Depending on the severity of prematurity, individuals may experience challenges with motor skills and coordination. This can affect both fine and gross motor skills. Preterm infants may be at an increased risk for sensory processing disorders. Sensory processing challenges can affect how individuals respond to sensory stimuli, potentially leading to over-sensitivity or under-sensitivity to certain sensations, which may affect the quality of life. Individuals born preterm may have a higher risk of certain health issues, and these health concerns can also influence their behavior. Chronic health conditions may impact daily functioning and overall well-being. **CONCLUSIONS:** It is important to note that while preterm birth can increase the risk of certain challenges, many individuals who were born preterm lead healthy and successful lives. Early intervention and appropriate support systems, including educational and therapeutic interventions, can make a significant difference in mitigating potential challenges associated with preterm birth. Regular monitoring and early intervention are crucial to addressing any developmental or behavioral concerns that may arise. Systematic data collection in this group of patients will allow the study of variations in the human brain development.

UNRAVELLING CORTICAL EXCITABILITY DURING SPIKE AND WAVES AND ITS CONSEQUENCES FOR SEIZURE INTERRUPTION IN A GENETIC EPILEPSY MODEL. G van Luijtelaar, B de Ruiter, Donders Centre for Cognition, Radboud University, Nijmegen, Netherlands. **INTRODUCTION:** The neuronal activity during the spike-wave complex, a constituent of spike-wave discharges (SWD) typical for generalized epilepsies, consists of synchronized neuronal firing in a group of neurons, followed by neuronal silence; this pattern can be observed in widespread cortical zones and the thalamus. The probability of SWD abortion by cortical single-pulse stimulation was determined in freely moving rats of the WAG/Rij strain during the ascending and descending phases of the spike and three wave intervals in the first second (early) and after one second (late) of the spontaneous occurring SWDs. This was related to an excitability measure (P1 of the electrical evoked potential). **METHOD:** Male rats of the WAG/Rij strain were chronically equipped with two cortical stimulation electrodes near the focal area and recording electrodes in the cortex and thalamus. An automatic spike detection system delivered single monophasic 1 msec pulses contingent upon a detected spike with varying and adjustable delays in free-moving rats. It was decided off-line whether stimulation occurred in one of the five intervals. Grand Average EEPs were made per interval in the early and late phase of SWDs. **RESULTS:** Single-pulse stimulation could interrupt ongoing SWDs at

any of the five SWD intervals in the cortex and thalamus. However, the probability was higher during the spike than the wave intervals, but this was only the case in the first second of SWDs. Different intervals and opposite early-late effects were found for the P1. Intrinsic excitability differences were found between the two spike-related intervals: low during the ascending phase of the spike and high during the descending phase. The responses during the wave were low but increased towards the last wave interval. **CONCLUSIONS:** There is no relation between the local excitability and the probability of interruption given the opposite interval and early-late effects on the probability of SWD interruptions and the excitability measure. Rather, the probability of an SWD interruption is mainly based on the state of the cortico-thalamo-cortical and cortico-cortical networks and is not dependent on local excitability. The heterogeneity in excitability found among the five predefined SWD intervals revealed not only the more often reported differences between the spike and wave, and within the wave, but even more pronounced within the spike.

AGE-RELATED FEATURES OF THE FUNCTION OF NEUROENDOCRINE SYSTEMS UNDER CONSTANT LIGHTING. ND Goncharova, AM Ermolaeva, OA Chigarova, TE Oganyan, NV Timoshenko, National Research Centre “Kurchatov institute”, Sochi, Russia. The problem of studying age-related changes in the function of adaptive neuroendocrine systems and their relationship with age-related stress-related diseases is extremely relevant due to the sharp increase in the incidence of age-related pathologies (cardiovascular, psychiatric, oncological, metabolic, neurodegenerative, etc.) due to the expansion of the range of stress factors, among which significant role is given to light pollution of the environment with an increase in illumination at night. The purpose of the study was to assess the functioning of the hypothalamic-pituitary-adrenal (HPA) axis, the hypothalamic-pituitary-thyroid (HPT) axis and the pineal gland under conditions of chronic round-the-clock lighting (CL, 4-7 weeks) (330-400 lux) on a translational monkey model. The experiments used 14 young and 14 old female rhesus monkeys, half of which were exposed to CL using conventional LED lamps designed for use in residential and office environments, and the other half to standard lighting (SL) with natural light during the day and darkness at night. During the basal period and against the background of CL or SL, animals were subjected to acute stress exposure (ASE, 2-h non-rigid immobilization, beginning at 15.00, 7 weeks of CL), a thyrotropin-releasing hormone injection (TRH, 9.00, 4 weeks of CL) and assessment of the circadian rhythm of the activity of the HPA axis, the HPT axis and the pineal gland. For the first time, the inhibitory effect of CL on the cortisol response to ASE was revealed in all animals, and in young animals it was associated with a decrease in the secretion of corticotrophin (ACTH), and in old animals it was not accompanied by changes in the ACTH response. As in the case of the HPA axis, TRH activation of thyroid function by CL in all animals was accompanied lesser increase in thyroxine level, but significantly more marked in old animals. At the same time, only minimal changes were noted in the functioning of the pituitary corticotrophs. No changes in MEL secretion were detected. Thus, a weakening of the reaction of the adrenal cortex to ASE and the thyroid gland to the administration of TRH on the background of CL was revealed, which was more pronounced in old individuals; the formed hormonal imbalance may play an important role in the pathogenesis of different age-related pathology. In turn, the identified inhibitory effect of CL on the functioning of adaptive neuroendocrine systems under conditions of their activation indicates the possibility of disruption of the body's adaptive abilities under conditions of constant lighting. **RESEARCH SUPPORT:** National Research Centre "Kurchatov Institute" (Russia), project 123011300084-1.

CLUSTERING TECHNIQUE TO STUDY NEURAL ACTIVITY IN GENETIC AND NON-GENETIC PATIENTS WITH PARKINSON’S DISEASE. EM Belova, PN Pavlovskiy, UN Semenova, NN Semenov Federal Research Center for Chemical Physics RAS, Moscow, Russia. **INTRODUCTION:** Neurodegeneration in Parkinson’s disease (PD) cause dysfunction in basal ganglia network and alteration in brain activity that manifest in various motor symptoms. Deep brain stimulation (DBS) of subthalamic nucleus (STN) has proven to be effective PD treatment that provides unique opportunity to perform neural recordings in subcortical structures of the human brain. However, progress in understanding of fundamental mechanisms of motor control as well as the development of personalized approaches to DBS rely on progress in methods to describe the complex features of neuronal activity affected by PD. **METHODS:** Here we apply clustering technique to identify patterns of single unit activity in PD patients with disease onset after 40 years as well as young onset PD with and without mutation in Park2 gene based on MLPA assay analysis. Clustering was also used to search for specific frequency ranges displaying the excessive synchronization of STN local field potentials (LFP) in PD. Both methods are observer independent and may help to describe diverse neuronal processes based on relatively stable features of neuronal activity. **RESULTS AND DISCUSSION:** In the STN, we described 3 patterns of neuronal activity: regular, burst and pause activity. Pause pattern was associated with hypokinetic symptoms severity, while 8-20 Hz oscillations

of these units correlated with bradykinesia score. Clustering analysis of LFP spectral peaks revealed 2 sub-bands of stable high amplitude oscillations within 8-30 Hz range that were shifted from commonly defined alpha/beta frequency bands. Excessive synchronization in the lower frequencies were always concurrent to stable peaks in higher frequencies marking patients with longer disease duration and more severe motor symptoms. We found that although there were no differences in pattern prevalence across young onset PD patients, burst and pause neurons in non-genetic group displayed significantly greater synchronization in the 8-20 Hz range. This was also evident on populational level within the range 8-25 Hz when analyzing spectral features of LFP recordings. Additionally, we have found significant differences in the slope of aperiodic spectral component in LFP recordings as well as in coefficient of variation for inter-spike intervals when considering single unit activity in young onset PD. We believe that observer-independent approaches may provide researchers with valuable descriptors of neuronal activity that help to elucidate brain processes associated with general pathology a well as differentiate between specific features of individual clinical picture. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00344.

ONLINE TALK: PSYCHOSOCIAL RISK ASSESSMENT IN SMALL GROUPS. Ph. Fauquet-Alekhine, JAK Erskine, Group INTRA robotics, France; SEBE-Lab-Behavioural and Psychological Science, St George's University of London, London, UK. **INTRODUCTION:** The assessment of psychosocial risks in companies has become an obligation for companies in many countries for the past several decades. Numerous books and publications have focused on this topic (e.g., the recent handbook of occupational stress by Fauquet-Alekhine and Erskine, 2023). Usually, this type of assessment is carried out on the basis of questionnaires that the company's employees fill in and that specialists analyze, or on the basis of collective interviews; some developments combine the two, with questionnaires allowing for prior identification of difficulties before interviews. Many scientifically validated questionnaires are available, and several reviews have discussed the advantages and disadvantages in depth. The choice of questionnaire depends on what the specialist wishes to target in the assessment, as well as the time available to administer the questionnaire to the participants: depending on the questionnaire, the number of items varies from 10 to over 100, which impacts the completion time as well as the time taken to analyze the results. **METHODS:** Many specialists agree to assess psychosocial risks by profession in companies, supplemented by an inter-occupational cross-analysis. Indeed, many psychosocial risk factors are induced by interactions between occupations. Depending on the company and the profession, the collectives can vary from 2 to more than 10 people. For example, the JSS (Job Stress Survey, Spielberger, 1994), proposes 30 questions are evaluated in terms of intensity in the first step and then later in terms of frequency during a second step, the product of the intensity by frequency gives an index per item. This questionnaire is interesting because it covers a wide range of psychosocial risks while inducing a relatively short duration of assessment and analysis. It is therefore particularly well suited to the assessment of psychosocial risks, which will then make it possible, during group interviews by profession, to focus the discussion on the difficulties highlighted by the results obtained from the questionnaire. **RESULTS AND DISCUSSION:** In practice, during a company psychosocial risk assessment, it has happened more than once that a group of professions brings together only 2-5 participants. This is the case, for example, with managers or departmental assistants. When the evaluation is renewed from year to year, some sponsors have questioned the validity of the scores averaged by profession when the collective has so few participants. Our position is that the results should not be approached with a statistical approach. Indeed, considering the scores obtained according to a statistical approach would assume that the results would correspond to a normal distribution, which might not be the case with so few participants. We therefore think that the results should be considered as the reflection of images at a given moment of the psychosocial state of the collective under consideration. In the case of an annual re-evaluation, the comparison between these two images should be considered in absolute values and not according to a statistical approach. In our opinion, the information provided by these psychosocial images of a group is perfectly acceptable provided that it is supplemented by group interviews by profession in order to validate or not what emerges from the results obtained in the questionnaires. According to our own experience as analysts of psychosocial risks, once out of 100 cases studied the sponsor refused to accept the validity of the results obtained from the questionnaire on the pretext that within a given collective, from one year to the next, the people constituting this collective had been renewed by a third: 2 out of 6 people had been replaced within the year. 1) The sponsor felt that the year-to-year comparison between the two psychosocial images was not comparable because of the change in people and the small number of participants in the group. During the same intervention, for another occupational group, a few days after the questionnaire was taken, some participants, dissatisfied with the organization of work, claimed to have forced negative responses by answering the questionnaire. 2) The sponsor considered that the results

were not admissible insofar as these people represented half of a collective of 4 people and that the answers were not honest. On these two points, our respectively position is as follows. As explained above, the results of the questionnaires give a psychosocial image of the group at time t. This psychosocial image reflects the state of mind of the people who make up the collective in the context of their work at the time t. This is precisely what is sought by using such a questionnaire. The difference in perception between the two assessments is relevant as an input for the interviews to be followed. It is as relevant as if it were a difference in the perception of a collective made up of the same people from one year to the next. The group interview that follows makes it possible to analyze and understand this difference and to know if the difference comes from personalities or from the Negative forcing of the responses to the questions should not be seen as a bias, but as a message from the participants in the analysis. The group interview to be followed is therefore an opportunity to analyze the message and integrate it into the understanding of the psychosocial situation. **CONCLUSIONS:** The use of scores averaged by occupational groups is acceptable in the assessment of psychosocial risks regardless of the number of participants in the groups. Importantly, for small groups, the score obtained cannot be used for a statistical study that would then be predictive for a larger population but as an input for analysis. Then the collective interviews are mandatory to analyze the scores.

ISBS TALK: REGULATED EXOCYTOSIS IN HUMAN GLIOBLASTOMAS. V Parpura, V Montana, International Translational Neuroscience Research Institute, Zhejiang Chinese Medical University, Hangzhou, China. **INTRODUCTION:** Glioblastomas (GBMs) are the most common primary malignant brain tumors in adults. They are one of the deadliest cancers, having a median survival of 14 months despite of standard of care (surgery, radiotherapy, and chemotherapy with temozolomide). GBMs are characterized by extensive dispersal throughout the brain, indicative of their highly invasive nature. Identifying novel treatments that stop/attenuate the progression of GBMs will be life altering. We propose a novel hypothesis that human GBM invasiveness is promoted by regulated exocytotic secretion of glutamate (Glu), a transmitter known to stimulate GBM cell motility and invasion. GBM invasiveness can be stimulated by bradykinin (BK), a signaling molecule generated at the interface between the brain parenchyma and vasculature. BK activates B2 receptors (B2Rs). **METHODS:** BK-evoked exocytosis were blocked in B2R high-expressing PDX GBM cells by icatibant and via transcriptional silencing of VAMP2. The effects were studied in both *ex vivo* and *in vivo* settings: A) Real-time visualization of human PDX GBM cell invasion into the normal brain parenchyma was examined in mouse acute slice preparations using laser scanning confocal microscopy. B) In mice bearing implanted PDXs, we will assess animal survival, tumor volume and GBM cells invasiveness. **RESULTS AND DISCUSSION:** Our data demonstrate that B2Rs are abundantly expressed on a subset of human GBMs. Our data further reveal that B2R activation in GBM cells causes exocytotic/vesicular glutamate release from human GBM patient-derived xenolines/xenografts (PDX), the best pre-clinical model of GBM. Blocking this pathway increasers survival time and decreases the GBM tumor progression in vivo. We posit that BK-evoked vesicular release of Glu could be a common mechanism of Glu release from GBMs and a therapeutic target to reduce invasiveness. The data generated is highly relevant for the development of adjuvant treatments for people suffering from this cancer. **RESEARCH SUPPORT:** Cheung Kong (Yangtze River) Scholar Program, Ministry of Education, China and the Kun Peng Action of Zhejiang Province, China.

VESICULAR GLUTAMATE RELEASE MODULATION BY PRESENILIN FROM ASTROCYTES. V Montana, V Parpura, International Translational Neuroscience Research Institute, Zhejiang Chinese Medical University, Hangzhou, China. **INTRODUCTION:** Alzheimer disease, AD is a progressive neurodegenerative disease characterized by severe disruption of functional connectivity of neural networks. Astrocytes are implicated to have a central role in the cellular phase of AD as they are responsible for controlling neurotransmitter homeostasis and maintaining connectivity by releasing gliotransmitters in Ca^{2+}-dependent manner. Ca^{2+} is delivered from both intracellular and extracellular sources. In addition to γ-secretase activity, presenilins, PS function as leak Ca^{2+} channels while residing in the ER membrane. A number of mutations of PS disturb Ca^{2+} permeability and result in throwing intracellular Ca^{2+} dynamics out of balance. Although astrocytes express both forms of presenilin, PS1 and PS2, the role of their mutated forms on Ca^{2+} homeostasis, Ca^{2+} dynamics and signaling pathways, such as Ca^{2+} -dependent gliotransmitter release, has not been extensively studied. **METHODS:** Primary mouse cultured astrocytes were used to co-express three different PS mutants, PS1ΔE9, PS1M146V and PS2N141I together with reporter dsRed2-C1. Cyclopiazonic acid, a blocker of ER Ca^{2+}-ATPase, was bath applied to observe outcomes on store operated Ca^{2+} entry. Fluorescently based calcium imaging and glutamate dehydrogenase assay were used to study effects of PS mutants on the process of regulated exocytosis after bradykinin stimulation, while mobility of

VGLUT3-EGFP labelled glutamatergic vesicles was monitored by time-lapse imaging. **RESULTS AND DISCUSSION:** Our data demonstrate that presenilin mutations dramatically affect capacity and dynamics of intracellular Ca^{2+} stores. Dysregulation in their function was further confirmed by bradykinin-invoked Ca^{2+} response, which was significantly decreased. As a consequence, exocytotic glutamate release was also significantly reduced in the presence of the mutants, as well as spontaneous mobility of glutamatergic vesicles. These effects could have profound impact in early stages and progression of AD as astroglia play an active role in synaptic strength and integration of synaptic processes by monitoring and modulating neuronal activity at tripartite synapse. **RESEARCH SUPPORT:** Cheung Kong (Yangtze River) Scholar Program, Ministry of Education, China and by the Kun Peng Action of Zhejiang Province, China.

Day 2, May 17, 2024

Venue – Yerevan State Medical University

NEUTRAL SPHINGOMYELINASE DETERMINES THE COMORBIDITY TRIAS OF ALCOHOL ABUSE, MAJOR DEPRESSION AND BONE DEFECTS. LS Kalinichenko, Department of Psychiatry and Psychotherapy, University Clinic, Friedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany. **INTRODUCTION**: Mental disorders, such as depression and alcohol abuse, possess high comorbidity with peripheral diseases, such as osteoporosis. Shared pathogenic pathways might determine these comorbidities. Crucial members of biological membranes, ceramides, contribute to the pathogenesis of single disorders, while role of the ceramide system in their comorbidities remains unclear. We hypothesized that natural variations in the activity of neutral sphingomyelinase-2 (NSM), a key enzyme of ceramide synthesis, is a common origin of the comorbidity trias of alcohol abuse, major depression and bone defects. **METHODS**: A genetic association analysis of *SMPD3* gene haplotypes, coding for NSM, with alcohol consumption, depression, and bone density was performed on 456,693 participants. Female transgenic mice with reduced NSM activity (fro) were tested in a battery of behavioral tests or exposed to alcohol on the model of free-choice drinking (Kalinichenko et al., 2021). **RESULTS AND DISCUSSION**: NSM determining ceramide synthesis contributes to the comorbidity trias of alcohol abuse, depression and bone defects. A genetic association analysis in 456,693 volunteers found associations of *SMPD3* haplotypes coding for NSM with alcohol consumption, anxiety and depressive symptoms, and bone mineralisation. Functional analysis in female heterozygous NSM knockout mice (fro) confirmed these findings. Fro mice possessed reduced alcohol consumption and depression/anxiety-like behavior compared to wild type controls. Voluntary alcohol drinking reversed the low-depression phenotype in fro mice, probably by affecting monoaminergic system functioning. Alcohol altered the extracellular levels of dopamine and serotonin, expression of their receptors and transporters, and affected serotonin uptake in synaptosomes in a genotype-specific manner. NSM also controlled bone–brain communication by enhancing signalling of osteocalcin, an inductor of bone mineralisation, in fro mice. Osteocalcin administration independently supressed alcohol consumption and reduced depressive behavior in a way similar to NSM effects. Altogether, we identified a single gene source, which interlink disorders of a mental–physical comorbidity trias of alcohol abuse—depression/anxiety—bone disorder. Targeting NSM and osteocalcin signalling may thus provide a new systems approach in the treatment of a mental–physical co-morbidity trias. **RESEARCH SUPPORT**: German National Science Foundation grants MU2789/8-2, GU335/29-2, GU335/29-3, KO947/13-3, KO947/15-2, HU306/27-3, TRR265.

SYMPOSIUM 2: NEUROMOLECULAR BASIS OF NORMAL AND PATHOLOGICAL BEHAVIOR (Chair: VN Naumenko)

INTERACTIONS OF SEROTONIN RECEPTORS IN THE REGULATION OF BEHAVIOR AND CENTRAL NERVOUS SYSTEM FUNCTION. VS Naumenko, EM Kondaurova, TV Ilchibaeva, AS Tsybko, AYa Rodnyy, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia. Our study showed that heterodimeric complexes could be formed both by different receptors of the same brain system and by receptors of different brain systems even if receptors belong to different superfamilies. Thus, the ability to form heterodimers was shown for 5-HT_{1A} and 5-HT_7 receptors from the serotonin G-protein-coupled receptors family as well as for serotonin G-protein-coupled receptor 5-HT_{2A} and brain-derived neurotrophic factor TrkB receptor, belonging to the family of receptors with enzymatic

activity. It was demonstrated that formation of heterodimeric complexes significantly affects the function of one or both composing receptors. Growing body of evidence indicate that receptors heterodimerization is an additional factor in the regulation of the functional activity of the brain neurotransmitter and neurotrophic systems and, hence, behavior. The obtained data draw attention to receptor complexes as new targets for pharmacological correction of behavioral pathologies. **RESEARCH SUPPORT***:* Russian Science Foundation grant 22-15-00011.

EFFECT OF PHD INHIBITION ON BIOELECTRICAL NEURAL NETWORK ACTIVITY DURING IN VITRO HYPOXIA MODELING. MV Vedunova, TA Mishchenko, EV Mitroshina, Lobachevsky State University Nizhny Novgorod, Russia. **INTRODUCTION:** Hypoxia represents a prevalent pathological state often accompanying various central nervous system pathologies, including ischemic injury, trauma, neurodegenerative diseases, and tumors. Hypoxia-inducible factor (HIF-1) serves as a pivotal transcription factor initiating the cell survival program in response to oxygen deprivation. HIF prolyl hydroxylase (PHD), the oxygen-sensitive enzyme, plays a critical role in the degradation of the α-subunit of the HIF-1 complex. **AIM:** To investigate the effects of PHD inhibition and HIF-1 stabilization on bioelectrical activity and functional reorganization of neural networks in primary cultures of mouse hippocampal cells during hypoxia simulation. **METHODS:** Primary neuronal cultures of hippocampal cells derived from embryonic brain tissue of C57BL/6 (E18) mice and cultured on MEA60 multielectrode arrays (Multichannel Systems, Germany) served as the object of research. Acute normobaric hypoxia was induced on Day 14 of in vitro culture development (DIV 14). During and immediately after hypoxia induction, the experimental group of cultures was supplemented with the original PHD inhibitor D014-0030 (0.5 μM). Electrophysiological data were analyzed using the original MEAxtd software. **RESULTS AND DISCUSSION:** In the hypoxia group, during acute hypoxia simulation, we found suppression of neural network burst activity and a prevalence of non-network, single electrical events. Two hours post-reoxygenation, small network burst impulses appeared, followed by an increase in both small and large network bursts after 24 h. The application of the original hydroxyquinoline PHD inhibitor D014-0030 under hypoxic conditions resulted in significant suppression of complex network burst events and the emergence of scattered single spikes. However, it contributed to maintaining the number of network bursts in the spontaneous bioelectrical activity profile, with an average of 100-300 spikes, while preserving active network centers responsible for generating network burst impulses. After 24 h, the analyzed parameters returned to baseline activity levels, comparable to the intact group. **RESEARCH SUPPORT:** Contract 075-15-2022-293 «Center of Photonics» by the Ministry of Science and Higher Education of Russian Federation.

IMPACT OF 5-HT4R ACTIVATION ON CA^{2+} NETWORK ACTIVITY AND INTERCELLULAR SIGNALING IN VITRO. EV Mitroshina, EA Marasanova, MV Vedunova, Lobachevsky State University, Nizhny Novgorod, Russia. **INTRODUCTION:** There is growing evidence suggesting involvement of various serotonin (5-HT) receptor subtypes, notably 5-HT4, in the pathogenesis of depressive disorders. While 5-HT4 receptors may modulate neurotransmitter release and play a role in regulating fundamental cellular processes underlying synaptic plasticity, their impact on neural network activity remains poorly understood. **AIM:** To investigate the influence of 5-HT4R activation on network calcium dynamics and intercellular signaling in neural cell cultures in vitro. **METHODS:** Primary cultures of hippocampal cells and monoastrocytic cultures from the cerebral cortex of C57BL/6 mice were carried for the study. Serotonin receptor stimulation was achieved using the selective 5-HT4R agonist BIMU8 (Sigma, Germany) through two protocols: chronic activation with each medium change at a concentration of 100 nM, initiated from the first day of cultivation, and acute single activation of 10 μM administered 1 h prior to activity recording. Calcium intercellular signaling was recorded on the 14th day of cultivation using an LSM 800 confocal microscope (Zeiss, Germany), with subsequent imaging data processing conducted using the proprietary Astrocyte Laboratory program (State registration of software 2021612870, 2021). **RESULTS AND DISCUSSION:** Acute activation of 5-HT4R was found to have no discernible effect on the number of active cells but negatively impacted the correlation of activity within neuron-glial networks in primary hippocampal cultures and the number of functionally significant connections between cells in the culture. Conversely, chronic activation of 5-HT4R significantly increased the proportion of cells involved in generating calcium activity (from 45.6±9.1% in Intact group to 64.5±19.8% in the Chronic BIMU8 group), while the level of calcium correlation dynamics remained unchanged. To assess the contribution of glial cells to changes in neural network calcium dynamics induced by 5-HT4R activation, we analyzed the influence of acute and chronic 5-HT4R activation on calcium activity in monoastrocytic cultures. No significant alterations in network characteristics of calcium activity or parameters describing individual calcium events (duration, frequency) were observed. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00178.

THE 5-HT1A RECEPTOR IN BTBR MICE AUTISM. EM Kondaurova, TV Ilchibaeva, AS Tsybko, VS Naumenko, NK Popova, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia. **INTRODUCTION**: Autism spectrum disorder (ASD) is currently one of the most commonly diagnosed neurological disorders. It is known that serotonin 5-HT_{1A} receptor participates in the mechanisms underlying social and repetitive behaviors as well as learning and memory, which are impaired in ASDs. Particular attention is drawn to the transcription factor Freud-1 (encoded by the *Cc2d1a* gene), which regulates many intracellular signaling pathways and suppresses the expression of 5-HT1A receptor gene. It is known, that dysfunction of Freud-1 leads to the development of various psychopathologies. We investigated the effects of 5-HT_{1A} receptor overexpression and suppression of *Cc2d1a/Freud-1* gene expression, induced by administration of corresponding adeno-associated viral constructs (SynH1-2_HTR1A-EGFP and SynH1-2 H1-2_shRNA-Freud-1) into the hippocampus of BTBR mice, on the behavior and functional state of the brain serotonin system. **METHODS:** Five weeks after the AVVs constructs injection the behavior of mice were analyzed in open-field, marble burying, three-chambered, elevated plus maze (EPM), Morris water maze (MWM) tests. The “operant wall” was used to estimate the impact of 5-HT_{1A} receptor overexpression on associative learning in BTBR mice. The mRNA and protein levels were assessed by real-time RT-PCR and western blot correspondently. The data were analyzed using one-way ANOVA. Results of MWM were analyzed using repeated measures ANOVA. **RESULTS AND DISCUSSION:** Five weeks after administration of the AVV “SynH1-2 H1-2_shRNA-Freud-1” construct, an increase in anxiety in the EPM test as well as the time spent on the platform and the time required to cover the distance to the platform in the MWM were found. However, Cc2d1a/Freud-1 knockdown did not affect spatial memory in MWM, and had no effect on the phosphorylation of the transcription factor CREB, the expression of 5-HT1A receptors and key genes of NF-κB signaling pathway (*Nfkb1* and *Rela*). 5-HT_{1A} receptor overexpression reduced stereotyped behavior in the marble-burying test and extended the time spent in the center in the open field test. On the molecular level, 5-HT_{1A} receptor overexpression raised hippocampal 5-HT_7 receptor mRNA and protein levels. Additionally, the 5-HT_{1A} receptor overexpression lowered both mRNA and protein levels of TrkB receptor. Thus, obtained results suggest (i) the involvement of the 5-HT and BDNF systems’ interaction mediated by 5-HT_{1A} and TrkB receptors in the mechanisms underlying autistic-like behavior in BTBR mice and (ii) that the transcription factor Freud-1 plays a role in the pathogenesis of anxiety and in the mechanisms of active stress avoidance in autism. **RESEARCH SUPPORT:** Russian Science Foundation project 22-15-00028. Mouse maintenance: Basic Research Project FWNR-2022-0023.

BDNF IS IMPLICATED IN THE MECHANISMS OF AUTISTIC-LIKE BEHAVIOR IN BTBR MICE. AS Tsybko, TV Ilchibaeva, AI Sherbakova, YP Kaminskaya, DV Eremin, VS Naumenko, Institute of Cytology and Genetics SB RAS; Novosibirsk State University, Novosibirsk, Russia. The mechanisms underlying autism spectrum disorder (ASD) are still poorly understood, but impaired neuroplasticity undoubtedly plays an important role in the development of the disease. Brain-derived neurotrophic factor (BDNF) significantly implicated in regulation of neuronal plasticity and behavior. In addition, a large number of human and animal studies indicate the involvement of BDNF in the pathogenesis of ASD. The reduced BDNF mRNA and protein levels in the hippocampus and the frontal cortex of BTBR mice (validated as the model for ASD) have been demonstrated in a few studies but these data are scarce and incomplete. Here we investigated *Bdnf* exon transcripts expression as well as BDNF and its precursor proBDNF proteins in the hippocampus (HC), frontal cortex (FC), striatum (ST) and midbrain (MB) of BTBR mice in comparison with normosocial C57Bl/6 mice. The mRNA levels of *Bdnf* exons 1-4 decreased in HC of BTBR mice. In the ST of BTBR mice, the number of transcripts *Bdnf* exons 1, 2, 4 also decreased. The mRNA levels of *Bdnf* exons 1 and 6 decreased in FC of BTBR mice. The proBDNF level, as well as proBDNF/BDNF ratio, increased in HC and ST of BTBR mice. Next, we tried to compensate deficits of mature BDNF in BTBR mice by either i.c.v. injection of recombinant BDNF protein or its overexpression in neurons using AAV vectors encoding *Bdnf* gene under synapsin promoter. Administration of BDNF protein failed to alter behavior of BTBR mice. However, a decrease in the proBDNF/BDNF ratio in ST was detected after i.c.v injection of BDNF. Hippocampal overexpression of BDNF significantly reduced anxiety-related and stereotyped behavior of BTBR mice without affecting their social interest. In contrast, overexpression of BDNF in the FC of BTBR mice exclusively increased social interest, but not other types of behaviors. Thus, we found, for the first time, significant changes in expression of specific *Bdnf* transcripts that may underlie impaired BDNF maturation in BTBR mice, as evidenced by the proBDNF prevalence. We also demonstrated that direct compensation of mature BDNF deficit by induction of BDNF overexpression can ameliorate autistic-like behavior in BTBR mice, but this effect strongly depended on the target brain structure. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00028.

SEROTONIN 5-HT$_4$ RECEPTOR AFFECTS AGGREGATION AND PHOSPHORYLATION OF TAU PROTEIN. TV Ilchibaeva, VS Snisar, NA Shved, VV Kumeiko, VS Naumenko, Institute of Cytology and Genetics SB RAS, Novosibirsk State University, Novosibirsk, Far Eastern Federal University, Vladivostok, Russia. The accumulation of hyperphosphorylated forms of Tau protein in CNS cells causes neurodegenerative diseases, including Alzheimer's disease (AD). Mounting evidence indicates that the serotonergic (5-HT) system is directly related to the development of taupathies. Although the molecular mechanisms of Alzheimer's disease remain unclear understood, the role of 5-HT receptors in its pathogenesis may be significant. It is known that in people suffering from AD, the number of serotonin receptors type 4 (5-HT$_4$) is significantly reduced. It was demonstrated in animal studies that 5-HT4 receptors are implicated in memory formation. To investigate a possible link between 5-HT$_4$-mediated signaling and Tau protein phosphorylation, N2A neuroblastoma cells were transfected with vectors carrying sequences encoding hemagglutinin (HA)-5-HT$_4$-tagged and green fluorescent protein-tagged Tau[R406W]-eGFP mutant protein of human. It was shown that co-expression of 5-HT$_4$ with Tau[R406W] led to pronounced hyperphosphorylation of Tau protein, which was accompanied by an increase in the total amount of Tau protein. Interestingly, phosphorylation of Tau in Thr181 decreased both upon stimulation of the receptor with the highly selective agonist BIMU-8, and upon exposure to the inverse agonist GR-113808, as well as after blocking of the 5-HT$_4$ receptor with its antagonist GR-125487. However, these drugs did not prevent receptor-induced Tau accumulation. Using Förster resonance energy transfer approach (Cdk5-mTurquoise2 and 5-HT$_4$-YPet served as the donor and acceptor, respectively) we identified heterocomplex between 5-HT4 receptor and Cyclin-dependent kinase 5 (Cdk5) known to be essential for Tau hyperphosphorylation. Thus, we have shown for the first time that 5-HT4 receptors promote the accumulation and hyperphosphorylation of Tau protein, which is reversed by blockade of the receptors. We also hypothesized that the effects of 5-HT4 receptor on Tau protein may be mediated by physical interaction and potential modulation of Cdk5. The data obtained allow us to rethink the role of the 5-HT$_4$ receptor in the AD pathogenesis. **RESEARCH SUPPORT**: Russian Science Foundation grant 22-15-00011.

EFFECT OF THE 5-HT7 RECEPTOR GENE OVEREXPRESSION IN THE MIDBRAIN ON BEHAVIOR AND NEUROPLASTICITY IN MICE DURING LONG-TERM ETHANOL CONSUMPTION. DV Bazovkina, AS Oreshko, AYa Rodnyy, VS Naumenko, Federal Research Center Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia. **INTRODUCTION:** The brain-derived neurotrophic factor (BDNF) and serotonin (5-HT) neurotransmitter system are involved in regulation of neuroplasticity and behavioral disorders, including those associated with long-term alcohol consumption. The 5-HT7 receptor is involved in autoregulation of 5-HT system, as well as in the development of psychopathologies such as anxiety and depression. **AIM:** To study the effects of adeno-associated viral (AAV) construct SynH1–2_HTR7–EGFP injection into the midbrain, driving the 5-HT7 receptor gene overexpression, on behavior, the 5-HT system and BDNF expression in the brain structures during long-term ethanol consumption in C57BL/6 mice. **METHODS:** For 6 weeks after AAV construct injection, the animals consumed 10% ethanol (control mice drank water). Behavior was assessed in the open field test, dark-light box, forced swimming test. The mRNA levels were determined by real-time RT-PCR, protein contents were evaluated by Western blot. Levels of 5-HT and its metabolite 5-HIAA were measured using HPLC. Data were processed by two-way ANOVA followed by Fisher's multiple comparisons. **RESULTS AND DISCUSSION:** Locomotor activity in the open field test was not different between mouse groups. The injection of construct with *Htr7* gene led to increase in the anxiety level in mice that received both water and ethanol ($p<0.05$). Mice injected with the target gene construct showed a significant increase in *Htr7* mRNA level only in the midbrain ($p<0.001$). Ethanol decreased the *Htr1a* mRNA level in the frontal cortex and hippocampus ($p<0.001$) and increased it in the midbrain ($p<0.05$). AAV construct injection decreased the level of *Htr1a* mRNA in the hippocampus only in mice drinking water ($p<0.001$). Alcoholization led to augmentation of 5-HIAA/5-HT ratio in the hippocampus and midbrain ($p<0.001$), while AAV construct injection with *Htr7* gene led to increase in this ratio in the midbrain only in mice drinking water ($p<0.05$). Moreover, *Htr7* gene overexpression caused decrease in *Bdnf* gene mRNA level in the frontal cortex of mice treated with ethanol ($p<0.05$). Only in animals drinking water, AAV construct injection led to increase in proBDNF level in the midbrain ($p<0.01$), frontal cortex ($p<0.05$) and hippocampus ($p<0.01$), as well as an increase in BDNF content in the frontal cortex ($p <0.05$). Thus, the *Htr7* gene overexpression in the midbrain increased anxious behavior in mice, regardless of ethanol consumption. In addition, long-term alcoholization weakened the effects of overexpression on the 5-HT system and the proBDNF and BDNF proteins levels in the brain structures. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00011.

SYMPOSIUM 3: ZUKOVSKA-PASTUKHOV SYMPOSIUM ON TRANSLATIONAL NEUROSCIENCE (Chairs: AV Kalueff, AV Semyanov, IV Ekimova)

BEHAVIORAL TESTS OF THE MOUSE VISUAL FUNCTION UNDER OPTOGENETIC THERAPY USING TRANSFORMER MAZE. VI Ni, EV Filatova, IY Morina, ML Firsov, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia. **INTRODUCTION:** Studies of the mechanisms of visual impairment and restoration require an assessment of the work of visual function at all levels. At the behavioral level, there are various tests such as maze-based tests, alternative forced-choice task, looming visual stimuli, black white box, optokinetic nystagmus and others. These methods, however, have some disadvantages. Some of them require previous learning, some of them depend on individual emotional features. The Transformer maze allows us to study separately different navigation strategies under identical conditions. **METHODS:** We use the Transformer maze for study mouse visual in two tasks. The first task is following the black line drawing on the floor. The second task is free wandering through maze compartments with different level of illumination within some of them. This task is the variant of the black white box. However, unlike it, the animal has a choice between the white or black at every point of the space. A cross was being built inside the transformer maze. In one case, the animals explored the space with the same illumination, in another, the periphery was dark and the center was light, and in the third, on the contrary, the periphery was light and the center was dark. Adult C57BL/6 mice were used in these studies. For the first task animals previously were trained following the black line. One group got retinal damage by intravitreal injection of the tunicamycin. Control animals got PBS injections. The electroretinogram was used for test the retinal function. Half of blind animals got optogenetic therapy with plasmid contains rhodopsin. **RESULTS AND DISCUSSION:** Unlike the control animals, all retinal damage animals had difficulties with following the black line in the first test. They had visiting cul de sacs, often returning and spending long time finding the reinforcements. The second test also showed the differences between groups. The control animals spent time in the center and the periphery of the maze in the similar proportion in case with the same illumination of all parts of the maze. In case with different illumination, they spent more time in the dark area regardless of the geometry. All the retinal damage animals spent more time at the peripheries regardless of illumination. However, animals that received optogenetic therapy showed more time in the center than animals without therapy. It can be assumed that blind animals are completely switched to the tactile navigation and had exploring the environment only based on peripheral edge. At the same time, animals that received optogenetic therapy showed less attraction for the periphery, which may indirectly indicate to the incomplete switch to the tactile orientation, which may be a consequence of the visual system activity. **RESEARCH SUPPORT:** State task 075-00264-24-00.

EFFECT OF INTRAVENOUS ADMINISTRATION OF CAFFEINE MODULATED SPLENOCYTES IN THE DEVELOPMENT OF NEUROINFLAMMATORY PROCESSES IN THE MODEL OF LASER-INDUCED TRAUMATIC BRAIN INJURY IN ZEBRAFISH. TG Amstislavskaya, EV Markova, EV Nehoroshev, WS Hao, MA Kleshchev, AA Akopyan, MA Tikhonova, IV Savkin, EV Serenko, AV Kalueff, Novosibirsk State University, Scientific Research Institute of Neurosciences and Medicine, Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia. **INTRODUCTION:** Traumatic brain injury (TBI) is accompanied by multiple pathophysiological changes that may also be lethal. Neuroinflammation is one of the key pathophysiological mechanisms of TBI, often exacerbating pathological processes in the brain and preventing its recovery. Thus, reducing neuroinflammation may provide a positive effect in the treatment of neurological disorders caused by TBI. Previously, we were the first to demonstrate that intravenous administration of caffeine-modulated splenocytes activates neuroplastic processes in the brain during neurodegenerative changes, including by reducing neuroinflammation. **AIM:** To study the effect of intravenous administration of caffeine-modulated splenocytes on neuroinflammation in the model of laser-induced traumatic brain injury in zebrafish (*Danio rerio)*. **METHODS:** Here, we assessed the differential expression of genes of interest involved in the control of neuroinflammation, the production of the microglial activation marker IBA1, determined the levels of interleukins in the brain, and tested

the effects of intravenous administration of splenocytes stimulated by pre-culturing *in vitro* with caffeine (150 μg/ml for 20 min) on these parameters and fish behavior 1 and 3 days after TBI. **RESULTS AND DISCUSSION:** On Day 3 post-TBI, the administration of caffeine-modulated splenocytes lowered the expression of interleukin 1 beta (*Il-1b*), metalloproteinase 9 (*mmp9 and cd40*) genes, and the production of the protein IBA-1 (a marker of activated microglia). Overall, splenocytes treated *in vitro* with caffeine had a stimulating effect on the production of proinflammatory cytokines (IL-1β and IL-6) on Day 1, and an anti-inflammatory cytokine IL-10 on Day 3 past TBI. Increased production of a pro-inflammatory cytokine IL-6 following intravenous administration of caffeine-modulated immune cells persisted on Day 3, whereas this effect was absent in control fish. Behavioral analyses using controlled machine learning protocol showed that the administration of caffeine-modulated splenocytes rescued behavioral deficits evoked by TBI on Days 1 and 3, whereas caffeine itself did not have such an effect. Overall, intravenous administration of caffeine-modulated splenocytes may represent a promising therapeutic approach for neurotrauma of various origins. **RESEARCH SUPPORT:** Russian Science Foundation grant 20-65-46006.

ADAPTIVE AND PATHOLOGICAL RESPONSES TO STRESS: REEVALUATING PTSD PATHOPHYSIOLOGY. AP Sarapultsev, MV Komelkova, EY Gusev, South Ural State University, Chelyabinsk, Russia. **INTRODUCTION:** The delineation between adaptive physiological responses and pathological outcomes in stress and trauma presents a nuanced challenge in understanding Post-Traumatic Stress Disorder (PTSD) and related disorders. This exploration suggests that responses traditionally classified as pathological may, under certain contexts, represent necessary physiological adaptations aimed at resilience and survival. **RESULTS AND DISCUSSION:** Research supported by Richter-Levin et al. (2019) highlights that early life stress and predator stress models may initially trigger adaptive and resilience-building physiological, structural, and molecular changes following trauma. For instance, maternal deprivation, rather than being purely pathological, might be an accelerated physiological preparation for independent life, induced prematurely. This is conceptualized through the 'training reaction' - nonspecific adaptive reaction to weak stimuli, increasing sensitivity to subsequent stress without pronounced behavioral effects initially. The 'activation reaction' follows the 'training reaction', representing a nonspecific adaptive response to medium stimuli, such as olfactory stress, that prepares the body for future challenges by activating its regulatory and protective systems. Similarly, classical fear conditioning, a fundamental survival mechanism, can become pathological only when adaptive fear responses to severe trauma fail, suggesting a collapse of these mechanisms. This balance between adaptive responses and pathological processes is crucial for understanding PTSD, emphasizing the need to consider the context under which physiological responses may become maladaptive. Examples of potentially non-pathological effects further illustrate this perspective. Stress-induced neurogenesis and acute neuroinflammatory responses, typically seen as negative, may serve as preparatory mechanisms for future stressors or recovery from trauma, respectively. Additionally, HPA axis hyperactivity and heightened autonomic nervous system reactivity, while often associated with stress pathology, are vital for survival responses in the face of immediate threats. In conclusion, the reevaluation of stress responses from adaptive mechanisms to pathological outcomes offers a framework for understanding the complex interplay between physiological adaptations and the development of pathology. This perspective challenges traditional views, advocating for a nuanced interpretation of experimental models, with the ultimate aim of enhancing our comprehension of PTSD and informing the development of effective interventions.

CHRONIC SLEEP RESTRICTION: CONSEQUENCES FOR THE BRAIN AND ENDOCRINE FUNCTIONS. IV Ekimova, MB Pazi, KV Lapshina, KV Derkach, AO Shpakov, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. **INTRODUCTION:** Chronic sleep restriction (CSR) is one of the most substantial problems of our time and is considered one of the root causes and predisposing factors of daytime sleepiness, cognitive deficits, anxiety and depression. These disturbances indicate serious functional disorders in the central nervous system, which currently remain largely unexplored. A growing body of epidemiological data link short sleep with impaired hormonal and metabolic status, which is considered as a factor contributing to an increasing incidence of obesity, type 2 diabetes mellitus, hypertension and erectile dysfunction. However, specific endocrine disorders induced by lack of sleep and the mechanisms of their development remain unclear. The aim of the study was to assess cellular and molecular rearrangements in the monoaminergic systems of the brain that control neurobehavioral functions, and their link to changes in metabolic and hormonal parameters of the thyroid, gonadal and adrenal systems in CSR in rats. **METHODS:** A model of CSR was studied in six-month-old male Wistar rats which underwent cycles of 3 h of sleep deprivation (SD) and 1 h of sleep opportunity continuously for

5 days on the programmed orbital shaker. The control group of rats lived in the same conditions, but without SD. Markers of neurodegeneration, endoplasmic reticulum (ER) stress and indicators of hormonal and metabolic status were evaluated after day 5 of CSR and on day 56 of the recovery period. **RESULTS**: CSR leads to structural rearrangements (apoptotic neurodegeneration) in the locus coeruleus noradrenergic system and dopaminergic mesolimbic systems, which mediate the regulation of the sleep-wake cycle, endocrine-metabolic, vegetative and behavioral reactions of the brain. Irreversible damage to neurons in these systems was caused by the activation of the PERK/CHOP proapoptotic pathway of ER stress. CSR decreased the secretion of leptin, insulin and testosterone, and increased serum triiodothyronine T3 and corticosterone in rats. Elevated corticosteroid levels may be one of the root causes of thyroid and androgenic status disorders, and may also be associated with a weakening of the insulin and leptin systems. Despite the fact that these indicators recover over time, repeated cases of sleep deficit can lead to persistent cumulative disorders in the neuro-endocrine systems. **CONCLUSIONS:** The present study shows detrimental effects of CSR on the brain and endocrine functions and highlights the need to develop a therapeutic strategy to protect the body from the damaging effects of sleep deficit. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation (agreement with the World-class Research Center “Pavlov Center” 075-15-2022-296).

THE ROLE OF WATER CHANNEL AQP4 IN THE NEUROPROTECTIVE MECHANISMS IN A RAT MODEL OF PARKINSON’S DISEASE. KV Lapshina, MV Khanina, MA Guzeev, MP Kaismanova, IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. **INTRODUCTION:** Water channel aquaporin-4 (AQP4) is tightly associated with the control of brain water homeostasis and glymphatic clearance of brain parenchyma from various metabolites, such as amyloidogenic proteins, contributing to the development of Parkinson’s disease (PD) and other neurodegenerative diseases. The key role in PD pathogenesis belongs to the misfolded α-synuclein and its toxic oligomers. **AIM:** To evaluate the effect of AQP4 knockdown in the substantia nigra pars compacta (SNpc) on the development of α-synuclein pathology, neurodegeneration rate, and compensatory processes in the nigrostriatal system in a rat model of PD. The knockdown of AQP4 was induced by nigral microinjection of the lentiviral construct with a nucleotide sequence encoding the hairpin RNA to the mRNA of AQP4 protein. The model of the clinical stage of PD was reproduced using microinjections of the selective proteasome inhibitor lactacystin (LC) into the SNpc 3.5 weeks after the administration of the lentiviral construct. Behavioral tests, immunoblotting, and immunohistochemistry were used to assess motor disturbances, α-synuclein pathology, and neurodegenerative changes in the nigrostriatal system. The model of the clinical stage of PD is characterized by the development of motor disturbances, α-synuclein pathology, loss of 68% of dopaminergic neurons in the SNpc, and a decrease in the level of tyrosine hydroxylase (TH), a key enzyme in dopamine (DA) synthesis, and vesicular monoamine transport 2 (VMAT2) in SNpc neurons. Knockdown of AQP4 in the SNpc in a PD model led to the appearance of more severe disturbances in fine motor skills, an extreme degree of sensorimotor deficit, and signs of hypokinesia and dystrophy. The pathomorphological analysis revealed an increase in the number of α-synuclein aggregates, an increased loss of DA neurons of the SNpc (by 1.4 times) and its axons in the dorsal striatum (by 1.2 times) compared to LC alone, and a decrease in the levels of TH and VMAT2 in the SNpc neurons, which could indicate a weakening of compensatory mechanisms aimed at maintaining DA transmission. **CONCLUSIONS:** Overall, this is the first study to show that AQP4 knockdown in the SNpc evoked the development of the terminal phase of the clinical stage of PD, causing aggravation of α-synuclein pathology, death of 89% of DA neurons in the SNpc and their axons in the striatum, attenuation of compensatory mechanisms, and aggravation of the severity of motor disorders and signs of dystrophy. Our findings suggest that the AQP4-mediated glymphatic system plays an important role in the protection of brain functions from neurotoxic factors in the development of Parkinson-like pathology. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-25-00607.

ISBS TALK: HIPPOCAMPUS AND AMYGDALOID NUCLEI - THE BRAIN STRUCTURES MOST RESISTANT TO VOLUME DECREASE IN PHYSIOLOGICAL AGING: MR VOLUMETRIC STUDY. D Kozic, S Stojanoski, J Boban, University of Novi Sad Faculty of Medicine, Novi Sad, Serbia. **BACKGROUND:** The differentiation between physiological aging and initial or subclinical forms of dementia is a rather demanding task. The main goal of this study was to determine which brain structures are most prominently prone to aging. **METHODS:** The study group was composed of 40 healthy patients who were, based on age, divided in two groups, younger with average age 26,75 +/- 2,47 SD and older group which averaged 68,5 +/-5,26 SD years. All patients were scanned with an MR scanner and volumes of their brain structures were calculated by voxel-based morphometry. **RESULTS:** In the group of older patients compared with younger group, there was a

significant decrease of total cerebral volume ($p<0.001$), total gray matter volume ($p<0.0001$), total white matter volume ($p<0.024$), average thalamic volume ($p<0.0001$), average putamen volume ($p<0.0001$) and average caudate volume ($p<0.004$), while the average volumes of lateral ventricles presented statistically significant increase ($p<0.002$). There was no significant decrease of hippocampal ($p=0.438$) and amygdala ($p=0.373$) volumes between two groups. **CONCLUSIONS:** Hippocampi and amygdala seem to be the most resistant to volume loss in healthy brain aging compared to other brain structures.

ISBS TALK: INNOVATIVE APPROACHES TO NEUROMODULATION AFTER SPINAL CORD INJURY. PE Musienko, Laboratory of Neuroprostheses, St. Petersburg State University, Pavlov Institute of Physiology RAS, St. Petersburg, Neurobiology Department, Sirius University of Science and Technology, Sirius, Neurorehabilitation Technologies Laboratory, LIFT (Life Improvement by Future Technologies) Center, Moscow, Russia.

SYMPOSIUM 4: EXECUTIVE FUNCTION IN ONTOGENESIS (Chairs: EI Nikolaeva, KI Kunnikova, Discussant: M Lebedev)

THE ROLE OF EXECUTIVE CONTROL IN THE EFFECTIVENESS OF COGNITIVE TRAINING. OM Razumnikova, Novosibirsk State Technical University, Novosibirsk, Russia. **INTRODUCTION:** Executive functions (EFs) involved such cognitive functions as planning, attention, and cognitive flexibility that associated with regulating thought, emotion, behaviors and are important to student success during professional training. EFs are measured using both rating scales and performance-based tests. However, divergent evidences indicate cross-method associations between the approaches. The main purpose of the present study is to evaluate the relation between different components of EFs measured using self-assessment approach (Executive Skills Questionnaire (ESQ)) and the neuropsychological testing by the Attention Network Test (ANT) and Working Memory (WM). Other aim was to study the association between EFs and efficiency of both WM and visual-spatial memory training. **METHOD:** The sample comprised 110 university students, aged 18.3±1.8 years. The ESQ consists of 40 items to measure executive skills on a 7-point Likert scale (from never/rarely (0) to very often (7). The ESQ has twelve factors: Response Inhibition (RI), Working Memory, Emotional Control (EC), Task Initiation (TI), Sustained Attention, Planning, Organization, Time Management, Flexibility, Metacognition (M), Goal-Directed Persistence, Stress Tolerance (ST). A higher score indicates higher level of executive functioning. ANT is designed to evaluate alerting, orienting, and executive attention is a response inhibition task in which a motor response (RT) must be executed or inhibited based on a stimulus cue (Fan et al., 2002). The computerized tests were used to evaluate self-regulated training one-back working memory (WM) and visual-spatial memory (VSM) while their performing at home using psytest.nstu.ru site. **RESULTS AND DISCUSSION:** In ESQ profile, TI and ST have minimal scores whereas RI and M are characterized maximal self-assessment. Significant correlations are found between RT while stimulus selection due to ANT and EFs measured by ESQ, namely, between alerting function and EC, P and ST ($0.02<p<0.04$). The detected positive correlation between RT due to executive attention and WM performing ($p<0.01$) is consistent with the idea of an increase in inhibitory processes after the realization of WM error, which is reflected by a slowdown in decision making in the system of attention executive control. Computerized training of WM and VSM has a positive effect. However, the success of WM training is a result already in the first ten sessions that determined by the summation of the EFs components including both WM and processing speed. A significant increase in short-term VSM is achieved only after twenty training sessions ($p<0.001$). It can be assumed that the more complex the mental function being trained, the more time and more executive control reserves are required to achieve success. Given the known individual differences in baseline levels of memory and executive functions, the findings are consistent with the view that cognitive training programs should incorporate adaptive task difficulty to optimize efficiency of task-related brain activity. Regarding the research results, EFs performance and their self-ratings in university students showed a significant association. Cognitive training may have positive impact on the EFs components and increasing the flexibility of the brain and cognitive reserves toward repeating and practicing in learning processes.

THE INFLUENCE OF SCREEN TIME ON THE QUALITY OF EXECUTIVE FUNCTIONS OF PRESCHOOL CHILDREN. Nikolaeva EI, Kalabina IA, Sutormina NV, Isachenkova MV, Herzen State Pedagogical University, St. Petersburg, Russia. The purpose of the study was to describe the effects of screen time associated with the use of gadgets on the executive functions of preschool children.

The study involved 95 children aged 4 to 7 years. Study design: An interview with children about their experiences using gadgets, followed by testing their working memory (Razumnikova and Nikolaeva, 2019) and inhibitory control (Vergunov and Nikolaeva, 2013). EEG was next recorded at rest for 5-10 min (depending on the child's behavior), after with the child played the game "Tom for Gold" on a smartphone for 5 min, and EEG was recorded again at rest. The researcher recorded the number of errors the child made during the game. An error is a collision with an obstacle. An Italian BE Plus LTM electroencephalograph from the EBNeuro family of amplifiers was used to collect EEG data with 61 electrodes. During the preprocessing stage, artifacts were removed manually using the Matlab-based EEG LAB program. Further processing was carried out using the Python programming language using the MNE and networkX modules. The connectivity pattern was assessed using the phase lag index (PLI). Global Connectivity Index, Network Density, Average Connectivity Strength and Clustering Coefficient were calculated. It was shown that children who spend 1-3 h with gadgets on weekdays made fewer errors when tested on the maturity of inhibitory control. Children with more experience using gadgets performed more successfully and more slowly on a task assessing inhibitory control. Global network connectivity indicators increased after the game, as did overall connectivity between different brain regions.

FORMATION OF EXECUTIVE FUNCTIONS IN CHILDREN WITH EXPERIENCE OF INSTITUTIONALIZATION. E Dydenkova, G Portnova, K Minin, Nizhny Novgorod State Pedagogical University, Nizhny Novgorod, Institute of Higher Nervous Activity and Neurophysiology, Moscow, Russia. **INTRODUCTION:** The experience of institutionalization has a negative impact on the development of children, including the development of executive functions. Thus, fostered children have lower levels of attention, planning and working memory, a significant deficit in visual memory, and the lack of adequate social interaction in early childhood leads to a decrease in self-regulation functions. Moreover, problems of cognitive development are observed even after seven years of stay in a foster family. **METHODS:** The study involved 165 fostered (53.4%) and blood children aged from 4 to 16 years, who made up 5 age cohorts: junior preschoolers (N=45; 5.12±0.53); older preschoolers (N=32; 6.39±0.28); junior schoolchildren (N=53; 9.06±1.37); younger adolescents (N=15; 13.27±0.72); and older adolescents (N=16; 15.65±0.44). Working memory and inhibitory control were assessed using computer-based psychophysiological techniques. An anamnesis of each child was collected, including features of the early biography. **RESULTS AND DISCUSSION**: Blood children are more attentive ($p<.001$), better able to resist fatigue ($p<.001$) and more inclined to learn ($p=0.003$). Children with early experience of institutionalization are less likely to learn ($p<0.001$), have worse speed indicators of reactivity ($p<0.05$), are less attentive ($p<0.05$) and get tired more quickly compared to children who received the same experience, but at a later age. However, when assessing the influence of the duration of institutionalization experience on the propensity to learn, significant differences were found both in the group of children staying in an orphanage for up to 12 months ($p=0.032$) and over 36 months ($p=0.002$), and in the group of fostered children, but without experience in an orphanage ($p=0.041$). All this speaks to the critical importance of preserving the biological family, the need for programs to prevent the removal of children from their biological family and to support the resilience of mothers in vulnerable situations. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00324 "Social tactile contacts and their role in psycho-emotional rehabilitation".

THE SPECIFICS OF EXECUTIVE FUCTIONS IN YONGER CHILDREN WITH INTELLECTUALL DISABILITIES. E Dunaevskaya, Herzen State Pedagogical University of Russia**,** St. Petersburg, Russia. The article presents the results of a study of the executive functions of primary schoolchildren with intellectual disabilities and normatively developing children. It has been revealed that children with intellectual disabilities have limited abilities to plan and organize activities, focus attention and switch it from one task to another, work with information in working memory and regulate their emotions and behavior. **METHODS:** software package for determining the characteristics of visual-spatial memory systems, interference; ReBOS technique (Vergunov, 2009); Raven's progressive matrices. The number of remembered stimuli and the speed of task completion are significantly lower than in children with normative development. A decrease in the number of stimuli from series to series indicates a decrease in reproduction and a weakening of inhibition processes. A simple sensorimotor reaction determines the reaction speed of selecting a particular stimulus. When a complex sensorimotor reaction occurs, it is prohibited to react to one of the stimuli. In this case, the number of erroneous reactions serves as a measure of inhibitory processes in a person. The results of simple and complex sensorimotor reactions in schoolchildren with intellectual disabilities indicate a longer time for completing tasks, a large number of errors when pressing when a stimulus appears when there is no need to press. When studying a complex sensorimotor reaction, the time to complete the

task is prolonged and the requirement becomes more complicated when you cannot click on the red circle when it appears on the screen. The difficulty of completing the task was determining the sequence and monitoring one's actions. This is due to the maturation of the prefrontal cortex, which from an evolutionary point of view is considered a relatively late-emerging structure, shaped during the first ten years of a child's life by the development of lower order sensorimotor and visual cortices. The quality of inhibitory processes determines the accuracy of sensorimotor integration, which depends on maturational processes in the brain.

PSYCHOPHYSIOLOGICAL FACTORS OF RESISTANCE TO SUBSTANCE DEPENDENCE. P Ivashina, Herzen State Pedagogical University of Russia, St. Petersburg, Russia. **INTRODUCTION:** The protective abilities of the individual are associated with executive functions, which are controlled by the brain region that emerged late in evolution and matured late in ontogenesis - the prefrontal cortex. None of the existing models of chemical dependency treatment is effective enough to be unconditionally accepted in different countries. New approaches to both prevention and correctional work with addicts are required. The purpose of the study is to identify factors influencing a person's resistance to psychoactive substances: psychophysiological, psychological, socio-demographic. A total of 232 people were examined. The control group included 82 people aged 34.7±9.4 years (of which 48% were women and 52% were men) who did not use psychoactive substances. The experimental group consisted of 150 people aged 35.6±7.8 years (39% women and 61% men) with long-term 5-20-year drug and alcohol use. The subjects did not differ in age, level of education and gender. **METHODS:** Questionnaire of socio-demographic characteristics, Methodology "Scale of Progressive Matrices" by Raven, Abbreviated Multifactor Personality Questionnaire, Methodology for diagnosing formal dynamic by Strelyau, methodology for assessing braking processes, Methodology for describing working memory mechanisms. **RESULTS AND DISCUSSION:** Nonverbal intelligence decreases in all groups of subjects with experience of using psychoactive substances. These changes are more pronounced the more complex and non-trivial the task. Formal dynamic characteristics indicate that people with experience of using psychoactive substances turn on compensatory mechanisms that allow them to cope with the changes that occur temporarily. There seems to be a significant connection between the level of development of executive functions in adulthood and the age of the mother at the birth of the child: the older the mother is at the birth of the child, the more developed the executive functions of her child are in adulthood. Executive functions may be protective factors that prevent a person from becoming addicted.

PRECURSORS OF FEATURES OF COGNITIVE DEVELOPMENT OF PREMATURE CHILDREN IN PRESCHOOL AGE. OA Ivanova, Voronezh State University, Voronezh, Russia. **INTRODUCTION:** Each year, about 10,6% of babies, or 14,84 million, are born before 37 weeks of gestation. These children are more likely than other infants to die before age 5 years (Lee et al. 2019). Up to 20,0% of preterm infants are considered moderately preterm (32–33 weeks' gestation) and 60,0–70,0% are considered late preterm (34–36 weeks' gestation) (Goldenberg et al. 2008). At the moment, the statistics of disability as a consequence of prematurity are as follows: 22–24 weeks (500–600 g): total 20–80%; disability 90–100%; 24–26 weeks (600–700 g): total 16–40%; disability 40–60%; 26–28 weeks (700–1000 g): only 7 – 20%; disability 20 – 40%; More than 28 weeks (more than 1000 g): only 5–10%; disability up to 20%. Such data indicate the extreme relevance of research into the precursors of the characteristics of cognitive development of premature children in preschool age. However, the problem lies in the contradictory data that currently exists regarding this category of children. Thus, in most studies, observation of premature babies continues only during the first year of life. At the same time, the need to predict the consequences of prematurity is explained by their extreme diversity, because very severe children at birth may not have deterioration in cognitive abilities in the future, and, on the contrary, a child who seemed quite well at birth later showed severe impairments, including the inability to attend general education institutions. There is also evidence that long-term outcomes of perinatal stroke, in association with characteristics of the stroke lesion (size and location), may act as prognostic factors for somatic, but not cognitive, development. Thus, the high inconsistency of the available data on the cognitive development of children born prematurely necessitated the need for a study, the purpose of which was to compare data obtained from premature children with different severity of pathological manifestations at birth, with the peculiarities of lateral preferences and parameters of executive functions in these same children aged 3-9. The sample consisted of premature children born with I, II, III, IV degrees of prematurity. The total sample size is 17 children, of which 8 are boys and 9 are girls. There were 11 children with I and II degrees of prematurity, 6 with III and IV degrees. 11 children were diagnosed with cerebral ischemia of varying severity. The sample consisted of children 3-9 years old. The research bases were the Perinatal Center and the Children's Clinic No. 11 (Voronezh, Russia). **METHODS:** Analysis of documents (extracts from the Perinatal

Center) - analyzed data obtained as a result of one of the most important indicators of the condition of a premature baby - neurosonography, which allows you to determine the possibility of hemorrhage in the child, and, accordingly, assess the severity of brain damage. Assessing lateral preferences – the more left-leaning a child is, the more likely it is to expect slower myelination of brain structures. Left-handedness has both genetic and pathological reasons. In our case, the increased incidence of left-handedness could be the result of early brain pathology. Children's handedness was assessed using three tests (lock test, shoulder test, and drawing performed alternately with both hands). Assessment of inhibitory control (Vergunov et al., 2019) and working memory. Determination of the level of general and non-verbal intelligence (Raven's progressive matrices). Questioning of parents to determine the composition of the family, the age of the parents at the time of the birth of the child, the order of birth of the child being examined, the number of close adults caring for the child. Study of maternal emotional intelligence. Methodology for diagnosing formal dynamic characteristics by Strelyau. **RESULTS AND DISCUSSION:** Thus, the results of neurosonography in the first month of a child's life in the perinatal center, correlate with the maximum number of studied indicators: preference for the left hand in the «lock» test, the average time of a simple sensorimotor reaction, the number of stimulus omissions in the training series, in a simple sensorimotor reaction, in a complex sensorimotor reaction. Therefore, the more severe the child's hemorrhage at birth, the later he or she was more likely to use his left hand, respond more slowly to the cue, and make more omissions when presented with the cue. The degree of prematurity is determined at birth based on medical parameters, including neurosonography. It reflects the severity of brain damage. The germinal matrix located around the lateral ventricles has been associated with the formation of new neurons during the prenatal period. It should be reduced by the time the child is born, but in premature babies this process is not yet complete. All this leads to possible hemorrhages, including in the area of the lateral ventricles of the brain. The more severe the damage at birth, the more likely the child will be to prefer the left hand later, respond more slowly, and miss more stimuli. It is worth emphasizing that with genetically determined left-handedness, children, on the contrary, have faster response rates in both simple and complex sensorimotor reactions. The most important prognostic parameter for future changes in cognitive functions at the birth of a premature baby are the results of neurosonography. Our results confirm the literature that the further cognitive development of a premature infant cannot be accurately predicted by initial data obtained in the perinatal center. To study the psychological characteristics of mothers of premature babies, data on the cognitive development of which are presented above, a sample was formed comprising mothers of premature babies born between 2014-2020 in Voronezh Perinatal Center. Overall, dynamism indices were medium in 88%, low in 12%; persistence was high in 12%, medium in 59%, low in 29%; sensory sensitivity scores were medium in 88%, and low in 12%; endurance high in 24%, medium in 64%, low in 12%; emotional reactivity increased in 17%, medium in 59% and low in 24%; activity was medium in 82% and low in 18% of subjects. Qualitative processing of data using the «Emotional Intelligence Questionnaire» by Lyusin showed for general emotional intelligence that 13% of mothers showed a very low value; 27% low; 270% medium, 13% high and 20 very high levels. Further detailed studies of the psychological characteristics of mothers of premature babies and their impact on the child are necessary to introduce psychological support into the practice of nursing them, develop support programs, correct mental stability and increase the sensory sensitivity of their mothers. Mounting evidence shows that positive home environment and relationship with the mother, along with neurosonogram data, is a precursor to the characteristics of the cognitive development of premature children in preschool and primary school age.

PSYCHOPHYSIOLOGICAL MECHANISMS OF COGNITIVE DEVELOPMENT IN CHILDREN WITH ARTERIAL ISCHEMIC STROKE: RESEARCH DESIGN. KI Kunnikova, Ural Federal University, Ekaterinburg, Russia. **INTRODUCTION:** Executive functions (EF) are skills that regulate lower-level cognitive processes, allowing for the formation of goal-directed behavior (Alvarez, Emory, 2006). They include: 1) working memory; 2) cognitive control; 3) cognitive flexibility (Cristofori et al., 2019). Most researchers agree that the dynamics of EF formation influence a child's academic performance, intellectual abilities and social interaction. Of particular importance is the study of the psychophysiological foundations of EF during preschool childhood, since it is at this time that the most intense morphofunctional changes occur in various structures of the brain. The dynamics of brain maturation depend on a whole range of factors, including physiological characteristics and social conditions in which the child develops. Arterial ischemic stroke is a factor that has a very dramatic effect on brain development and, as a consequence, on the quality of human life. The prevalence of perinatal stroke is approximately 1 in 1100 births. Up to 60% of children who have suffered perinatal ischemic stroke have cognitive and emotional impairments. The study of the consequences of strokes in children is usually aimed at identifying risk factors for somatic complications and motor disorders,

while for the child to fully recover, it is also necessary to pay close attention to impaired cognitive functions. **AIM:** To reveal the relationship between the features of executive functions and the dynamics of restoration of nervous tissue in children of preschool age (6 years) who suffered an ischemic stroke at the age of up to 18 months. **METHODS:** Currently, there are data from a neurological assessment of 60 children with the onset of ischemic stroke before the age of 18 months. All participants have MRI images of the brain in the acute period. It is planned to conduct an assessment of a group of children during the outcome period. Morphometric parameters of the brain and the dynamics of neural tissue recovery will be analyzed using MRI images obtained during the outcome period. The level of development of EF will be assessed using a battery of psychological tests. To assess the distribution of attention, the «Software package for determining the characteristics of visual-spatial memory systems» was used (Razumnikova, Savinykh, 2016). To assess inhibitory control in go/no-go paradigms, a computer version of the author's complex reflexometry program ReBOS was used (Vergunov, Nikolaeva, 2009). This test allows to measure children's ability to navigate the flow of sensory signals and identify the quality of inhibitory processes. To assess cognitive flexibility, the «Raven's Colored Progressive Matrices» was chosen, which allows to evaluate the flexibility of switching between strategies for solving assigned problems. Also, using this test, it is possible to determine the level of non-verbal intelligence. A computerized version of the Corsi visuospatial test will be used to assess working memory. It is based on a computer program repeating the sequence of selecting elements on the screen. To assess the development of verbal intelligence, the standardized methodology (Determination of the level of mental development of preschoolers and primary schoolchildren) by Zambatsevičienė was used. **RESULTS AND DISCUSSION:** The expected results of the research will contribute to the understanding of the fundamental mechanisms of the brain and its functions in health and disease. In addition, early detection and prediction of cognitive impairment may be critical in recovery strategies after perinatal or pediatric ischemic stroke. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-78-01251.

RELATIONSHIP OF ONLINE INFORMATION SEARCH AND EXECUTIVE FUNCTIONS IN CHILDREN. N Sutormina, Herzen State Pedagogical University of Russia, St. Petersburg, Russia. **INTRODUCTION:** Executive functions are cognitive processes that are necessary to perform tasks that require planning, time management, decision making, and behavioral control. The development of executive functions is extremely important for the child, since it is the executive functions that contribute to the benefits of learning and are regulatory processes that allow the child to concentrate for a long time. It is possible to investigate executive functions using connectivity studies. Functional connectivity in the brain can be measured as a network using electroencephalography (EEG) signals. The electroencephalogram connectivity is little studied regarding children education. **METHODS:** The children had to find the answer to the question on the Internet. The search time and the correctness of the answer were measured. To study executive functions, two computer methods were carried out to assess inhibitory control and working memory. The study leveraged an EEG performed with eyes closed using a BE Plus LTM electroencephalograph with 64 channels. EEG pre- and processing used Python modules MNE, NetworkX and others. **RESULTS AND DISCUSSION:** Inhibitory control and working memory are significantly correlated with correct performance of an educational Internet based task. In addition, more successful task completion is associated with the Small-World organization pattern EEG**.** Connectivity. The study also showed a connection between the completion of an educational task and such global indicators of connectivity as Modularity, Global Efficiency and Average Path Length.

A COMPARATIVE ANALYSIS OF CORRELATION BETWEEN THE DEVELOPMENT OF EXECUTIVE FUNCTIONS AND INTERNAL HEALTH IN PRIMARY SCHOOLCHILDREN AND ADOLESCENTS. VS Merenkova, SA Burkova, Bunin Yelets State University, Yelets, Herzen State Pedagogical University of Russia, St. Petersburg, Russia. **INTRODUCTION:** An analysis of executive functions generation in ontogenesis is important, since their early development predetermines both academic success and health quality. It is important to compare the effectiveness of executive functions development (inhibitory control and short-term memory) with the level of internal health picture (IHP), since both indicators are sensitive to influence from the immediate environment. **METHODS:** To clarify the age-related characteristics of correlation, we used reflexometric technique "REBOS" (Vergunov and Nikolaeva, 2009), the model of proactive interference (Razumnikova and Savinykh, 2016), and child IHP diagnosis (Nikolaeva et al., 2014). The study involved 167 participants of two age groups: primary schoolchildren (9.8±0.8, n=66) and teenagers (12.8±1.5, n=101). Overall, not a single parameter of short-term memory was associated with the IHP level, suggesting that the main function of short-term memory in the chosen age range (not relevant in this case) is long-term planning. Furthermore, in the group of primary schoolchildren, IHP was associated only with omissions

of a stimulus in a simple sensorimotor reaction, and not associated with a complex sensorimotor reaction. This can be explained by the very beginning of maturation of the prefrontal cortex at this age, whose activity may hence be insignificant while making decisions regarding healthy behavior. In the teenage age group, all parameters of sensorimotor integration were associated with IHP: the higher the IHP level is, the faster the subject reacts to the assigned task, making less mistakes.

DYSFUNCTION OF THE HIPPOCAMPAL ASTROCYTES OF KRUSHINSKY-MOLODKINA RATS DURING EPILEPSY DEVELOPMENT. MV Glazova, YS Grigorieva, AA Naumova, SD Nikolaeva, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. **INTRODUCTION:** Epilepsy progression is tightly correlated not only with alterations of excitatory/inhibitory neurotransmission, but also with dysregulation of glial functions. The main epilepsy-associated astrocyte deficit, reactive astrogliosis, is characterized by multiple morphological and molecular changes. Epilepsy-associated changes in astrocyte physiological functions are associated not only with GFAP increase, but also with alterations in such specific proteins, including excitatory amino acid transporters (EAATs), glutamine synthetase (GS), nuclear factor I-A (N FIA), AQP4 and Kir4.1 and others. Here, we analyzed the astrocytes in the hippocampus of adult naïve vs. exposed to audiogenic kindling KM rats. We also examined the effects of nootropic drug piracetam on the hippocampal astrocytes of Wistar and KM naïve and audiogenic kindling-exposed rats. Piracetam improves cognitive functions, and is used as add-on therapy of epilepsy. However, how piracetam may affect astrocytes in the normal and epileptic brain, remains unclear. **METHODS:** Adult Wistar and KM rats were used. During audiogenic kindling each KM rat was subjected to acoustic stimulus (10 kHz) daily during 14 days. Piracetam (100 mg/kg) was injected i.p. daily for 21 days starting a week before audiogenic kindling. Analysis of astrocytes functional state used immunohistochemistry, Western blotting and qPCR. The expression of key astrocyte proteins assessed GFAP, EAATs, GS, NFIA, AldoC. **RESULTS AND DISCUSSION:** Naïve KM vs. Wistar rats demonstrated altered expression of key astrocytal proteins in the hippocampus, including increased NFIA and altered EAATs expression. These data show genetically determined changes in astrocytes of KM rats. Audiogenic kindling altered the expression of astrocyte proteins, demonstrating the participation of astrocytes in the development of limbic epilepsy, but piracetam had no effects on the astrocytes of KM rats, either naïve or kindled. At the same time, piracetam induced some alterations in the hippocampal astrocytes of rats of parental Wistar strain. Thus, our data showed inherited aberrations in the astrocytes of KM rats which may be involved in the genetically determined audiogenic epilepsy and the development of limbic seizures in KM rats. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-24-00342.

POSTER SESSION 1

THE ROLE OF TRANSCRIPTION FACTOR NEUROD1 IN MOUSE CORTICOGENESIS. MS Gavrish, AD Okhalnikov, AO Motorina, VS Tarabykin, Research Institute of Neurosciences, Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia; Institute of Cell Biology and Neurobiology, Charité Medical University, Berlin, Germany. **INTRODUCTION:** The mammalian cerebral neocortex is a highly organized structure that is responsible for many of the higher-level cognitive functions in humans, including language, memory, learning, decision making, and motor planning. Expanding of our fundamental understanding of molecular mechanisms of neocortex development, organization, and function is a key to investigating brain developmental disorders and elaborating new therapeutic approaches. Key members of the Neurod family of transcription factors – Neurod1, Neurod2, and Neurod6, are known to be important regulatory factors for the differentiation and specification of neurones during corticogenesis, and are also critically required in postnatal life. The main function of Neurod1 has been discovered to be promoting terminal neuronal differentiation in progenitor cells. Its expression is found in the subventricular zone in mitotic and early postmitotic neuronal cells and is involved in the differentiation of neuronal progenitor cells and contributes to the generation of most excitatory neurons that form the mature cortex. **METHODS:** In order to test if the role of Neurod1 in callosal development, we used in utero electroporation (IUE) of conditional expression plasmids into the developing neocortex. Genetic construct was activated by Cre-mediated Neurod1 recombination under control of the endogenous Neurod6-promoter (NexCre) in mouse embryos at the embryonic stage e13.5. Material collection and subsequent immunohistochemical staining was performed at e18.5. **RESULTS AND DISCUSSION:** Paramount, Neurod1 ectopic expression under postmitotic doublecortin (DCX) promoter activity was activated. The results of our experiments showed that overexpression of Neurod1 affects the laminar distribution of migrating

neuronal cells and also markedly alters their cell fate. **RESEARCH SUPPORT:** Russian Science Foundation (project 22-14-00232).

BEHAVIORAL CHARACTERISTICS OF DIFFERENT LINES OF ZEBRAFISH. DS Galstyan, TO Kolesnikova, AN Ikrin, AM Moskalenko, AV Kalueff. Institute of Translational Biomedicine, St. Petersburg State University, Institute of Experimental Medicine, Almazov National Medical Research Centre, St. Petersburg, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION**: A freshwater teleost fish, the zebrafish (Danio rerio) has become a popular model species in translational neuroscience research. In addition to outbred wild-type zebrafish populations, there are several well-characterized inbred zebrafish strains with distinct behavioral patterns, such as aspers (lacking melanocytes and iridophores). The purpose of the work is to study the behavioral characteristics of Caspers and the wild type. **METHODS:** A total of 5–7-month-old 60 experimentally naïve adult zebrafish (30 Casper and 30 wild type fish, 50:50 female to male ratio) were used in the study. To assess the behavioral characteristics of wild-type Caspers, a 6-day battery of 6 behavioral tests (1 test per day) was administered, organized according to the principle of increasing relative severity of stress exposure, such as novel tank test (NTT, day 1), the shoaling test (ST, day 2), the light-dark test (LDT, day 3), the social preference test (SPT, day 4), the novel object test (NOT, day 5), the aggression test (AT, day 6). Behavioral parameters in the tests were calculated using Noldus EthoVision XT11.5 software. Statistical data were analyzed using the Kruskal-Wallis (KW) test followed by Dunn's post hoc test to obtain significant KW data ($p<0.05$). **RESULTS AND DISCUSSION:** Compared to Caspers the wild type showed statistically significant low values of the total time in the top of the tank ($p<0.01$) in the NTT, the average distance between individuals in the ST ($p<0.001$), as well as the average distance to a new object ($p<0.05$) in the NOT test, but without statistically significant differences in the PBC test. In addition, it was found that the wild type spent more time in the zone with conspecifics ($p<0.01$), but less time in the middle zone ($p<0.001$) in the SPT. The aggression test also did not reveal statistically significant differences. Thus, the wild-type was found to exhibit greater anxiety and a greater level of socialization compared to Caspers. **RESEARCH SUPPORT:** Russian Science Foundation project 23-25-00412.

ANXIETY AND DEPRESSION-LIKE BEHAVIOR OF ZEBRAFISH IN A MODEL OF UNPREDICTABLE CHRONIC STRESS. MM Kotova, SV Amikishiev, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** Studies show a link between stress and various neuropsychiatric disorders (e.g., anxiety and depression). In order to reveal potential cures for these states, mostly rodent models are used. Indeed, comorbidity between depressive and anxiety disorders is common. Previously, a 20-day chronic stress model in mice showed a switch from anxiety to depression at the level of gene expression. Nevertheless, the zebrafish (Danio rerio) has established itself as an important model organism in translational biology, including chronic stress research. However, the temporal changes in affective disorders are still poorly understood. **AIM**: To evaluate anxiety and depression-like behavior of zebrafish in a 12-week unpredictable stress model **METHODS**: The total number of fish (160 wild type short-fin zebrafish) was divided into 2 equal groups: experimental and control. The experimental group was exposed to unpredictable chronic stress for 12 weeks. During the experiment, 3 time points were chosen: week 1, week 5, week 12. At each time point, fish were slaughtered after the behavioral tests for subsequent assessment of cortisol levels by ELISA method. Behavioral tests included novel tank test (NTT) and zebrafish tail immobilization (ZTI) test. Statistics were analyzed using the Kruskal-Wallis (KW) test followed by Dunn's post hoc test for significant KW data ($p<0.05$). **RESULTS AND DISCUSSION**: There were no differences in NTT in the experimental group compared to controls at 1 week. At week 5, chronically stressed individuals spent less time in the upper zone had a shorter total distance traveled, and had a longer latent period than control fish in the NTT. At week 12, experimental fish also had a decreased stay in the top zone, reduced top entry frequency and increased top entry latency period, indicating increased levels of anxiety. Moreover, some indicators of anxiety were revealed in the group of males. The ZTI test showed no differences at weeks 1 and 5. At 12 weeks, stressed fish showed less activity compared to the control group, indicating depressive-like behavior. In addition, the amount of cortisol was greater at 5 weeks, whereas by 12 weeks it was secreted less compared to the control, showing depletion of cortisol production. **CONCLUSIONS**: The combined NTT and ZTI tests show that fish at 5 weeks exhibited anxiety-like behavior and fish at 12 weeks more depression-like behavior. This may illustrate a progression from anxiety behaving to depression-like behavior during prolonged stress on zebrafish that has not been shown previously.

INVESTIGATION OF THE EFFECT OF DRUGS ON ZEBRAFISH BEHAVIORAL PATTERNS USING MACHINE LEARNING. DA Lukovikov, TO Kolesnikova, AA Korotaev, AV Kalueff, Sirius University of

Science and Technology, Sirius Federal Territory, St. Petersburg State University, Almazov National Medical Research Centre, St. Petersburg, Russia. **INTRODUCTION:** Zebrafish are a valuable model organism in biomedical research due to their genetic similarity to humans, rapid reproduction, and transparent embryos. They're increasingly used in preclinical drug research, particularly for drugs targeting the central nervous system (CNS). Video-tracking technologies enable the recording and analysis of their behavioral patterns, aiding in the identification of neuroactive drug candidates. However, manual analysis of zebrafish behavior is time-consuming, prompting the exploration of AI technologies to automate the process. Therefore, we developed our system to analyze different patterns of zebrafish behavior based on translating visual data into behavioral indicators. We validated this approach on well-studied CNS drugs with distinct effects on zebrafish behavior and then tested its predictive capabilities on independent drug. **METHODS:** We used a novel tank test to record and analyze zebrafish behavior. Fish were individually exposed separately to caffeine (100 mg/L for 20 min), ethanol (2% for 20 min), arecoline (10 mg/L for 20 min), fluoxetine (0.1 mg/L for the 20 min), and nicotine (10 mg/L for 5 min). We employed several machine learning models to obtain zebrafish location data (like the YOLOv8 model and the Segment Anything Model). Subsequently, we converted the zebrafish location data, using a custom-made algorithm designed specifically for this research, into distinct behavioral indicators, including distance travelled, average speed, time spent in bottom of the tank, the frequency and average duration of freezing bouts and hyperactivity. To differentiate between different behavior patterns, we trained the Random Forest classifier from Scikit-learn package (1.2.2). **RESULTS AND DISCUSSION:** Using our approach we were able to successfully identify the 4 groups of compounds (under nicotine, caffeine, ethanol, and control group) to which zebrafish were exposed with 81% accuracy, as well as correctly predict the pattern of zebrafish behavior under fluoxetine and arecoline based on visual data alone. We identified that indicators such as the initial position, total time at the bottom of the tank, the number of freezing episodes, average freezing time, and the frequency of hyperactivity episodes contributed the most to our classifier. This shows that with the help of modern machine learning models, it is possible to extract enough data from visual observations to classify different drug manifestations, which opens new possibilities in analyzing the influence of various factors on zebrafish condition. **RESEARCH SUPPORT:** Sirius University of Science and Technology.

EXTRACT OF *AMANITA MUSCARIA* INDUCES ANXIETY-LIKE BEHAVIOR IN ZEBRAFISH. AE Makhortykh, VD Riga, NO Prokhorenko, TO Kolesnikova, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** In modern society, there is a significant increase in the production and consumption of dietary supplements (DS), yet many of these products lack comprehensive research into their effectiveness and safety. One substance that is gaining popularity among users of DS is the fly agaric (Amanita muscaria). While the study of bioactive substances on laboratory animals is a common practice, the number of research articles on dried Amanita muscaria (AM) on animals is limited, which emphasizes the relevance of studying fly agaric using animal models. **AIM:** To study the effect of AM on adult zebrafish, we analyzed the acute and chronic behavioral effects of the fungus and assessed the impact of AM treatment cessation. **METHODS:** A total of 76 wild-type zebrafish were used for the study. Animal behavior was evaluated using the novel tank test (NTT) for 5 min, capturing data on latency (s) and number of top entries, time spent in the upper and lower section of the tank, freezing behavior duration and frequency, travelled distance, frequency and duration of mobility and immobility states using the Ethovision XT17 software. To estimate social behavior and anxiety level we used a shoaling test (ST), that assessed inter-fish distance and shoal area for 10 min. The Y-maze task (YT) was used to assess memory. First, we evaluated the acute effects of 300 and 600 mg/L AM in NTT on zebrafish compared to the control after a standard 20-min pretreatment. Then we measured the behavioral effects of chronic 1-week treatment with AM at doses of 100 mg/L, 200 mg/L, and 300 mg/L compared to the control in NTT, ST and YT. Fish behavior in NTT was also analyzed after 17 h of AM treatment cessation. **RESULTS AND DISCUSSION:** The acute effect of AM had an anxiogenic effect on the 600 mg/L group, with top frequency significantly decreased ($p<0.01$). Similarly, chronic exposure to 200 mg/L AM in zebrafish revealed anxiety-like behavior as evidenced by decreased distance traveled ($p<0.05$), top frequency ($p<0.01$), frequency and duration of immobilized state ($p<0.01$) in NTT. Notably, the higher dosage of AM (300 mg/L) had an effect only on the frequency of immobilization ($p<0.05$). The common effect for all AM exposure was the transformation of the movement trajectory into a smooth wall-to-wall movement. No significant differences were found in YT with the control group, which may indicate that there were no negative effects of AM on memory. Chronic exposure to 200 mg/L AM led to an increase in body contact cumulative duration in ST compared to other groups ($p<0.01$) and a decrease in distance between fish compared to control animals ($p<0.01$), which may indicate an anxiogenic effect of 200 mg/L AM. However, when the dosage was increased to 300 mg/L, fish did not show differences

in distance parameters. In the group with chronic 300 mg/L exposure we report fish mortality (60%) and belly swimming, which indicates the toxicity of high doses of fly agaric. AM extract cessation caused no significant behavioral changes. Thus, we observed heterogeneity of AM effects on zebrafish behavior depending on the dosage. **RESEARCH SUPPORT:** Sirius University of Science and Technology, project NRB-RND-2116.

USING EEG BIOMARKERS FOR PHENOTYPING SOCIAL DEFICITS IN RATS. VD Riga, AA Rebik, IS Midzyanovskaya, Sirius University of Science and Technology, Sirius Federal Territory, Institute of Higher Nervous Activity and Neurophysiology RAS, Moscow, Russia. **INTRODUCTION:** Epilepsy is often comorbid by autism spectrum disorder (ASD). Although the exact nature of the relationship between the two pathologies is still not clarified, it is known that EEG epiphenomena, such as focal interictal spikes (FIS), are associated with dysfunction of the cerebral cortex, and are often seen ASD patients. **AIM:** To examine whether rats with latent audiogenic epilepsy and social deficits exhibit changes in EEG similar to the clinical data of ASD patients. Phenotyping ASD-epilepsy rat models may shed light on the underlying mechanisms of the two comorbid pathologies. **METHODS:** To model the comorbiding latent genetic epilepsy and ASD symptoms, male rats from the KM strain were crossed with the Wistar maternal strain, and their offspring (hereafter referred to as WSKM, n=16) was used. In order to study patterns of electrical activity accompanying social testing, epidural electrocorticogrammes were recorded. Target areas were the right prefrontal cortex (2.5 AP, -1 ML), right parietalcortex (Par1; -1 AP, -4.5 ML), retrosplenial cortex (RSA; -4.5 AP, -1.0 ML), visual cortex area (Oc2L; -5.5 AP -4.5 ML), with grounding and reference electrodes placed in the cerebellum area and frontal bone, respectively. Primary analysis was performed using the EEGLab toolbox in MATLAB. Two main types of focal interictal spikes (FIS) were considered: spikes and polyspikes. **RESULTS AND DISCUSSION:** Based on the FIS mapping, two main areas of abnormal cortical hyperexcitability were identified: in the primary parietal (Par1) and retrosplenial (RSA) cortex. In the literature, abnormal excitation of these areas is often associated with autistic behavior. For the RSA and Par1 areas, statistically significant ($p<0.05$) increased numbers of polyspikes and spikes were registered when a new stimulus animal was introduced (social novelty test), indicating a disruption of network excitability in brain areas sensitive to social interactions. A sharp decrease ($p<0.05$) in the theta rhythms in the occipital leads (Oc2L) and RSA during the social novelty test may be associated with negative emotional affect during the increased social load. Therefore, WSKM reproducibly exhibit abnormal cortical activity in at least two areas (Par1 and RSA) associated with human ASD. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-25-00484

CRISPR/CAS9 MEDIATED INACTIVATION OF THE KCNQ3 GENE CAUSES MALFORMATION OF THE CORPUS CALLOSUM. AA Babaev, MS Gavrish, SA Tutukova, AD Okhalnikov, VS Tarabykin, Research Institute of Neurosciences, Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia; Institute of Cell Biology and Neurobiology, Charité Medical University, Berlin, Germany. **INTRODUCTION:** The corpus callosum contains ~80% of the commissural fibers of the brain, the function of which is to coordinate a wide range of tasks that require direct processing and exchange of information between different regions of the cortex and hemispheres. Complete or partial agenesis of the corpus callosum is one of the most common congenital malformations. During the initial stages of cerebral cortex development, processes such as neuronal specification, differentiation, migration and axonal orientation are controlled by transcription factors. Among them, factors from Neurod family and their target genes play a key role. **METHODS:** To identify molecules under the control of Neurod transcription factors, transcriptional analysis was performed together with ChIP-Seq (chromatin immunoprecipitation), and the localization of Kcnq3 expression was investigated by situ hybridization. Genetic constructs for CRISPR/Cas9 regulated inactivation of the Kcnq3 gene were generated. These constructs were used in in utero electroporation (IUE) at the embryonic stage e13.5. Material collection and subsequent immunohistochemical staining was performed at e18.5. **RESULTS AND DISCUSSION:** We demonstrated a decrease in Kcnq3 expression at e15.5 and e18.5 in Neurod2/6 DKO and Neurod1/2/6 TKO mutant mice. It has also been shown that axons, in the absence of Kcnq3, defasciculate and stop growing towards the midline. Kcnq3 appears to be required for logical axonal navigation of the corpus callosum and its formation. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-14-00232.

BEHAVIORAL CONSEQUENCES OF GENETICALLY DETERMINED DYSFUNCTION OF STRIATAL-ENRICHED PROTEIN TYROSINE PHOSPHATASE STEP IN MICE. VS Moskaliuk, PD Komleva, NV Khotskin, DV Bazovkina, EA Kulikova, Institute of cytology and genetics SB RAS, Novosibirsk, Russia. **INTRODUCTION:** striatal-enriched protein tyrosine phosphatase STEP, encoded by the gene Ptpn5, is involved in key signaling cascades regulating neuroplasticity and is connected

to the glutamate-, dopamine- and serotonergic systems of the brain. STEP also takes part in the pathogenesis of neurodegenerative and psychiatric disorders. Furthermore, STEP inhibitor exerted an anxiolytic, antidepressant and anti-aggressive effects as well as corrected the pathologic behavior in animal models of neurodegenerative disorders. These data suggest a possible role of STEP in the mechanisms of behavior and affective states. **AIM:** To evaluate the effects of *Ptpn5* gene functional knockout on behavior of mice. **METHODS:** Behavior of two-month-old male C57BL/6 mice and *Ptpn5* knockout (STEP KO, this strain has a deletion which leads to the absence of substrate-binding domain in the structure of STEP) mice was evaluated in the open field test (OF), elevated plus-maze test (EPMT), marble burying test (MBT), novel object recognition test (NOR), rotarod, Morris water maze (MWM), 3-chamber social test and social interaction test. **RESULTS AND DISCUSSION:** In the OF *Ptpn5* knockout mice did not differ from the wild-type in locomotor and exploratory activity. However, in the EPMT they displayed lower anxiety and higher exploratory activity. STEP KO mice buried less marbles, showing reduced stereotypic behavior. In the MWM they spent more time finding the platform in the learning phase of the test and spent less time in the target quarter in the memory testing phase. *Ptpn5* knockout did not affect social behavior, locomotion in the rotarod test and memory in NOR. Thus, *Ptpn5* knockout affected anxious and stereotypic behavior of mice, as well as spatial learning and memory, which suggests a profound role of STEP in the regulation and behavior and cognition. **RESEARCH SUPPORT:** Basic Research Project for a Young Researcher FWNR-2022-0010.

ACUTE AND CHRONIC EFFECTS OF GBR 12909, FLUOXETINE AND THEIR COMBINATION ON ADULT ZEBRAFISH (*DANIO RERIO*). AN Ikrin, AM Moskalenko, AD Shevlyakov, SV Amikishiev, TO Kolesnikova, DS Galstyan, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia. AN Ikrin, AM Moskalenko, AD Shevlyakov, SV Amikishiev, TO Kolesnikova, DS Galstyan, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Russia. **INTRODUCTION:** Monoamine reuptake inhibitors (MRIs) are important drugs in biomedicine for treatment of CNS disorders, mostly psychiatric ones (e.g., depression, anxiety, substance dependencies). To enhance or expand the range of action of monoamine reuptake inhibitors, multiple-acting inhibitors can be used. Combination effects of MRIs are poorly studied in zebrafish. GBR 12909, a dopamine reuptake inhibitor, and fluoxetine (FLU), a serotonin reuptake inhibitor, are frequently used MRIs. A study of the combination of these drugs in zebrafish (*Danio rerio*) suggests a promising approach to treating CNS disorders. **AIM:** To evaluate the acute and chronic effects of GBR 12909, FLU, and their combination on adult zebrafish. **METHODS:** We exposed 56 zebrafish to 1 mg/L of FLU, GBR, and their combination (GBR+FLU, 1 mg/L each) for 20 min, exhibiting acute drug exposure. Additionally, 60 zebrafish were chronically exposed to 0.1 mg/L of FLU, GBR, and GBR+FLU (0.1 mg/L each) for 7 days. The Novel Tank Test (NTT) was performed to assess zebrafish behavior for 5 min. Total distance moved (cm), time spent in the top (s), number of transitions from bottom to top, and highly mobile and immobile state frequency and duration (s) were measured during the NTT assessment. **RESULTS AND DISCUSSION:** Acute FLU exposure decreased time in the top compared to control group. Acute GBR+FLU decreased top frequency and increased mobile state duration compared to control. There were no differences in the acute GBR group compared to control. Chronic exposure to FLU decreased the frequency of top transitions, increased the duration of immobility and increased time in the top vs. control. In the chronic GBR+FLU group top frequency decreased, while top time increased compared to the control group. There was no altered behavior in the chronic GBR group compared to control. Overall, NTT showed that in acute exposure, GBR+FLU, but not GBR or FLU, had anxiolytic effects on zebrafish. In chronic exposure, GBR+FLU and FLU significantly reduced anxiety rather than GBR, which was inactive. **CONCLUSIONS:** Overall, these results confirm the sensitivity of zebrafish to dopamine and serotonin transporter inhibitors, assuming GBR+FLU drug combination as a new approach in treatment of psychiatric disorders (e.g., depression) acutely but not necessary chronically since both chronic GBR+FLU and FLU lowered anxiety in zebrafish. **RESEARCH SUPPORT:** Neurobiology Program (NRB-RND-2116) and Graduate Program in Genetics and Genetic Technologies, Center of Genetics and Life Sciences, Sirius University of Science and Technology.

A NEW SENSOR FOR NON-INVASIVE ASSESSMENT OF STRESSOR CONDITIONS OF THE ORGANISM. LG Simonyan, GG Karamyan, AM Manukyan, VR Sargsyan, HL Kostanyan, LH Misakyan, RSh Sargsyan, Laboratory of Integrative Biology, LA Orbeli Institute of Physiology NAS RA, Armenia. Research on the search for alternative methods for assessing the physiological state of biological systems led to the development of the hardware complex "Bioscope". Its principle of operation is based on measuring the intensity of light scattered in a light-tight chamber. When approaching the Bioscope of inanimate objects with ambient temperature, the readings of the

equipment do not change. However, already from 5-6 m, Bioscope reacts to the presence of a person. Various biological objects effect on the readings of Bioscope to varying degrees, at the same time, the signals of the equipment also change when their physiological state changes. This indicates the possible application of the developed equipment for non-invasive assessment of the functional state of biological systems in various biomedical research. Experiments on the influence of stressors of various modalities revealed the high sensitivity and specificity of Bioscope signals to changes in the physiological state of the body, both in animals and in people. The absence of analogues of Bioscope on the ensures preserving the priority of Armenia in its wide use in medical practice.

THE ROLE OF EVOLUTIONARY NEW ENHANCERS ON NEOCORTEX DEVELOPMENT. AO Kustova, A Newman, JCC Suescún, VS Tarabykin, Research Institute of Neurosciences, Lobachevsky State University of Nizhny Novgorod, Nizhny Novgorod, Russia; Institute of Cell Biology and Neurobiology, Charité Hospital, Berlin, Germany. **INTRODUCTION:** Mammalian brain has undergone significant changes during the evolution. Modern placental (*Eutheria*) mammals demonstrate amazing cognitive abilities and diverse social behavior because of higher neuronal activities. It became possible in virtue to neocortex development and reforming of communication between hemispheres. In marsupial (*Marsupialia*) and monotreme (*Monotremata*) mammals contralateral neurons in cortex interact via anterior commissure, while placental (*Eutheria*) mammals have more effective path, the corpus callosum. A possible explanation for the complication of the neuronal activities and the formation of a new commissure is in molecular changes during cortex development. **METHODS:** We compared an epigenetic marker for active gene enhancers - the acetylation levels of histone H3 on lysine 27 (H3K27ac) in genomes of the house opossum (*Monodelphis domestica*) and the house mouse (*Mus musculus*), identifying several evolutionary new enhancers. We used in utero electroporation and CRISPR/Cas9 system to completely delete the active gene enhancer in developing neocortical cells of mouse embryos at day 14 of embryonic development (E14,5) and investigated neocortex after 4 days (E18,5) by IHC. **RESULTS AND DISCUSSION:** A new active enhancer was identified for *Tbr1* gene. We first estimated Tbr1 expression after deletion of the active enhancer to confirm relationships between detected enhancer and Tbr1 gene expression level, noting reduced Tbr1 expression (to 30% vs. 96% in the control group). Moreover, the majority of electroporated neurons remained in the deeper layers of the cortex (49% vs. 18% in the control group) while in the upper layers were only 33% (vs. 70% in the control group). This indicates a considerable delay in neuronal migration. The direction of axonal growth remained unchanged: callosal axons effectively crossed the midline. Thus, expression of the evolutionary novel Tbr1 enhancer is important for Tbr1 expression and neuronal migration during corticogenesis. However, its contribution to the development of the corpus callosum is not fully understood. A detailed analysis of the corpus callosum morphology in post-enhancer deletion brains will be necessary. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation project FSWR-2023-0029.

THE CHEMOGENETIC MODULATION OF DAT-KO RATS BEHAVIOR IN HEBB-WILLIAMS MAZE. AA Gromova, TS Shemyakova, AD Belskaya, NP Kurzina, RR Gainetdinov, AB Volnona, Institute of Translational Biomedicine, St. Petersburg State University Faculty of Biology and University Hospital, St. Petersburg, Russia. **INTRODUCTION:** One of the relevant topics in modern neurobiology is revealing the mechanisms underlying the complex cognitive processes. It is well known that biogenic amines such as dopamine and norepinephrine modulate brain function and that these two neurotransmitter systems have reciprocal relationships in striatum and prefrontal cortex (PFC). **AIM:** To investigate the features of these reciprocal relationships using an animal model of pronounced hyperdopaminergia (DAT knockout rats, DAT KO). **METHODS:** We used a chemogenetic approach using Designer Receptor Exclusively Activated by Designer Drug (DREADDs) which allowed us to modulate the level of norepinephrine released by Locus Coeruleus (LC) neurons to the PFC. Genetic material was delivered to the LC retrogradely using the viral vector CAV-2 injected into the PFC. The effects on cognition were estimated using the Hebb-William maze. Rats were trained to find the correct path from the start to the finish in order to obtain a food reward. After training the configurations of the arena were modified by changing the position of the inner walls of the maze. In different types of arenas rats were received injections of saline or the DREADDs ligands clozapine (Clzp, 1 mg/kg) or clozapine-N-oxide (CNO, 1 mg/kg). Immunofluorescence analysis was performed to confirm the transfection of LC norepinephrine neurons. **RESULTS AND DISCUSSION:** Before activation of DREADDs, DAT KO rats demonstrated pronounced hyperactivity, they travelled significantly longer distance and spent more time on the task completion than WT rats; after Clzp injection these parameters reduced to the levels similar to WT control group. It also led to the decreasing of the time spent in error zones and disappearance of stereotypical behavioral patterns in DAT KO rats. CNO as a DREADDs activation was less effective, however general trends of effects were similar. WT rats have not shown significant

behavioral differences after activation of DREADDs. Chemogenetic methods used on knock-out animal model have great potential for further understanding the brain functional connectivity and its influence on behavior. **RESEARCH SUPPORT:** Russian Science Foundation grant 21-75-20069.

ASSESSMENT OF AGE-RELATED BEHAVIORAL EFFECTS OF CHRONIC STRESS IN LABORATORY RATS (RATTUS NORVEGICUS). TO Kolesnikova, AM Moskalenko, AN Ikrin, NO Prokhorenko, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** The chronic effects of stress are a pressing problem in the present society. Current research indicates a link between stress and accelerated aging of the body and neurodegeneration. However, the role of chronic effects of stressors on behavioral performance is not well disclosed, which provides a great space for research activities. This work will present the effects of 5-week chronic stress on the development of depressive and anxious behaviors in young and old rats. **METHODS:** chronic stressing of experimental groups of animals for 5 weeks with randomized stressor agents; assessment of depressive development using the Forced Swim test (frequency, duration of freezing and activity, and the latency before the first episode of freezing); assessment of anxiety development using the Elevated Plus-Maze test (entries in the dark and light arm frequency, durations, latency, freezing, climbing and stretching behavior frequency and duration), comparing groups using the Kruskal-Wallis and/or pairwise Mann-Whitney tests. **RESULTS AND DISCUSSION:** Intergroup comparison of the results of the Elevated Plus-Maze test showed statistically significant differences between the control group of young rats and the experimental groups in the latency of entering the light arm of the maze ($p=0.036$ and $p=0.041$ for the experimental groups of young and old rats, respectively), as well as differences between the duration of entries in the light arm between the control group of young rats and the experimental group of old rats ($p=0.044$), with the control group showing an earlier and more active visit to the light arm. A pairwise comparison, however, showed that the control groups of young and old rats differed in the frequency of the stretching behavior ($p=0.015$), with the old rats being less active. In addition, the Forced Swim test revealed that mean activity time differed significantly between controls of young and old rats ($p=0.006$), and between experimental groups of young and old rats ($p=0.045$), with both young rats being more active. These results may indicate that chronic stress has a more pronounced anxiogenic effect on young animals than on old animals, which are affected by chronic stress as a depressant. **RESEARCH SUPPORT:** Russian Science Foundation project 23-25-00246.

EFFECTS OF LOW-DOSE 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN EXPOSURE ON THE DEVELOPMENT OF RAT OFFSPRING. KV Pakhomov, DS Vasilev, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. **INTRODUCTION:** Dioxins are highly toxic anthropogenic environmental pollutants with a half-life of up to 11 years. They are proven to have teratogenic, carcinogenic, mutagenic and immunosuppressive effects on the body. The most famous of them is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), its' toxic equivalency factor (TEF) is 1. TCDD exposure is extremely dangerous during pregnancy due to the possibility of the offspring's impaired development. While TCDD and its' effects on the organism are studied all over the world, the experiments are mostly conducted using doses that significantly exceed current regulation standards, whereas effects of low doses remain poorly researched. Our goal was to characterize the effects of pregnant rats' low-dose TCDD exposure on the development of the offspring. **METHODS:** On the 14th day of pregnancy, female Wistar rats were administered *per os* with TCDD diluted in 1 ml of vegetable oil (0.1, 0.5 and 1 μg/kg body weight), control animals were administered with oil only. Daily weight gain and sensory-motor reflexes development of the offspring from P0 to P30 were analyzed. Behavior and cognitive abilities were assessed from P25 to P30 and after P90 using open field (OF), novel object recognition (NOR) and platform search tests in the Morris water maze (MWM). **RESULTS AND DISCUSSION:** Significant differences were found in the performance of rats in the MWM and OF tests. Among young animals during MWM training, no significant differences were found between the groups, in the final test pups of the 1 μg/kg TCDD group performed worse than the control group. After P90, the TCDD 1 μg/kg group lagged behind the control during training, and all TCDD groups performed worse than the control in the final test. In the OF the locomotor activity of adult rats of the TCDD groups was higher than that of the control group. Prenatal administration of TCDD negatively affects the cognitive abilities of rat offspring, even at low doses. Continued research into the effects of low doses is necessary to update regulations of acceptable TCDD levels in the environment and food. **RESEARCH SUPPORT:** State budget assignment 075-00264-24-00.

PERSEVERATION IN ADHD SYNDROME: MODEL EXPERIMENTS ON DOPAMINE KNOCKOUT RATS. AB Volnona, AD Belskaya, AA Gromova, RR Gainetdinov, NP Kurzina, Institute of Translational

Biomedicine, St. Petersburg State University Faculty of Biology and University Hospital, St. Petersburg, Russia. Impairment in dopamine transmission is occurs in developing of many neuropsychiatric disorders. The DAT-KO rats are one of the valuable models of attention deficit hyperactivity disorder (ADHD). These animals are characterized by a significant increase of the extracellular dopamine levels, marked hyperactivity and cognitive disorders: they have impairments in spatial working memory and perform many behavioral tasks much worse in comparison with wild type (WT) rats. **AIM:** To reveal and analyze peculiarities of perseverative behavior in DAT-KO rats during training in different mazes. We investigated the behavior of DAT-KO rats in spatial (8-arm radial and Hebb-Williams mazes) and non-spatial (the RedBox setup) tasks. It was found that DAT-KO rats are able to learn and perform all tested cognitive tasks. However, they spent more time on task performance and covered a significantly longer distances in all mazes in comparison with WT rats. In the spatial tasks (8-arm and Hebb-Williams mazes), DAT-KO rats learned task rules less successfully than WT rats. This may be due not only to the motor hyperactivity and inattention of knockout animals, but also due to the presence of perseverative activity during learning. The DAT-KO rats demonstrated multiple returns to the start in the Hebb-Williams maze which led to the significant increasing of the number of errors. In 8-arm radial maze they often revisited the previously visited arms. In the non-spatial RedBox setup, animals were trained to manipulate and distinguished objects. DAT-KO rats performed the behavioral task more successfully than WT rats and made fewer errors distinguishing familiar and novel objects. This fact may be explained by the plausible effect of the stereotypy on the learned motor skills: rigid tactic provided stable task performance. The data obtained allows us to suggest that abnormal dopamine transmission leads to the appearance of marked perseverative activity in knockout rats not found in WT animals. Therefore, the perseverative reactions in DAT-KO rats in spatial tasks reduce the efficiency of tasks performance whereas in non-spatial task this type of behavior enhances it. This comparative analysis makes it possible to assume that DAT-KO rats can be used not only as a model of ADHD, but also as a model for studying the mechanisms of compulsivity and maniacal behavior. **RESEARCH SUPPORT:** Russian Science Foundation grant 21-75-20069.

EMOTIONAL-PAINFUL STRESS IN RATS WITH CONTRAST EXCITABILITY AFFECTS THE CELL GENOME STABILITY OF CENTRAL NERVOUS SYSTEM DIFFERENTLY. VD Shcherbinina, MB Pavlova, NA Dyuzhikova, EV Daev, Pavlov Institute of Physiology RAS, St. Petersburg State University, Saint Petersburg, Russia. **INTRODUCTION:** During ontogenesis, the central nervous system (CNS) reacts to various stressors at different levels, including at the genome level of its cells. The stress response leads to functional changes in the genome as well as to structural changes. Destabilization of the brain cell genome is one of the possible mechanisms for the formation and maintenance of neuropathological conditions. **METHODS:** In this study, we assessed the degree of DNA damage in cells of the hippocampus, amygdala, and prefrontal cortex of rats at various times after the end of prolonged emotional-painful stress (PEPS) in order to identify the dynamics of DNA destabilization and reparation after stress. We used male rats of two strains with genetically determined differences in the threshold of the nervous system excitability, as well as unselected Wistar rats, subjected them to PEPS, and then the level of DNA damage was assessed by single-cell gel electrophoresis. **RESULTS AND DISCUSSION:** Significant differences were revealed (both upward and downward) in the degree of destabilization of the genome of the cells of all three studied brain structures at 2 h, 2 weeks and 2 months after the end of the stress procedure. The dynamics of DNA damage induction and repair were complex, nonlinear, and specific for each of the rat strains studied. The genome of CNS cells is a target for stressors of a psychoemotional nature, which can lead to the formation of post-stress pathologies. The specificity of the genomic response of cells of various brain structures may depend on genetically determined excitability. Individual genotype-specific differentiation features of stressor-sensitive target cells determine the specificity of changes in the functioning of various areas of the central nervous system and PTSD peculiarities. **RESEARCH SUPPORT:** State Program 47 “Scientific and Technological Development of Russian Federation” (2019–2030), theme 0134-2019-0002.

ACUTE BEHAVIORAL EFFECTS OF RACLOPRIDE, A SELECTIVE D2 ANTAGONIST ON ADULT ZEBRAFISH. KV Apukhtin, VS Nikitin, AV Kalueff, Sirius University of Science and Technology, Russia. **INTRODUCTION:** Dopamine is a neurotransmitter that plays a key role in various brain functions, such as cognition, motivation, reward, and movement. Dopamine is also involved in several neurological and psychiatric disorders, such as Parkinson's disease, schizophrenia and addiction. Zebrafish have distinct clusters of dopaminergic neurons in the forebrain, which project to various brain regions and modulate different aspects of behavior. Raclopride is a selective dopamine receptor type 2 (D2) antagonist. **AIM:** To understand the effects of acute doses of a D2 antagonist drug on zebrafish behavior. **METHODS:** A total of 88 wild type short-fin outbred zebrafish (~50:50 male:female

ratio) were assayed in the novel tank test (NTT) for 5 min, scoring distance moved, latency (s), number and time of top entries, freezing behavior, mobility and immobility, turn angle and angular velocity using the EthoVision XT11.5 software. First, we evaluated acute effect of 10 and 50 mg/L of raclopride in adult zebrafish following acute 20-min pre-treatment in NTT. We then also evaluated the effects of 0.2, 1 and 5 mg/L S(−)-raclopride (+)-tartrate salt from Sigma-Aldrich. **RESULTS AND DISCUSSION:** Acute effects at concentrations of 10 and 50 mg/L did not show marked differences in automatic counting, but there was a distinctive phenotype of stereotypic "jumpy" swimming. In the second experiment, there was a marked increase in frequency and duration of mobility and immobility as well as turn angle, angular velocity at a concentration of 1 mg/L compared to control. At 1, 5, 10 and 50 mg/L fish start to show "jumpy" swimming without erratic movements. Differences in turn angle, angular velocity indices are explained by the fact that fish after the drug circle more often and do not make smooth up- or downward movements, unlike controls. It is possible that absent effects in NTT at 10 and 50 mg/L was because raclopride, like other neuroleptic drugs, has a dose-dependent effect, binding to pre- and postsynaptic D2 receptors. Thus, the analyzed concentration range should be extended and other tests (e.g., Y-maze), can be used. Overall, zebrafish respond to raclopride with characteristic dose-dependent stereotypic "jumpy" swimming behavior. **RESEARCH SUPPORT:** Sirius University of Science and Technology.

THE EFFECTS OF NEUROLIPINS ON LIPOPOLYSACCHARIDE-INDUCED NEUROINFLAMMATION IN VITRO. KA Arsentiev, SP Konovalova, MYu Bobrov, VV Bezuglov, PE Musienko, Sirius University of Science and Technology, Sirius, Russia. **INTRODUCTION:** Neuroinflammation is a common feature of many CNS pathologies. The pro-inflammatory microenvironment also reduces the bioavailability of monoamines. Neurolipins are a class of endogenous amidic and etheric derivatives of fatty acids, which theoretically have an anti-inflammatory action and are able to stimulate monoamine systems. **AIM:** To evaluate the anti-inflammatory effect of N-arachidonoyl-serotonin (AA-5-HT), N-arachidonoyl-dopamine (NA-DA), N-docosahexaenoyl-dopamine (DHA-DA) and N-eicosopentaenoyl-serotonin (EPA-5HT) on a neuroinflammation model in vitro. **METHODS:** The experiments were carried out on rat C6 glioma cultures cultured in DMEM/F12 medium containing 10% fetal bovine serum (FBS), 2 mM glutamine, 250 U/ml penicillin and 250 μg/ml streptomycin. To model neuroinflammation, lipopolysaccharide (LPS) was added alone to the culture at a concentration of 1 μg/ml, or in the presence of various neurolipin concentrations (2.5, 5, 10 and 20 μM) for 24 h. Dimethyl sulfoxide (DMSO) was added to the control groups as a vehicle at a concentration of 0.1%. Cytotoxicity was assessed using an MTT test, and the cell migration rate was evaluated using a scratch assay. To assess proliferation, acridine orange (AO) staining was used to further measure the fluorescence intensity. Data analyzed by ANOVA and appropriate post hoc tests. **RESULTS AND DISCUSSION:** All substances at 20 μM significantly reduced the viability of glioma cells to 30-40% at 20 μM ($p<0.001$). DHA-DA had the greatest cytotoxicity, already seen at 5 μM ($p<0.01$). In low concentrations, compounds have been shown to inhibit the LPS stimulated cell migration in the scratch assay ($p<0.05$). Among tested compounds, NA-DA and AA-5HT (up to 5 μM) reduced LPS-stimulated migration to intact control levels, while other neurolipins were less active. At the same concentration range, all compounds had no influence on glioma cells proliferation. Notably, LPS action may stimulate redox metabolism in glioma cells and this effect was abrogated by tested compounds among which AA-5HT was the most active. Overall, our data show that neurolipins do not exhibit an antiproliferative effect, but are able to reduce the migration rate of LPS-induced glioma C6 cells. **RESEARCH SUPPORT:** Sirius University of Science and Technology.

RELATIONSHIP BETWEEN SPEECH AND READING IN CHILDREN WHO SURVIVED POSTERIOR FOSSA TUMORS. S Mironets, M Shurupova, A Karelin, Neurocognitive Laboratory, Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, RAE Data Center, Federal Center of Brain and Neurotechnologies, Moscow, Russia. **INTRODUCTION:** In recent years, experimental studies concerning the role of the cerebellum in the implementation of cognitive functions and a variety of language deficits have been conducted. The goal of the investigation is to evaluate the correlation between speech and reading. **METHODS:** 46 children (12.17±2.72) survived posterior fossa tumors (remission period 43.2±36.21); We performed a dysarthria rating scale. We also assessed oculomotor parameters: gaze holding score (gaze holding on a static object) and six parametres during reading seven literary texts. The children read passages presented on a screen, scoring total reading time for each text; total number of fixations; average fixation duration; the number of fixations per word; saccadic amplitude; and percentage of saccadic regressions, all averaged across 7 texts for each patient. The eye movements were recorded every 1/60 s monocularly with an Arrington eye tracking system. Data were analyzed using Spearman’s rank

correlation coefficient. **RESULTS AND DISCUSSION:** We revealed significant positive correlations between unstable gaze holding and dysarthria score (r=0.347, p=0.019), and significant correlations between reading parameters and dysarthria score: total reading time (r=0.328, p=0.028), number of fixations/s (r=-0.339, p=0.023), total number of fixations (r=0.300, p=0.045), number of fixations per word (r=0.326, p=0.029), percentage of saccadic regressions (r=0.575, p<0.001). We did not observe correlation between dysarthria score and fixation duration (r=0.252, p=0.095) and saccadic amplitude (r=-0.181, p=0.234). Thus, these findings should be considered for neuropsychological rehabilitation of children undergoing treatment after cancer to improve reading skills and future academic achievement.

MOUSE REPEATED AGRESSION PARADIGM: DEPRIVATION FROM FIGHTING RESULTS IN HIGHTENED ANXIETY AND AGRESSION IN MALE CD1 MICE. AS Mutovina, KA Ayriyants, AA Sapronova, PE Kisaretova, NP Bondar, Novosibirsk State University, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia. **INTRODUCTION:** Numerous psychopathologies, namely substance misuse, posttraumatic stress disorder and schizophrenia can cause recurrent aggression. Unfortunately, little is known about the mechanisms underlying the recurrence of aggressive behavior. The mice's behavioral findings after they were repeatedly put through agonistic encounters imply that winners receive positive reinforcement, which may account for their tendency to revert to aggressive behavior. It is still unclear whether the winners' pathological aggression is temporary or persistent, and what other behavioral changes may accompany this pathology. **METHODS:** Using the sensory contact model, robust aggressive behavior was developed in male CD1 mice. The mice that have won 30 consecutive encounters were then subjected to fighting deprivation for 30 days after their most recent confrontation. The development of pathological aggression was assessed using encounters with immobilized male CD1 mice three times: after 3d aggressive confrontation; after the last aggressive confrontation, and after deprivation of fighting. Anxiety-like behavior was assessed using the elevated plus-maze test on the next day after the final aggressive encounter, and in the light-dark box test after fighting deprivation. **RESULTS:** Male CD1 mice developed abnormal aggression, hostility and other behavioral phenotypes. Based on pathological aggression and aggression to a free moving conspecific male, we conducted cluster analyses to categorize individual aggressive mice into distinct subgroups. First group (40%) included mice with only territorial aggression; second group (44.4%) showed enhanced aggression the more fighting they experience, and have heightened levels of aggression after a fighting deprivation; and third group (15,6%) exhibited high aggression to the free-moving conspecific male from the start of aggressive encounters, but have low levels of pathological aggression. Second and third groups of aggressors also demonstrated heightened anxiety in the elevated plus maze and light-dark box tests. Thus, long experience of fighting evokes pathological aggression in most mice. These results will foster further studies of mechanisms that control the aggressive behavior in CD1 male mice. **RESEARCH SUPPORT:** Russian Science Foundation grant 24-25-00189.

INTENSITY DEPENDENCE OF AUDITORY-EVOKED POTENTIALS AS AN INDICATOR OF DEPRESSION SYMPTOMS SEVERITY. S Prasad, DG Mitiureva, OV Sysoeva, Institute of Higher Nervous Activity and Neurophysiology RAS, National Research University Higher School of Economics, Moscow, Russia. **INTRODUCTION:** Auditory-evoked potentials, particularly the intensity dependence of auditory-evoked potentials (IAEP), are used as indirect markers to assess central serotonin activity. IAEP, derived from peak-to-peak N1/P2 amplitudes, reveals changes in auditory-evoked potential slopes in response to tone loudness variations. While IAEP offers insights into central serotonin function, its correlation with depressive symptomatology is understudied. **AIM:** To explore the relationship between IAEP, quantified as the Amplitude-Stimulus Function (ASF), and Beck Depression Inventory (BDI) scores. **METHODS:** The study included 77 participants (20 males) aged 30±2.2. Participants completed the Beck Depression Inventory (BDI-II). EEG recordings were conducted using 64 electrodes arranged in the 10-20 system (actiCHamp Plus, Brain Products GmbH). Participants listened to audio stimuli of different tone loudness while EEG recordings were made. Stimuli of 500 Hz and durations of 0.1 s were presented at 50, 60, 70 and 80 dB SPL in randomized order. Each intensity step had 180 repetitions with interstimulus intervals varying between 0.7 and 1.1 s. Participants were isolated from external noise and wore headphones while watching muted videos on a screen, and had no explicit task concerning auditory stimuli. **RESULTS AND DISCUSSION:** The analysis revealed a significant positive correlation between ASF scores and BDI results (r = 0.432, p<0.001), indicating that higher BDI scores correspond to elevated ASF scores, suggesting deficient serotonergic neurotransmission. This links depressive symptoms and serotonergic neurotransmission and suggests ASF as a potential indicator of depression severity. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-18-00676.

MODELING OF PTSD IN SEXUALLY MATURE MALE RATS BORN TO MOTHERS STRESSED DURING PREGNANSY CAUSES MEMORY IMPAIRMENT AND HORMONAL DYSFUNCTION OF THEIR OFFSPRING. ED Shigalugova, GI Kholova, NE Ordyan, Pavlov Institute of Physiology RAS, St. Petersburg, Russia. **INTRODUCTION:** Prenatal stress (PS), caused by maternal stress during pregnancy, has complex neurological, behavioral and physiological manifestations in later life. Currently, there is an acute problem of identifying factors that increase the predisposition to the development of mental illnesses caused by strong psycho-emotional stressors. It has been shown that PS males are characterized by increased sensitivity to stressors. Previously we showed that stress in male fathers in the “stress-restress” paradigm (PTSD model) manifests itself in their offspring, predominantly males, in the form of various disorders of behavior, memory and hormonal functions. **METHODS:** This study was conducted on adult Wistar males born from females subjected to daily immobilization for 1 h from days 15-19 of pregnancy (PS males). During the period of spermatogenesis, PS males were exposed to traumatic stress and subsequent restress after 6 days. These males were mated with intact females 48 days after restressing. Further experiments were performed on their offspring of both sexes. The memory of adult offspring was studied in the passive avoidance test, insulin-like growth factor 2 (Igf2) gene expression in the hippocampus and neocortex was assessed using real-time PCR. Testosterone and estradiol levels were determined by ELISA. **RESULTS AND DISCUSSION:** Prenatal stress contributes to lower brain *Igf2* expression in offspring of both sexes and memory impairment in males, if males were additionally stressed before mating. We found lower testosterone levels in male, and estradiol levels in female, offspring. Thus, poorer memory of the offspring of PS males in whom PTSD was modeled before conception may be due to reduced brain expression of *Igf2* caused by impaired secretion of sex steroid hormones.

EEG FACE ODDBALL PARADIGM AS THE TEST FOR EMOTIONAL REACTION. A Popyvanova, E Pomelova, D Bredikhin, M Koriakina, AN Shestakova, E Blagovechtchenski, Centre for Cognition and Decision Making, Institute for Cognitive Neuroscience, HSE University, Moscow, Russia. **INTRODUCTION:** One method for assessing human emotional reactions is considered paradigms involving the presentation of affective images, including facial expressions, which are among the most familiar and noticeable stimuli in our visual environment. Electroencephalography (EEG) event-related potentials (ERP) to various stimuli is used as sensitive tests for determining categorical perception of specific stimulus modalities. We hypothesized that the oddball ERP paradigm, with the presentation of angry and happy faces, could serve as a test for determining a person’s emotional reaction. **METHODS:** EEG were recorded in 5 adults (3 males, mean age 22.3) in the ERP oddball paradigm. In this paradigm, repeated images of faces with a happy expression (80%, standard stimulus) were mixed with angry faces expression images (20%, deviant stimulus). 160 images were the set of standard stimuli, whereas 40 images were present in the set of deviant stimuli. Additionally, during the presentation of images with faces, participants experienced an auditory cognitive load in the form of an audio recording to make the experiment paradigm more passive. Participants were instructed to listen to a narrative, remember it, and list the items mentioned in the audio recording after the experiment. **RESULTS AND DISCUSSION:** In the study, ERP data revealed major response peaks at 116, 252, 480 and 784 ms (measured by global field power) presumably corresponding to P2, N170 and P3 ERP components. All the peaks exhibited differences in the amplitude of responses to the standard and deviant, suggesting variations in the processing of faces with happy and angry expressions. We conclude that facial expression detection happens automatically, even when mixed in a task in a different sensory modality. Further research is needed to ascertain whether this paradigm can effectively determine a person's emotional status. **RESEARCH SUPPORT:** The study was conducted within the project “Mirror Laboratories” of HSE University.

ANTIMICROBIAL, ANTIPROLIFERATIVE, AND POTENTIAL ANTISEIZURE PROPERTIES OF *ARTEMISIA VULGARIS* AND *ARTEMISIA GLAUCA* FROM KAZAKHSTAN. O Karapina, A Trofimov, B Sailike, Y Yermagambetov, G Mamytbekova, D Birimzhanova, Y Suleimen, B Akbay, T Tokay, Nazarbayev University, Kazakh University of Technology and Business, Astana, Kazakhstan. **INTRODUCTION:** This preliminary study investigates the antimicrobial, cytotoxic, and antiproliferative properties of root extracts from *Artemisia vulgaris* (*AV*) and *Artemisia glauca* (*AG*), harvested from the Akmola region of Kazakhstan, to assess their potential for treating epilepsy. Due to the drug resistance of many epilepsy forms, there is a critical need for alternatives that can modulate neuroinflammatory responses, reduce oxidative stress, and enhance GABAergic transmission. We hypothesize that the broad pharmacological activities of these *Artemisia* species may help reduce brain vulnerability to seizures. **METHODS:** The neuro- and cytotoxic properties of the extracts were evaluated by their effects on brine shrimp (*Artemia salina*). Antimicrobial activity was assessed by testing the extracts

against clinical strains of *Staphylococcus aureus*, *Escherichia coli*, *Serratia marcescens*, *Candida albicans*, and *Aspergillus flavus*. The antiproliferative effects were determined using alamarBlue cell viability reagent *in vitro*. Evaluation of antiepileptic properties commenced with the establishment of a chronic seizure model in CD-1 mice through a series of i.p. pentylenetetrazole (PTZ) injections (6 x 40 mg/kg every other day), followed by behavioral testing. **RESULTS AND DISCUSSION:** The ethanol extract from *AV* root exhibits low cytotoxicity and no neurotoxicity, while *AG* extract shows both cytotoxicity and neurotoxicity. Antimicrobial evaluations suggest potential activity against numerous clinical strains for both extracts. Cell viability assays revealed dose-dependent reductions in the proliferation of astroglioma and astroglial cells by both *AV* and *AG* extracts. In behavioral experiments with adult mice, i.p. injections of *AV* extract (50-500 mg/kg) 30 min prior to PTZ injections showed no effect on seizure measures assessed by Racine's scale, nor did the positive control (naringin, 80 mg/kg). With no delayed behavioral effects observed in Open Field, Elevated Zero-Maze, and Barnes maze tests, our future studies will adjust the seizure model by increasing the number of lower-dose PTZ injections to induce chronic seizures and better evaluate the antiepileptic potential of these extracts. **RESEARCH SUPPORT:** Collaborative Research Program 2023-2025.

PECULIARITIES OF DEVELOPMENT IN CHILDREN WITH MOTOR DISORDERS: THE EEG ASPECT. MM Koriakina, DO Bredikhin, OE Agranovich, AN Shestakova, ED Blagoveshchensky, National Research University HSE, Moscow, Turner Scientific Research Institute for Children's Orthopedics, St Petersburg, Russia. **INTRODUCTION**: The primary emphasis of the present study is on children with only upper limb motor disorders, specifically obstetric brachial plexus palsy (OBPP) and congenital arthrogryposis (AMC). These conditions significantly impair their motor function and interfere with normal development. Previous studies have indicated that children with OBPP/AMC exhibit deficits of cognitive function in addition to motor impairments, suggesting that they have specific brain developmental features. In this study, our primary objective was to investigate the alterations in brain neuronal dynamics caused by OBPP/AMC pathologies. We specifically examined the long-range temporal correlations (LRTCs) within the electroencephalogram (EEG) signal and assessed the amplitudes of different rhythms to better understand the impact of these conditions on brain function. **METHODS**: 27 participants were included in the present study (11 female, 16 males; age ± SD: 8.63 ± 3.35). The patient group consisted of individuals with motor disorders, namely 13 patients with AMC and 14 patients with OBPP, who were recruited from the Turner National Medical Research Center for Pediatric Orthopedics and Traumatology. In this study EEG recording was conducted using the 21-channel NVX 36 system (MCS, Russia). Throughout the recording session, the participants were seated in a chair and passively received a combination of auditory and visual stimuli, known as multimodal sensory stimulation (MSS). Auditory stimulation consisted of the sequence of pseudowords and verbs. Visual stimulation consisted of short video clips of human movements and views of nature. Following the processing and filtering of the EEG signal we assessed LRTCs within the brain activity. LRTCs reflect the degree to which the signal exhibits fractal self-similarity in different time-domain scalings. We used detrended fluctuation analysis (DFA), one of the most popular methods used to quantify the presence of LRTCs in a time series. LRTCs reflect underlying patterns of participants' brain structure-dynamics. **RESULTS AND DISCUSSION:** The results of the analysis showed a positive correlation between the values of the alpha band DFA indicator and the motor development indicators of children with motor disorders. A negative correlation has been identified between the values of the alpha band DFA indicator and the cognitive development indicators of children with motor disorders. This suggests that motor impairments affect features of brain structure-dynamics, and that the relationship between motor impairments and cognitive functions may not be linear, as previously shown. **RESEARCH SUPPORT:** Basic Research Program at the National Research University Higher School of Economics (HSE University). The project utilized the HSE Automated system of non-invasive brain stimulation with the possibility of synchronous registration of brain activity and registration of eye movements. The study was conducted within the project "Mirror Laboratories" of HSE University

C.R.A.B.: THE PARADIGM TO STUDY READINESS POTENTIAL. E Pomelova, D Bredikhin, A Popyvanova, K Bartseva, A Kuznetsova, A Kirsanov, M Koriakina, E Blagovechtchenski, Centre for Cognition and Decision Making, Institute for Cognitive Neuroscience, HSE University, Moscow, Laboratory of Behavioural Neurodynamics, St. Petersburg State University, St. Petersburg, Russia. **INTRODUCTION:** Pre-movement neuronal activity, known as the readiness potential (RP), is shown to precede voluntary actions. The majority of the approaches to studying RP still depend on the introspective reports of the participants and are based on the paradigm by Libet et al. (1983). However, the validity of participants' introspective reports in Libet's paradigm is highly questionable. In this light, we decided to develop the paradigm for non-direct control over the various cognitive factors inferring

the development of motor intention throughout the unfolding of the RP waveform. **METHODS:** EEG was recorded in 14 volunteers participated in the study (10 females, mean age = 20.8, SD = 2.1). The "C.R.A.B." app allowed users to control the movements of the animated character during the hide-and-seek game using a response pad. The goal of the player was to guide the main character to the right lane (one of three) using the button press, and therefore to find a hiding character. Three trial types correspond to different gameplay levels. In EASY trials, the position of the hider was visible from the start and remained constant. In MEDIUM trials, the position of the hider could change during the trial. In HARD trials, the hider was never visible. The game included training trials to familiarize players with the mechanics and conditions, followed by 120 trials (40 per condition) in the main gameplay. **RESULTS AND DISCUSSION:** Overall, RP waveforms were underdeveloped (in terms of both amplitude and latency measurements) in the condition, where participants could choose the right movement immediately after trial onset based on visual hints (EASY) in comparison to conditions with a non-reliable hint (MEDIUM) and no-hint (HARD) conditions. We suggest that our results favor the interpretation of the RP as a counterpart of the contingent negative variation, reflecting rather an anticipation of a particular movement-related stimulus than the movement initiation (or movement-related intention) per se. **RESEARCH SUPPORT:** Basic Research Program at the National Research University Higher School of Economics (HSE University). The project utilized the HSE Automated system of non-invasive brain stimulation with the possibility of synchronous registration of brain activity and registration of eye movements.

FACILITATORY EFFECTS OF COLD PRESSOR TASK ON CORTICOSPINAL EXCITABILITY: A PILOT STUDY. KV Bartseva, UR Nikishina, MM Koriakina, MU Lukov, AS Kirsanov, DA Fomicheva, DA Andreeva, EA Levchenko, AS Dasaeva, ED Blagovechtchenski, St. Petersburg State University, St Petersburg, HSE University, Moscow, Russia. **INTRODUCTION**: Cold pressor task (CPT) is a common procedure to induce physiological stress. Previous studies described its effects on the autonomic neural system; however, very few studies examined how the induced stress may affect corticospinal excitability, even though it can be the key mechanism behind alterations in movement precision under stress. The current study aims to compare the level of excitation of the corticospinal system before and after physiological stress induction via CPT. **METHODS**: 7 volunteers participated in the study (6 females, M_{age} = 22, SD = 6,37). Each participant was informed of the experimental procedure and signed the consent form. CPT was conducted by immersing the participant's hand into cold water (3-5°C) for 3 min. The participants rated the unpleasantness of this procedure on a scale of 1 to 10 (average response: 7, SD 2,45). The level of corticospinal activation was assessed by amplitude of the motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) and measured by electromyography (EMG). In the preparatory stage, the representation of the *abductor pollicis brevis* (APB) muscle was found in the M1, and the individual motor threshold was assessed (the minimal level of stimulation that is able to produce MEPs no less than 50 mV in 50% or more cases). During the experiment, 5 sets of 20 TMS pulses were delivered 10% above the threshold: one for the baseline, one immediately after CPT, and three more - every 10 min after CPT. Data analysis for signal processing was performed using scripts in MATLAB R2023a (The MathWorks) and JASP 0.18.3 (JASP Team, 2024). EMG activity was filtered with a high-pass filter and a notch filter (50 Hz), baseline correction was applied. MEP peaks were identified inside a 20–62 ms time window from the TMS stimulus. The amplitudes were assessed peak-to-peak and then averaged for each probe, analyzed by Wilcoxon signed-rank test to compare the five probes pairwise. **RESULTS AND DISCUSSION:** The significant differences were found between the baseline probe (1st) and the probe immediately after the CPT (2nd), with the baseline amplitudes being slightly smaller: $Z = -2.03$, $p = 0.02$ (directional hypothesis). These results suggest that stress can be a facilitatory factor for the corticospinal excitability. Future elaboration on these results may provide new insights regarding the mechanisms of motor agitation and movement-based methods to relieve stress. However, given the small sample size of the current study, further research is needed to explore potential moderating factors, as well as the dynamics of the corticospinal system recovery from stress. **RESEARCH SUPPORT:** St. Petersburg State University.

mTOR, AUTOPHAGY AND SIRT-1 IN BRAIN DURING PRENATAL HYPERHOMOCYSTEINEMIA. AV Mikhel, IV Zalozniaia, AD Shcherbitskaia, SK Bochkovskii, YP Milyutina, DS Vasilev, AV Arutjunyan, Ott Research Institute of Obstetrics, Gynecology and Reproductive Medicine, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. Autophagy operates at basal levels under normal physiological conditions but can be influenced by cellular stress, potentially disrupting cellular homeostasis. This process is regulated by the mTOR pathway, and inhibition of this complex (mTORC) can activate autophagy. Additionally, SIRT1 has been shown to

deacetylate components related to autophagy (including LC3B) and may encourage autophagy activation via mTORC inhibition. Thus, prenatal hyperhomocysteinemia (PHHC), triggered by the cytotoxic amino acid homocysteine (HC), can induce autophagy. However, the impact of PHHC on the mTOR system, autophagy, and deacetylase levels in the fetal brain at various developmental stages remains poorly understood. Here, female Wistar rats received methionine (0.6 g/kg body weight) orally during pregnancy to model PHHC, while control animals received water. We conducted Western blot analyses to assess the levels of mTOR system markers (mTOR, p-mTOR, 4E-BP1, p-4E-BP1, rpS6 and p-rpS6), autophagy markers (Atg13, Beclin-1, Ambra-1, LC3B, p62, LAMP-2), and SIRT-1 in fetal brain tissues on days 14 and 20 of embryonic development (E14 and E20). Our findings revealed that PHHC led to a reduction in SIRT-1 and Beclin-1 levels, as well as an increase in LAMP-2 in the fetal brain on E14. However, no significant changes were observed in the levels of other autophagy markers. Moreover, elevated maternal HC levels in the fetal brain on E20 were associated with decreased levels of SIRT-1 and 4E-BP1, without significant alterations in other protein levels. Consequently, PHHC adversely affects fetal development: it decreases SIRT-1 levels, which are crucial for neurite and axon growth in the embryonic brain, and reduces 4E-BP1 levels towards the end of pregnancy, potentially impairing cap-dependent translation. Changes in autophagy markers observed only on E14 might suggest a shift in the balance between autophagy and apoptosis towards apoptosis in fetal brain on E20. These disturbances may predispose to neurodegenerative conditions in the postnatal period. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00393.

STRESS AND ELECTRICAL INJURIES IN LARGE FARM ANIMALS. NS Orlyansky, ON Eremenko, Trubilin Kuban State Agrarian University, Krasnodar, Russia. Electric injuries are becoming highly prevalent in the livestock industry. Although active measures are being taken to reduce this type of injury, severe injuries and frequent mortality among large farm animals due to electricity have become an important problem of this industry. In the present study, we performed a comparative analysis of electric shock-related injuries in pigs, cows and sheep (based on data surveys from livestock farms of 10 Agricultural universities in Russia). The study compared main types and major causes of electrical injuries and analyzed their stress mechanisms, treatment methods and physical impact for the three key farm animals. **RESEARCH SUPPORT:** Trubilin Kuban State Agrarian University

DYNAMICS OF BRAIN ELECTRICAL ACTIVITY DURING PROLONGED AUDIOVISUAL STIMULATION. NE Tadevosyan, BB Forghan, AA Tumanian, LV Vahradyan, AS Khachunts, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** The method of audiovisual stimulation (AVS) has attracted increased attention due to its mobility and ease of implementation. AVS is a type of neurostimulation, which influences by light and sound stimuli at the frequency of “healthy” biorhythms of the brain on its biological activity and state of consciousness, contributing to the improvement of the general functional state of the person. It is known that AVS, through modulating brain systems, creates a resonance effect and causes synchronization of previously unrelated sources of spontaneous brain rhythms. The aim of the study was to investigate the dynamics of EEG parameters during prolonged AVS. **METHODS:** Twenty-five males and females aged 23 to 27 years participated in the study. Each subject completed a 30-min AVS session for 15 consecutive days. The modern portable device "Photosonix Inner Pulse" was used for AVS training course, the interface of which allowed choosing the intensity and frequency of exposure (3-14Hz). EEG recordings were performed 4 times for 10 min each: one day before (background recording), and on days 5, 10 and 15 after, AVS session. Brain bioelectrical potentials were recorded using a "NeXus-10" electroencephalograph according to international 10-20 system of electrode placement. Computer analysis of bioelectrical activity of frontal, temporal, parietal and occipital regions of both hemispheres was performed. **RESULTS AND DISCUSSION:** During prolonged AVS, changes in absolute and relative power values of EEG components were observed starting from the 10^{th} day of stimulation. We found a significant increase in the power of alpha and beta rhythms in leads F3-P3 and F4-P4. At the same time, no significant changes were revealed in leads T3-O1 and T4-O2. The same dynamics was noted in relation to changes in the power of the theta rhythm. It should be noted that after the 10^{th} AVS day no significant changes in the power of the studied biorhythms were detected. Thus, the results of our studies show that AVS with a frequency of 3-14 Hz has a specific and selective effect on the components of brain bioelectrical activity. Thus, prolonged AVS, changing bioelectrical activity in frontal and parietal regions, can reduce psycho-emotional stress and increase the person’s activity and performance due to the realization of functional reserves through the brain modulating systems.

EVALUATION OF SIMPLE VISUAL-MOTOR REACTION TIME IN DIFFERENT AGE GROUPS DURING MENTAL LOAD. AA Tumanian, AS Khachunts, AR Sargsyan, NE Tadevosyan, LA Orbeli

Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** Age-related changes in the functional state of the CNS are characterized by morphological changes in the brain and their further functional manifestations, such as slowing of sensorimotor reactions and cognitive decline. One of the most informative methods for assessing the functional state of the CNS is the evaluation of simple visual-motor reaction (sVMR) time, which gives an idea of the integrity and processing capabilities of the CNS. **METHODS:** 88 subjects were divided into 3 age groups: 18-21 (n=29), 22-35 (n=33) and 36-60 (n=26) and performed computer-based sVMR time test before and after mental load. We analyzed a number of parameters: reaction time (M_t), standard deviation (SD), the functional level of the system, response stability, the level of functional abilities, and delayed and advanced responses. **RESULTS AND DISCUSSION:** The study results showed that before mental load the 3rd group had low sVMR speed and low values of functional parameters compared to the 1st group. In the 1st group, there was instability of nervous processes with the predominance of excitation strength, as evidenced by a significant prevalence of advanced responses over delayed responses. However, with age a balance of nervous processes is established with some decrease in the strength of excitation and an increase in inhibition processes. After mental load, the older group was inferior to the two younger groups almost in all parameters. The first two groups showed higher sVMR speed and stability, and the 2nd group also showed an increase in functional parameters. The older group revealed only higher sVMR speed. All groups demonstrated an increase in advanced responses and a significant predominance of advanced responses over delayed responses. The increase in reaction speed in the studied groups after mental load may be related to both the addictive factor and the so-called "speed-accuracy trade-off" phenomenon, when fatigue after mental load results in a decrease in reaction time with a simultaneous increase in delayed and advanced responses. Thus, we found age-related changes in CNS functional state, uneven in nature. Main changes, namely, a decrease in sensorimotor reaction speed and functional characteristics, occur in the older age group, most likely due to neurohumoral and morpho-functional CNS changes.

COMPARATIVE STUDY PARAMETERS OF HEART RATE VARIABILITY AND OF PSYCHOLOGICAL STATE OF THE ARTSAKH WAR PARTICIPANTS. AA Sahakyan, HG Galstyan, AV Sargsyan, LV Vahradyan, NE Tadevosyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** Military actions inevitably lead to significant mental stress, which may result in a variety of psychological and physiological disorders in the participants. Prolonged exposure to stress factors leads to an inability to adapt and withstand difficult conditions, and often to post-traumatic stress disorder. In recent years, the relevance of studying the functional state of military action participants has increased. **AIM:** To study the features of autonomic regulation of the cardiovascular system of the Artsakh war participants in the post-war period by analyzing heart rate variability, to evaluate the parameters characterizing the psychological state, as well as to consider the interrelation of the studied processes. **METHODS:** The study was conducted on 83 war participants aged 18-35 divided into three groups: army recruits, volunteers and war participants (who received injuries of varying severity). The control group included 36 men of the same age who did not participate in military actions and did not live in a military zone. Heart rate variability (HRV) was studied using the BioMouse Research hardware/software complex developed by NeuroLab Company. Short-term HRV recordings (5 min) were performed twice: before (baseline) and after performing mental tests. A wide range of HRV parameters was analyzed. To study the psychological state, we used adapted computerized psychological tests (Taylor Manifest Anxiety Scale (TMAS) and Pichot Inventory). The comparative study was carried out using correlation analysis. **RESULTS AND DISCUSSION:** The study results showed that the participants of the military actions, as compared to the control group, had lower HRV, some tension of the regulatory systems, and a shift in cardiac autonomic balance toward sympathetic predominance. The army recruit group had higher levels of anxiety, and other two groups had higher levels of depression and hypochondria vs. controls. We also found between-group differences of the studied parameters in the participants of military actions. The war participants, vs. other two groups, showed low HRV and high level of tension of regulatory systems, and had the highest levels of depression and hypochondria. After performing the tests, in all groups we noted reduced tension of the regulatory systems and increased parasympathetic activity, which may be linked to manifestation of fatigue. Comparative analysis of HRV and psychological parameters revealed a strong positive correlation between stress index and depression in all groups.

STUDY OF THE QUALITY OF LIFE AND ANXIETY OF THE POPULATION OF ARTSAKH IN THE POST-WAR PERIOD USING THE SF-36 QUESTIONNAIRE. HG Galstyan, AA Tumanian, GH Sakanyan, MA Mardiyan, LA Orbeli Institute of Physiology NAS RA, M Heratsi Yerevan State Medical University, Yerevan, Armenia. **INTRODUCTION:** Biomedical assessment of the quality of life (QOL) is a methodological tool that allows identifying the degree of human adaptation to changing functional

states and environmental factors. The association between areas of QOL as an integral characteristic of the physical, emotional and social functioning of a person, and anxiety as an individual psychological personality trait, has not been fully investigated. For the first time we tried to analyze the population's QOL and anxiety in post-war conditions, as well as the study of the "QOL-anxiety" complex with the identification of relationships between its components. **METHODS:** The study was conducted over 2021-2022 (a year after the end of the military events in the region), one hundred eighty Artsakh 16 to 60 years residents of both genders have been tested using a modified version of SF-36 questionnaire. Population anxiety was assessed by Spielberg. Statistical processing and analysis of the data were carried out using the SPSS 22.0 application package, the correlations between the studied indicators were determined by the Spearman method and the Kruskal-Wallis criterion. **RESULTS AND DISCUSSION:** The average values of the population's QOL indicators for the SF-36 questionnaire scales varies from 59.5 (the vital activity and mental health) to 84.2 points (physical functioning). In general, the entire population had a low level of mental health – MH (43.7 points), compared with physical health – PH (49.7 points). The average values for these personal (PA) and situational (SA) anxiety of the respondents are 46.1 and 43.6 points, respectively. An inverse relationship was found for the anxiety-MH (r=-0.602-0.697, p≤0.001). Weak negative associations were obtained for the ratios of anxiety-PH (r=-0.236-0.266 (p<0.001). For the relationships between the PH and MH, we found no reliable connection (r=-0.011, p=0.885). A direct relationship between SA and PA is indicated by correlation coefficient r=0.602-0.697 (p<0.001). Our results demonstrate the importance of QQL and anxiety research using questionnaires, as they complement each other and allow individualization of biomedical approaches to subjects. **RESEARCH SUPPORT:** Science Committee of Armenia project 23T/AA-003.

APPLICATION OF THE "WHO SHORT QUESTIONNAIRE" METHOD IN THE ANALYSIS OF HEALTH-RELATED QUALITY OF LIFE IN INDIVIDUALS DURING POST-WAR TIME ON THE EXAMPLE OF THE POPULATION OF ARTSAKH. AV Sargsyan, AA Sahakyan, NE Tadevosyan, HG Galstyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** At present a number of concepts are known in the biomedical field that reflects the mechanism of the post-war syndrome. Our study of health-related quality of life (QOL) as the main indicator of an integral assessment of the population health in 'hot spots' offers a new approach. The work presents the first results of a comprehensive QOL study in the post-war period on the example of Artsakh. **METHODS:** The study was conducted in 180 residents of both sexes, aged 16-60, one year after the end of the war in the region. A short version of the WHOQOL-BREF questionnaire (World Health Organization Quality of Life) was used as a tool for population's QOL assessment. We assessed the anxiety of the population according to Spielberg, with Student's t-test at p<0.05. Statistical data were processed using the SPSS 22.0 application package. Correlation between the level of anxiety and QOL domains according to WHOQOL and the assessment of its reliability were determined by the Spearman method and by the Kruskal-Wallis test. **RESULTS AND DISCUSSION:** The lowest value was obtained for physical domain (54.6 scores). The highest value was shown for social relationships domain (70.5 scores). Intermediate values – psychological and environmental domains (66.1 and 62.3 scores, correspondingly). At the same time, the male's population indicators of the QOL on all scales slightly exceeded those of the females. QOL indicators decreased with age. An inverse relationship was found for the ratios mental well-being-situational anxiety (r=-0.370, p<0.001) and environment-situational anxiety (r=-0.491, p<0.001). Weak negative relationships were also obtained for the remaining ratios, ranging from r=-0.230 (p=0.002) to r=-0.284 (p<0.001). For the ratio of personal physical well-being-anxiety, the absence of a significant relationship was revealed (r=-0.119 (p=0.110). Study results allow to designate the obtained values as regional population QOL's norms in the post-war period, and the established phenomenon of Artshakh requires further study. **RESEARCH SUPPORT:** Science Committee of Armenia, project 23T/AA-003.

REFINEMENT OF DECELLULARIZED GRAFTS FOR PERIPHERAL NERVE TISSUE ENGINEERING. VS Grigoryan, GP Sevoyan, SS Gasparyan, PV AnjanKumar, SV Karapetyan, ZI Karabekian, LA Orbeli Institute of Physiology NAS RA, University of Traditional Medicine, M Heratsi Yerevan State Medical University, Yerevan, Armenia; George Washington University, Washington DC, USA. **INTRODUCTION:** Nerve injuries are commonly encountered pathologies. In large defects, autografting is gold standard. However, it is associated with disadvantages (donor site limitation, functional impairment, neuromas, graft mismatch). With allo- and xenotransplantation, in addition, long-term immunosuppression is required. Biological, chemical, mechanical properties determine aspects of regeneration. ECM-derived decellularized scaffolds retain architecture, growth factors, adhesion molecules, and various intrinsic proteins. The potential benefits of adding electroactive compounds are underestimated due to conflicting experimental data. **METHODS:** Decellularization

was performed by a method developed by us, via a combination of freezing-thawing cycles and use of detergents (SDS, SDC, Triton-X100). We performed characterization and comparison of decellularized scaffolds with and without addition of graphene oxide (GO). Decellularization efficiency was studied by histological analysis (H&E, DAPI), confocal microscopy (using DiO dye). Cell viability and function were assessed in media conditioned by decellularized nerve scaffolds compared to intact nerves, as well as scaffolds supplemented with GO. MTT was the major method for viability assessment. **RESULTS AND DISCUSSION:** We developed methodology for decellularization. Histological analysis and confocal microscopy of decellularized samples showed efficient removal of the cellular component with preserved nerve structure after exposure to decellularizing materials. In compound scaffolds, evaluation showed decrease in cell viability in high GO concentrations, with further normalization. In contrast, controls (decellularized scaffolds without additives) and those with addition of low GO concentration showed comparable data. **RESEARCH SUPPORT:** Science Committee of RA Research project 23AA-1F037, co-funded by the AESA R&D Grant, EIF-PMI 2022.

USING TEMPORAL EEG SIGNAL DECOMPOSITION TO IDENTIFY NEUROPHYSIOLOGICAL MARKERS AMONG STROKE PATIENTS. DG Muhammad, N Syrov, A Medvedeva, Y Alieva, L Yakovlev, D Petrova, GE Ivanova, AY Kaplan, MA Lebedev, Vladimir Zelman Center for Neurobiology and Brain Rehabilitation, Skolkovo Institute of Science and Technology, Federal Center of Brain Research and Neurotechnologies, FMBA, Laboratory for Neurophysiology and Neuro-Computer interfaces, Faculty of Biology, Faculty of Mechanics and Mathematics, Lomonosov Moscow State University, Moscow, Russia. **INTRODUCTION:** Lateralized readiness potential (LRP) as a marker of motor cortex (M1) activation in motor preparation might be suggested as an objective functional marker for motor network disruption and their restoration during rehabilitation. Being strictly lateralized, LRP was also suggested to show interhemispheric activity balance during movement preparation. Therefore, it may be important to track each hemisphere's contribution during restoration in order to adjust rehabilitation for better outcomes. The inconsistent results from previous studies on LRP might be connected with the complexity of M1 functions during movement preparation and execution, specifically during visuomotor coordinations, where M1 activation depends on its connections with visual areas. In the current study, we included post-stroke subjects with upper limb impairments in order to separate M1 activation impairments related to stimulus processing (S cluster), stimulus-response mapping (C cluster), and execution (R cluster) using the Residue Iteration Decomposition (RIDE) algorithm. Due to the lack of detectable EMG responses in paralyzed limbs in most subjects, the response time (RT) calculation was not possible, so we didn't extract the R cluster, but we expect the R-related activity to likely be merged with the C cluster. **METHODS:** The experimental task required the participant to extend the wrist indicated as the target upon seeing a visual cue, which was a flash of light emitted from the button. The target wrist was identified by a sustained flash of light from either the right or left button, depending on which one was the target. Subsequently, both buttons flashed in a pseudorandom sequence, but participants were instructed to only extend their wrists when the target button flashed. **RESULTS AND DISCUSSION:** In the S cluster, the activity of the ipsilesional hemisphere is characterized by double LRP peaks in the unaffected hand movement and a single peak in the affected hand movement. While the former observation may suggest intact motor preparation, the latter may indicate stroke-induced altered motor preparation. Similarly, the contralesional hemispheres in both affected and unaffected hand movements exhibited a normal LRP waveform (positive peak) with a double peak during affected hand movements, suggesting compensatory mechanisms in the unaffected hemisphere. In the C cluster of the affected hand movement, the amplitude of the ipsilesional hemisphere LRP is nearly equal to the contralesional hemisphere; the ipsilesional hemisphere in the unaffected hand movement appears to have minimal contribution in movement preparation. Conclusively, both ipsilesional and contralesional hemispheres participate in movement preparation after stroke, with compensatory actions in the unaffected hemisphere. **RESEARCH SUPPORT:** Russian Science Foundation grant 21-75-30024.

NEURAL CORRELATES OF INDIVIDUAL DIFFERENCES IN TIME PERCEPTION. DG Mitiureva, OV Sysoeva, Institute of Higher Nervous Activity and Neurophysiology of RAS, Moscow, Russia. **INTRODUCTION:** Time perception is a fundamental cognitive function upon which other cognitive functions arise. While high inter-individual variability in subjective time was shown, underlying brain mechanisms are largely understudied. Their identification may shed light on psychiatric conditions accompanied by time perception distortions, such as depression and schizophrenia. Here, we aimed to explore the relation between brain response to the termination of a time interval in the duration comparison task (DCT) and individual characteristics of time perception. **METHODS:** The study included 93 participants (53 females, age 25.8±9), who were to compare durations of visual stimuli presented sequentially in pairs (9 pairs of stimuli with durations ranging from 3.2 to 6.4s presented

randomly 8 times) answering which stimulus lasted longer. Psychophysical curves were fitted to the data to assess the point of subjective equality (PSE) that was considered as an index of subjective time shrinkage or temporal order effect observed in such tasks (the more negative PSE, the greater subjective time shrinkage of the 1st stimulus relative to the 2nd one as the process develops in time). EEG (64-channels) was recorded simultaneously. The recordings were segmented in relation to stimuli offset separately for short (S: 3.2-4s), middle (M: 4.4-5.2s) and long (L: 5.6-6.4s) durations considering their position in a pair (1st or 2nd) and averaged over to obtain offset evoked potentials (off-EP). Then, we applied the spatiotemporal clustering test based on ANOVA interaction effect (position*duration). We suggested the mean off-EPs' amplitude differences between 1st and 2nd stimuli in a pair (particularly M1–S2 and L1–M2) of the clusters as potential neurophysiological correlates of inter-individual variability in duration shrinkage and examined whether the more negative PSE relates to the smaller off-EPs' amplitude differences between these stimuli, which in case of high subjective time shrinkage should be perceived as more similar in duration, while the 1st is objectively longer. **RESULTS AND DISCUSSION:** We detected 5 clusters of brain activity ($p<0.05$) responsible for the interaction effect. Most of them exhibited overt power distinction both between the durations (S>M>L) and their position in a pair (2nd>1st). Two of these clusters' differential amplitude correlated with PSE: the central cluster with latency 0.12-0.21s (M1–S2: R=.23, p<.05; L1–M2: R=.27, p<.01) and the frontal cluster with latency 0.26-0.36s (M1–S2: R=.296, p<.01). Therefore, the off-EP for a stimulus with a certain duration during the DCT carries information about the duration, and its amplitude is related to individual differences in time perception: the more negative PSE, indicative of greater subjective time shrinkage, the smaller the difference in off-EP between objectively larger first and smaller second time intervals. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-18-00676.

MOTOR LEARNING AND BELIEF UPDATING IN BIPOLAR DISORDER. M Ivanova, K Germanova, G Kopytin, A Ragymova, D Petelin, M Herrojo Ruiz, National Research University Higher School of Economics (HSE), First Moscow State Medical University, Moscow, Russia; Goldsmiths, University of London, London, UK. **INTRODUCTION:** Bipolar disorder (BD) is a chronic mental disorder present in approximately 3% of the population and is characterized by alternate episodes of mania and depression interspersed with episodes of remission. BD is often accompanied by misdiagnosis with such disorders as depression and borderline personality disorder. **METHODS:** We recorded brain activity of 27 healthy control participants (HC) and 22 bipolar patients (BD) using magnetoencephalography (MEG). Participants completed a validated motor-based decision-making paradigm. This task combined a probabilistic binary reward-based learning task, set in a volatile environment, with motor sequences for expressing decisions. We analyzed behavioral data using a computational model known as the Hierarchical Gaussian Filter (HGF). HGF is a Bayesian generative perceptual model which allows estimating multiple levels of model parameters. The model allows to interpret agent behavior using the model parameters. **RESULTS AND DISCUSSION:** Our results demonstrated that BD patients exhibited lower win rates compared to HC individuals, meaning their learning behavior was less optimal. They also showed lower win-stay rates and exhibited more stochastic decisions. Using MEG analysis, during prediction error processing we found alpha and beta suppression and gamma increase in the prefrontal, orbitofrontal, and anterior cingulate regions in healthy individuals, whereas participants with bipolar disorder demonstrated diminished effects across these areas. In conclusion, these findings provide some insights into the interactions between individuals with BD and their environment. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-18-00660 (MI, GK).

THE VULNERABILITY OF DOPAMINERGIC NEURONS IN MICE WITH CONDITIONAL INACTIVATION OF THE ALPHA-SYNUCLEIN GENE AND CONSTITUTION BETA-SYNUCLEIN KNOCK-OUT. R Karpov, A Krayushkina, O Morozova, T Ivanova, E Lysikova, K Chaprov, Institute of Physiologically Active Compounds at Federal Research Center of Problems of Chemical Physics and Medicinal Chemistry RAS, Chernogolovka, Russia. **INTRODUCTION:** Pathogenesis of Parkinson's disease (PD) is tightly linked to the gain-of function of alpha-synuclein. The aim was to study the late-onset alpha-synuclein depletion involved in various important steps of neurotransmission. Recently we produced a new mouse line for conditional knockout of the gene encoding *SNCA* (alpha-synuclein) on background of *SNCB* (beta-synuclein) knock-out and here we used its tamoxifen-inducible pan-neuronal inactivation to study consequences of the adult-onset (from the age of 6 months) and late-onset (from the age of 12 months) alpha-synuclein depletion to the nigrostriatal system. **METHODS:** To generate experimental groups of male mice with the SNCA$^{flox/delta\ flox}$/SNCB^{-}/SNCG^{+}-NSE-Cre-ER-T2-Hemi genotype, the core L1-SNCA$^{flox/flox}$/SNCB^{-}/SNCG^{+} and subsidiary L6-SNCA$^{delta\ flox/delta\ flox}$/SNCB^{-}/SNCG^{+}-NSE-Cre-ER-T2-Homo lines were crossed. Thus, it became possible to achieve a

tamoxifen-inducible pan-neuronal knockout. The behavioral tests employed for the purpose of phenotype description included the basic motor tests (Inverted grid, Grip strength, Accelerated rotarod, the Noldus Catwalk XT gait analysis system) and the cognitive 30-min Open field test. A morphometric analysis of the dopaminergic neurons in the substantia nigra (SNps) and the ventral tegmental area (VTA) was conducted at the conclusion of the testing period. The residual alpha-synuclein levels in the brain were quantified, and the concentrations of dopamine and its metabolites in the corpus striatum were determined using highly effective liquid chromatography. **RESULTS:** Conditional inactivation of alpha-synuclein-encoding gene in adult animals triggered gradual development of hyperactive phenotype in the 30-min Open field test. No significant changes of animal balance/coordination at the age of 12 and 18 months or the number of dopaminergic neurons in the SNpc were observed after adult and late-onset alpha-synuclein depletion. In ageing (18 month) adult-onset depleted mice we found significant reduction of dopamine in the striatum and the number of dopaminergic neurons in the VTA. This reduction can be attributed to the combined effects of dysfunction in alpha- and beta-synucleins on the process of dopamine neurotransmission. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-24-00450.

EFFECTS OF AGING ON THE DEVELOPMENT OF EPILEPSY IN THE KRUSHINSKY-MOLODKINA (KM) RATS. EP Aleksandrova, AA Kulikov, AP Ivlev, EV Chernigovskaya, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. **INTRODUCTION:** In contrast to epilepsy, aging causes a decline in glutamatergic system activity. Temporal lobe epilepsy is characterized by morphological and biochemical changes in the hippocampus, causing neuronal hyperactivity. A relevant model of temporal lobe epilepsy, audiogenic kindling involves repeated stimulation of the limbic system that triggers seizures. However, the role of aging in epilepsy and pathological changes in the hippocampus remain poorly understood. **METHODS:** The Krushinsky–Molodkina (KM) rats, genetically prone to audiogenic epilepsy, was used as a model to examine the contribution of inherited epilepsy in age-related impairment of hippocampal glutamatergic transmission. For this, we compared aged (16-18-months) KM rats with control Wistar rats of the same age. To study the role of epileptic state in long-term glutamatergic system, we compared naïve and kindled rats after 7 days of rest, followed by immunohistochemical and Western blot analyses. **RESULTS AND DISCUSSION:** Temporal lobe epilepsy develops in KM rats due to CNS glutamatergic deficits during kindling. Young KM rats demonstrate decreased expression of synaptic proteins contributing to the glutamatergic system, compared to Wistar rats. At the same time, young KM and Wistar rats have comparable levels of glutamatergic neuron activation, as shown by similar expression of neuronal activation markers. However, aged KM rats, in contrast to Wistar rats, have increased expression of neuronal activation factors pERK1/, FRA-1 and p-Creb in hippocampal glutamatergic neurons. Furthermore, aging did not reduce proteins of glutamatergic transduction (AMPA, NMDA, Vglut1/2) in KM rats as significant as in Wistar rats. Kindling in young and old KM rats alters hippocampal glutamatergic system, as shown by its biomarkers pERK1/2 and ERK-dependant transcriptional factors p-Creb, c-fos, glutaminase and Vglut1, glutamate receptors mGlur1 and mGlur5. Thus, genetic predisposition to epilepsy emerges as a damaging factor in aging hippocampus that affects the glutamatergic system. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-24-00101. Part of the analyses were performed at Research Resource Center 441590 at Sechenov Institute of Evolutionary Physiology and Biochemistry RAS.

ALTERATIONS IN MICROGROOMING STRUCTURE AND EXPLORATION-RELATED BEHAVIOR IN TPH2-KO RATS. NA Krotova, IS Zhukov, PD Shabanov, N Alenina, AV Kalueff, KA Demin, RR Gainetdinov, Institute of Translational Biomedicine, St. Petersburg University Hospital, St. Petersburg State University, Institute of Experimental Medicine, Almazov National Medical Research Centre, St. Petersburg, Higher School of Economics, Moscow, Neurobiology Program, Sirius University of Science and Technology, Sirius, Russia; Cardiovascular and Metabolic Diseases, Max-Delbrück-Center for Molecular Medicine (MDC), Berlin, Germany. **INTRODUCTION:** The tryptophan hydroxylase 2 (TPH2) gene, pivotal in serotonin biosynthesis, plays a critical role in the brain, including modulating mood and anxiety. Disrupted serotonin production, such as observed in TPH2 knockout mice, has been closely linked to alterations in affective behaviors and grooming habits, often used as indicators of underlying psychiatric conditions. Here, we tested TPH2-KO rat behaviors in the open field test (OF), elevated plus-maze test (EPM) and grooming assay, focusing specifically on self-grooming microstructure/patterning. **METHODS:** Tph2 knockout (Tph2–/–) rats were generated by a truncation mutation.55 Tph2–/–, wild-type (Tph2+/+) were derived by crossing heterozygous rats (dark agouti) that were out crossed with wild-type rats (DA/OlaHsd) (Jacob Human and Molecular Genetics Center, Medical College of Wisconsin, Milwaukee, USA). For behavioral testing, 16 isolated male rats (36 weeks, n=8 per group) of the same genotype were housed 2-3 per cage from weaning with 2 cm

sawdust bedding under controlled environmental conditions with food and water ad libitum. The 10-min EPM (50x30 cm) and 3-min circular OF (67 cm diameter) were performed using Open Science (Krasnogorsk, Russia) test systems. Grooming behavior was assessed in a small 20x45 cm glass cylinder for 5 min, video-recording and scoring manually by highly trained observers. **RESULTS AND DISCUSSION:** TPH2-KO rats exhibit only modest behavioral alterations in the tests studied, reducing OF hole exploration time ($p<0.05$, Mann-Whitney U-test) but unaltering other OF and EPM behavioral parameters, including distance moved in both tests, OF grooming, freezing, sniffing, wall rears and vertical rears and fecal boli numbers, and EPM time spent in open arms, closed arms and arena center. Similarly, TPH2-KO rats did not show pronounced behavioral alterations in general grooming endpoints, including total number and time spent grooming and rostral and caudal grooming behavior analyzed separately. However, TPH2-KO rats had decreased percent of correct grooming transitions ($p<0.05$, U-test), supporting their sensitivity to changes in grooming behavioral microstructure. **CONCLUSIONS:** TPH2-KO results in inhibition of rat exploration and rigid, more patterned self-grooming behavior, suggesting association with disorders involving anxiety and repetitive behavior in human. **RESEARCH SUPPORT:** St. Petersburg State University project 95444211.

THE FUNCTIONAL STATE OF ASTROGLIA IN THE HIPPOCAMPUS OF NORMAL AND EPILEPTIC RATS: ANALYSIS OF GENETICALLY DETERMINED DIFFERENCES AND THE EFFECT OF PIRACETAM. AA Naumova, YS Grigorieva, SD Nikolaeva, KA Ivanova, MV Glazova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. **INTRODUCTION:** A plenty of data indicate that epilepsy development is accompanied with abnormal functioning of the brain astroglia. On the other hand, the studies epilepsy-related genetic abnormalities have revealed a number of mutations and genetic polymorphisms in genes regulating astrocyte metabolism and functions. These data let to assume that impairment of glial functions can be not only the consequence of epileptiform activity but also the reason of hereditary epilepsy. However, this question needs further investigation. **AIM:** To analyze key astrocytal proteins in the hippocampus of Krushinsky-Molodkina (KM) rats genetically prone to reflex audiogenic epilepsy. In addition, it is known that nootropic drug piracetam and related drugs increase the effectiveness of anti-epileptic therapy. However, detailed mechanisms that underlie the action of racetams are poorly understood. Thus, out additional task was to study the piracetam effect on astroglial functions in Wistar and KM rats. **METHODS:** Adult (P120) Wistar and naïve KM rats were recruited in our experiments. Piracetam (100 mg/kg) was i.p. injected daily for 21 days. Control animals received the injections of saline. Astrocytic markers were analyzed with use of immunohistochemical, Western blot, and real-time PCR analyses. **RESULTS AND DISCUSSION:** Comparison of KM and Wistar rats revealed no difference in the hippocampal expression of such key markers of astrocytes as GFAP, ALDH1L1, aquaporin 4, GABA transporter 3, glutamine synthetase, SPARC, and SPARCL. However, expression of nuclear factor I-A (NFIA) in astrocytes of KM rats was significantly elevated indicating the increased astrocyte activity. Expression of glutamate transporters EAAT1 and 2 was increased as well pointing on enhanced activity of glutamate removal from synapses. These changes can provide a neuroprotective mechanism which prevents the spontaneous seizures in KM rats. On the other hand, in the hippocampus of these animals, we detected abnormally low level of aldolase C, probably, pointing on the lower production of lactate which is a necessary nutrient for neurons. Analysis of piracetam effect showed that piracetam treatments led to an increase in NFIA in the hippocampus of Wistar rats. This mechanism can mediate positive piracetam effects on cognitive functions, since NFIA participates in the regulation of synaptic plasticity. However, piracetam induced no pronounced alterations in the studied proteins of KM rats. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-24-00342.

EARLY SIGNS OF AUTISM SPECTRUM DISORDER. O Frolovskaia, Herzen State Pedagogical University of Russia, St. Petersburg, Russia. **INTRODUCTION:** deficits in social communication and interaction, repetitive behaviors, restricted interests or activities, and abnormal sensory sensitivities. Features of sensory processing is one of the criteria for autism in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). One of the most important areas is problems with auditory processing. A number of studies have shown that children with autism spectrum disorder (ASD) exhibit slower conduction of bioelectrical impulses along the auditory tracts of the brainstem compared to healthy subjects. We hypothesized that ignoring early symptoms of ASD in a child may be associated with the psychological state of the parent himself, but we did not find significant correlations between the level of depression on the Beck Inventory and ignoring ASD symptoms. This may indicate that ignoring disturbing manifestations in the child's behavior is the result of low awareness of parents and possible signs of ASD. **METHODS:** Questionnaire of socio-demographic characteristics, CASD (Checklist for Autism Spectrum Disorders), Testing using Beck Depression Inventory, BDI, Testing using the Questionnaire "Assessment of Expressions of Anger" (STAXI2) by Spielberger. **RESULTS**

AND DISCUSSION: Based on our findings, the use of the ABR as a universal screen for ASD may be particularly effective and efficient in identifying young children (in the first months of life) with milder ASD features and less severe developmental delays, who may have a favorable prognosis with early onset of EIBI. Thus, using ABR as a screening tool for ASD may increase the number of children identified at an early stage, when intervention is most successful.

MOUSE MODELS OF NEURODEGENERATIVE DISEASES. EI Leonova, II Akhmarov, OA Kirillov, AV Chirinskaite, JV Sopova, Center of Transgenesis and Genome Editing, St. Petersburg State University, St. Petersburg, Russia. **INTRODUCTION:** Active longevity is a primary focus of global biomedical research, dedicated to the improvement of health in older people. While life expectancy has increased in developed countries, the prevalence of age-related neurodegenerative diseases markedly decreases the life quality. Animal models have played a crucial role in enhancing our knowledge of the molecular mechanisms that contribute to neurodegenerative conditions in different brain disorders. Among these mechanisms, Catechol-O-methyltransferase (COMT) stands out as a key enzyme in mammals that plays a role in the breakdown of catecholamines like dopamine and norepinephrine. This process of catecholamine breakdown is essential for regulating the normal function of the nervous system, including emotions and responses to stress. Ionotropic receptors that specifically bind N-methyl-D-aspartate (NMDA) are ion channels activated by glutamate, which play a vital role in regulating various processes within the nervous system at different developmental stages. Disruptions in the structure and function of these receptors can result in cognitive impairments and neurodegeneration in a range of brain disorders. **METHODS:** To obtain two lines of *comt* and *grin3a* knockout mice, we microinjected the Cas9 nuclease/guide RNA ribonucleotide complex into mouse zygotes, which were transferred into the oviducts of pseudopregnant female mice. After 21 days, the newborn mice underwent genotyping by PCR. Brain metabolites were analyzed using high-performance liquid chromatography. **RESULTS AND DISCUSSION:** We created two mouse models with frameshift mutations in the *comt* and *grin3a* genes, that led to the absence of proteins and biochemical changes in brain metabolism. The roles of COMT and Glun3a in CNS function make mice lacking these genes a valuable tool for studying mental health disorders, such as cognitive functions, anxiety, pain sensitivity, and psychosis. **RESEARCH SUPPORT:** St. Petersburg State University research project 95445540.

Day 3, May 18, 2024

Venue – Yerevan State Medical University

ISBS PRESIDENTIAL LECTURE: A LONG HISTORY OF ISBS CONFERENCES – PROMOTING TRANSLATIONAL NEUROSCIENCE STRESS RESEARCH AND EDUCATION, AV Kalueff, ISBS Office, New Orleans, USA. The International Stress and Behavior Neuroscience conferences have been held annually since 1997, providing a platform for researchers and scientists to share their latest findings and advancements in the field of stress and behavior neuroscience and biological psychiatry of stress. From the very beginning, 'stress' was very broadly construed for our meetings, which attracted to the events a wide range of experts from neuroscience, psychiatry and psychology. The first conference was held in Kiev and has since been hosted in various locations around the world, including Moscow (since 2002), St. Petersburg (since 2004), and Yerevan (since 2023). Over the years, the conferences grew from 1 half-day 1-countly 40-delegate event (in 1997) to a fully blown 4-day international congress (e.g., gathering 800 delegates from 60 countries in 2004). In 2008, the Conference created the International Stress and Behavior Society (ISBS), which took the leading role in organizing and running the Stress and Behavior conferences. The society includes over 300 members – basic neuroscientists and clinical scientists who recognize the need for a global forum to discuss the growing research on stress and its impact on behavior and brain function. In addition to 30 main ISBS conferences, the Society has successfully organized 2 Neuroscience Summer Schools for Young Scientists (2008 Russia, 2009, Latvia), and 16 Workshops on animal models of brain disorders. Since 2010, ISBS has also convened 5 Regional conferences in the Caribbean (Caribbean Biomedical Research Days), 8 Regional (North America) meetings in USA, 3 Regional (South America) meetings in Brazil, 1 Regional European meeting (in 2013 in Armenia) and 8 Regional (Asia) meetings in China and Japan. The conference has since become a highly respected event in the scientific community, attracting renowned experts and researchers from all over the world. Over the years, the conference has covered a wide range of topics related to stress and behavior neuroscience, including the effects of stress on mental health, the relationship between stress and physical illness,

and the neurological mechanisms behind stress response. As our understanding of stress and its impact on the brain continues to evolve, the conference has adapted to cover new and emerging areas of research. In addition to presenting groundbreaking research, the conference also offers panel discussions to facilitate the exchange of knowledge and ideas among attendees. It has also become a valuable networking opportunity for scientists and researchers to collaborate and form partnerships, aiming to promote translational neuroscience and biopsychiatry research and education. We shall be proud of our accomplishments so far, and look forward to further successes and new frontiers.

INDUCTION OF INFLAMMATION IN EARLY POSTNATAL PERIOD: EFFECT ON ACTIVATION OF ASTROCYTES AND MICROGLIA IN BTBR MALE MICE. MM Kolesnikova, Novosibirsk State University, Novosibirsk, Russia. **INTRODUCTION:** Autism spectrum disorder (ASD) is the most common neurodevelopmental disorder, but the mechanisms of its development are still unclear. Patients with ASD are known to have numerous immune abnormalities, including neuroinflammation in post mortem samples; indicating the potential involvement of the immune system in the pathophysiology. However, it is still not known whether inflammation experienced during critical periods of brain development can aggravate the disorders observed in patients. **AIM:** To evaluate the effect of early-life induced inflammation on astroglial and microglial activation in the hippocampus of BTBR T+Itpr3tf/J (BTBR) males, which exhibit behavioral impairments resembling ASD patients, as well as similar immune features. **METHODS**: Inflammation was induced by the administration of bacterial (LPS, 50 μg/kg) and viral (Poly I:C, 10 μg/kg) mimetics or their combination on postnatal days 3 and 5. The control group received an equivalent volume of saline. On day 40 of the experiment, the expression of the Gfap (astroglia activation marker) and Aif (microglia activation marker) genes in the dorsal and ventral hippocampus was assessed using real-time PCR. **RESULTS AND DISCUSSION:** For the expression of the *Aif1* and *Gfap*, effects were found only in the dorsal hippocampus, with significant interstrain differences (Aif1: $F(1,71) = 6.802$, $p=0.01$; Gfap: $F(1,71) = 22.504$, $p<0.001$). At the same time, BTBR mice showed decreased expression of *Aif1* ($p=0.01$) and, conversely, increased expression of *Gfap* ($p<0.001$) compared to C57BL/6J mice. No significant influence of inflammatory agents on these parameters was identified. Thus, BTBR mice demonstrate reduced *Aif1* and increased *Gfap* expression in the dorsal hippocampus, indicating lesser microglial and higher astroglial activity. Experience of inflammation at an early age had no effect on astroglial or microglial activation in mice of either strain. **RESEARCH SUPPORT:** State Budget project FWNR-2022-0016.

SYMPOSIUM 5: ZEBRAFISH NEUROSCIENCE MINI-SYMPOSIUM (Chair: TG Amstislavskaya)

ACUTE AND CHRONIC EFFECTS OF NITROGLYCERIN IN ADULT ZEBRAFISH (*DANIO RERIO*). TO Kolesnikova, AN Ikrin, AM Moskalenko, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** Migraine is a highly prevalent, chronic neurological disorder, necessitating studying pathophysiological mechanisms in both clinical and experimental settings. Nitroglycerine (NTG) exposure has long been known to cause migraine-like states in humans and animals. The zebrafish (*Danio rerio*) is a popular model organism with physiological and genetic homology to humans, and sensitivity to a wide range of neuroactive drugs. **METHODS:** We used 128 adult male and female wild-type long-tailed zebrafish (7-9 months old). Acute 20-min exposure by water immersion involved placing zebrafish individually in a 1-L plastic beaker with 1, 5, and 10 mg/L NTG diluted in systemic water. Zebrafish were subjected to chronic exposure to NTG at concentrations of 1, 2 or 4 mg/L for 5 and 7 days. We then analyzed behavior in the novel tank test (NTT), shoaling test (ST) and zebrafish tail immobilization (ZTI) test. **RESULTS AND DISCUSSION:** Acute behavioral effects of 20-min NTG exposure, revealing increased immobility duration and meandering at 10 mg/L and decreased total distance and top entries at 10 mg/L in NTT. Chronic 5-day exposure to NTG also produces anxiety-like phenotypes and impaired social behavior at 4 mg/L. Increased average inter-fish distance also showed after 7-day chronic NTG treatment at 1 and 2 mg/L in ST. However, 7-day NTG did not alter anxiety-sensitive endpoints in NTT in adult zebrafish. Acute, but not chronic, NTG treatment also increased despair-like behavior in adult zebrafish at 10 mg/L, decreasing total distance moved, frequency and duration of high active states and total activity in the ZTI test. Here, we investigate the acute and chronic effects of NTG on adult zebrafish, aiming to mimic certain aspects of migraine pathobiology. Taken together, this confirms the sensitivity of zebrafish to central effects of NTG and suggests the potential utility of this model organism for studying the pathological mechanisms of migraine and preclinical screening drugs for its treatment. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-25-00246.

COMPARATIVE STUDY OF THREE NAVIGATION STRATEGY OF ZEBRAFISH IN THE TRANSFORMER MAZE. EV Filatova, Sechenov Institute of Evolutionary Physiology and Biochemistry, St. Petersburg, Russia. **INTRODUCTION:** Zebrafish is widely used as a model animal. Navigation skills are one of the basic cognitive functions, which provide survival and adaptation. Teleosts analyze the space and their position in it using a variety of sense modalities and different navigation strategies. Most experiments examining zebrafish navigation abilities typically offer a choice in the test to assess which strategies the animals prefer. The Transformer maze allows us to perform comparative studies of different strategies under identical conditions. The goal of the work was to study the zebrafish ability to learn and perform three different tasks, each requiring the use of a specific strategy. **METHODS:** Fish were trained to perform three tasks. The first one was an allocentric landmark-based navigation. The second was an egocentric sensory-based navigation (following a black line drawn on the floor). The third one was an egocentric route-based navigation (remembering the route). All three tasks were performed with food reinforcement. There were estimated the success of the task executions, the time spent in the start compartment, and the decision-making time, which was defined as the time spent by the animal at the points of choosing the direction of movement. **RESULTS AND DISCUSSION:** Zebrafish learn successfully in all three tasks. Comparative analysis of error-free trials and trials with errors showed that by the end of the training, the average decision-making time in error-free trials is significantly lower than in trials with errors. But in the probes, it becomes comparable. The decision-making time in trials with the errors does not differ in the three tasks, but in the error-free trials, it is significantly lower in the route-based task. The time spent in the start compartment is longer only during the learning the first task in the trials with errors, but a general comparison of all three tasks showed a significant delay in exiting the start compartment in the trials with errors. Because the Transformer maze does not allow the animal to use mixed or preferred strategies to achieve a goal, zebrafish success in all three tasks demonstrates their ability to use all three kinds of navigation separately. At the same time, the time of decision-making and the time to exit the start compartment are lower in confidently execution, than in the unsure. Other studies have suggested that slower explorer environment animals may be more accurate in decision making and more flexible in behavior. Our results show that in solving navigation tasks, decision-making time more likely depends on the animal's confidence and level of training and varies widely depending on the situation. **RESEARCH SUPPORT:** State task 075-00264-24-00.

INTRANASAL METHOD OF DRUG DELIVERY IN ADULT ZEBRAFISH USING NICOTINE TARTRATE. DS Galstyan, TO Kolesnikova, AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, Institute of Experimental Medicine, Almazov National Medical Research Centre, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** The nasal mucosa is an important and common target for the delivery of a wide range of drugs. Zebrafish have a highly developed olfactory system and use it to detect food, predators and potential mates, just like other vertebrates. **METHODS:** A total of 60 wild-type adult short-fin zebrafish were used for this study (male: female ratio ~50:50). All fish were divided into 4 groups: a group that received 30 mg/l nicotine tartrate by water immersion (20 min), fish that received the drug intranasally (10 mg/ml and 5 mg/ml) and a control group. Briefly, all fish were kept for 20 min in a plastic beaker (250 ml) containing the drug (30 mg/L water immersion) or in water. 5 min before filming the experiment, the fish were caught with a net and 1 µl of nicotine tartrate (5 or 10 mg/ml) or water (control and water immersion) were dropped into the nostrils. The novel tank test (NTT) was used to evaluate the behavior of zebrafish within 5 min of drug administration. Behavioral parameters (frequency, top entry duration and delay, distance traveled, frequency and duration of freezing) were calculated using Noldus EthoVision XT11.5 and analyzed using the Kruskal-Wallis (KW) test followed by Dunn's post-hoc test for significant KW data ($p<0.05$). **RESULTS AND DISCUSSION:** Fish receiving 30 mg/l nicotine tartrate by water immersion ($p<0.001$), as well as 10 mg/ml intranasally ($p<0.05$) showed a high anxiolytic effect with statistically significantly higher time in the top, compared with the control group. Thus, intranasal administration of nicotine tartrate produces similar effects in zebrafish with an acute 20-min effect by immersion in water. By employing this new method of drug administration, the duration of the acute experiment can be curtailed and the utilization of medications can be minimized. **RESEARCH SUPPORT:** Russian Science Foundation project 23-25-00412.

BIOCHEMICAL AND BEHAVIORAL EFFECTS OF PREDNISOLONE IN ADULT ZEBRAFISH. EV Nikiforova, AV Zhdanov, SL Khatsko, AV Kalueff, Ural Federal University, Yekaterinburg, Russia. **INTRODUCTION:** Prednisolone is a synthetic glucocorticoid, actively used clinically as an anti-inflammatory, antiallergic and immunosuppressive agent. Treatment with prednisolone, like with other glucocorticoids, is accompanied by various side effects, including on CNS. Humans and zebrafish

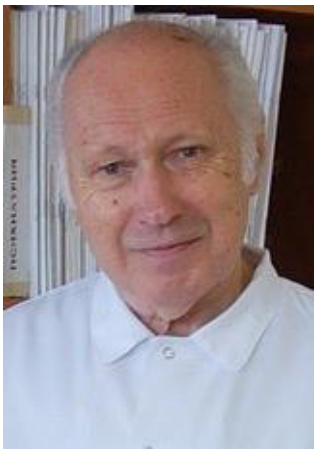
have similar structure and functioning of the endocrine systems. **METHODS**: The experiment involved a total of 59 wild-type short fin adult zebrafish, experimentally naive and kept in a 40-L hometank. Animal behavior was assessed in the 5-min novel tank test (NTT), using the EthoVision and RealTimer software, in control (n=12) and 4 experimental groups acutely exposed to prednisolone at 1, 10, and 50 mg/L (n=15-16 per group). The cortisol level was measured on 5 body samples of fish from each group by ELISA, and adjusted based on the body mass (ng/g). Statistical analyses used Statistica 12.0 and U-test at $p<0.05$. **RESULTS AND DISCUSSION:** Prednisolone at 10 mg/L significantly increased in the number ($p=0.039$) and duration ($p=0.019$) of freezing bouts and erratic movement frequency vs. controls. A significant increase in the level of cortisol was detected at 1 and 10 mg/L ($p=0.021$ and $p=0.012$) vs. control. Overall, prednisolone at low concentrations unalters fish behavior but increases cortisol levels, which shows its effectiveness and safety in binding to glucorticoid receptors even in small doses. Increasing its concentrations to 10 mg evokes anxiety-like bveahvior in fish without a significant dose-dependent increase in cortisol concentration. However, rising prednisone concentration to 50 mg does affect behavioral or cortisol endpoints. These results indicate binding and saturation of glucocorticoid receptors, which allows the use of prednisone to model hypocortisolism in zebrafish. Thus, prednisone exerts similar effects on behavior and the neuroendocrine axis in zebrafish and humans, making these fish a useful model of endocrine and neural disorders. **RESEARCH SUPPORT:** Ural Federal University, Yekaterinburg, Russia.

LOCOMOTION ACTIVITY OF THE ZEBRAFISH *DANIO RERIO* REGISTERED BY SFCO HYDROPHONE. AS Khachunts, SG Gevorgyan, AA Tumanian, AR Sargsyan, NE Tadevosyan, GS Gevorgyan, LA Orbeli Institute of Physiology NAS RA, Yerevan State University, Yerevan, Armenia. **INTRODUCTION:** Registration and analysis of behavioral characteristics of small laboratory animals (zebrafish, mice, and rats) are widely used in physiology, pharmacology, translational medicine, and other fields. Studying animal activity makes it possible to register social behavior, stress, and emotional manifestations (aggression, anxiety), track the movement of animals in a limited field (activity), record specific patterns of behavior and their changes by pharmaceuticals, other bioactive compounds or genetic mutations. An important place among behavioral physiology monitoring methods is animal activity tracking by recording microseismic oscillations generated by animal locomotion in the experimental chamber. **AIM:** To characterize locomotor activity of zebrafish registered by highly sensitive hydrophone based on Single layer Flat Coil Oscillator (SFCO) technology developed by PSI Ltd. **METHODS:** An acrylic plastic tank was used to study the behavioral activity of fish. Signals detected by the SFCO hydrophone were fed to the Counting and Processing Unit with appropriate software (high-speed, 8 channel SFFM-8 frequency meter) for detecting and processing the recorded data. The *SFFM-8* frequency meter registers dynamic changes of the frequency at a rate of 1000 measurements per second. Further additional processing of the measured data was performed using *"Diadem"* (NI), and *"Mat Lab"* (*Math Works*, *Inc*., USA) programs. Data processing was performed using digital filtering and Fourier-transform. To decompose the signal into intrinsic mode functions (IMFs), we utilized the empirical mode decomposition (EMD) method. Simultaneous video recording of animal behavior was paralleled with the signals registered by SFCO sensor. **RESULTS AND DISCUSSION:** Recording behavioral activity of fish with SFCO hydrophone and subsequent processing of signals obtained using empirical mode decomposition and spectral analysis methods allowed us to reveal and identify main components of the fish locomotor activity: low-, middle- and high-frequency. The first component extends from 0.3 to 10 Hz and may contain several peaks. The *high*-frequency component is bell-shaped with a maximum at a frequency of ~27-28 Hz in the 20-45 Hz range. Between these two components, middle-frequency unstable components typically occupy the 10-20 Hz range. The low-frequency component reflects the sweeping movements of the fish's body, while the high-frequency activity is most likely associated with the activity of the fin rays, which provide undulation movements of the fins. **RESEARCH SUPPORT:** PSI Ltd. (providing sensors and devices for signal registration for the present study).

ISRIB-INDUCED BRAIN TRANSCRIPTOMIC AND BEHAVIORAL EFFECTS IN TRAUMATIC BRAIN INJURY-EXPOSED AND CONTROL ZEBRAFISH. NP Ilyin, AD Shevlyakov, GA Boyko, AM Moskalenko, AN Ikrin, DS Galstyan, TO Kolesnikova, NV Katolikova, SA Chekrygin, AV Kalueff, KA Demin, Almazov National Medical Research Centre, Institute of Translational Biomedicine, Core facility center "Center Bio-Bank", St. Petersburg State University, St. Petersburg, Neurobiology Program, Sirius University of Science and Technology, Sirius, Scientific Research Institute of Neurosciences and Medicine, Novosibirsk, Russia. **INTRODUCTION:** Traumatic brain injury (TBI) is a significant health and social issue, affecting millions of people worldwide each year that is also linked to high mortality and various long-term disabilities. Despite the severity and profound impact of TBI, there are currently no effective, specific treatments available that can adequately recover neuronal

damage or address the associated behavioral and cognitive impairments. Increasing research suggests that TBI may be connected to an excessive activation of the integrated stress response (ISR) in the brain. Recently, a compound known as ISRIB has been discovered, which effectively counters the effects of eIF2α phosphorylation, a key process in ISR. Given ISR's involvement in brain degeneration, ISRIB is emerging as a promising agent to explore for its potential beneficial effects on brain health. In this study we for the first-time investigate neurotranscriptomic effects of ISRIB in vertebrates using zebrafish in both healthy animals and following TBI exposure. **METHODS:** The study utilized 80 wild-type naïve short-fin zebrafish randomly allocated into 4 groups (n=20). TBI treated group was subjected to TBI by insertion of 27 g needle into the right telencephalon through the scalp on the first experimental day. ISRIB group received intraperitoneal injections of 2.5 mg/kg on days 1-3. TBI+ISRIB group got the same treatment as TBI and ISRIB groups but simultaneously. Whereas sham control group got injected with a drug-free solvent on days 1-3 similar to ISRIB group. We assessed behavioral changes in shoaling test (days 1-3) and the free-movement pattern (FMP) Y-maze (day 3) to study potential cognitive, motor, social, and anxiety-related alterations. Following the last behavioral test, the telencephalon samples were collected and analyzed using RNA-seq, examining differential gene expression using two-factorial testing in DESeq2 package with post-hoc gene set enrichment analysis (GSEA) using STRING database. **RESULTS AND DISCUSSION:** Expectedly, TBI resulted in decreased locomotion and disturbed social activity in shoaling test and increased the number of repetitions in Y-maze suggesting memory deficits. Interestingly, ISRIB exposure alone didn't affect memory in Y-maze, increased social activity on the first day of shoaling test and decreased locomotion on days 2-3. Despite the lack of beneficial effects of ISRIB in the tests, exposure to ISRIB following TBI successfully attenuated most of TBI behavioral effects, suggesting existence of strong interaction effect. Our two-factorial RNA-seq analysis further supports the idea that ISRIB evokes different effects in healthy and TBI cohorts highlighting involvement of different inflammatory and neurogenetic pathways in those factors. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation agreement 075-15-2020-901.

ISBS SYMPOSIUM 6: LAPIN BIOLOGICAL PSYCHIATRY SYMPOSIUM (Chair AV Kalueff)



WHAT ARE THE EXPERIENCES AND CONSEQUENCES OF STRESS DUE TO EMOTIONAL ABUSE ON MARRIED WOMEN? HN Shilubane, R Mulaudzi, ET Nkhwashu, University of Venda, Thohoyandou, South Africa. **INTRODUCTION:** The rise in domestic violence and domestic homicide is a cause for concern and affects women psychologically, as they display signs and symptoms of stress. Emotional abuse is seen as an issue to be kept secret and not reported because there is no evidence of abuse until stress, sickness and death occur. **AIM:** To explore the experiences and consequences of stress due to emotional abuse amongst married women in a particular village within the Limpopo province. **METHODS:** The study used a qualitative descriptive phenomenological design. Purposive sampling was used to choose participants with lived experiences related to stress due to emotional abuse, with the assistance of a local healthcare expert. In-depth one-on-one unstructured interviews were held. Data saturation limited the number of married women interviewed to ten. The data were analyzed using Colaizzi's technique. **RESULTS AND DISCUSSION:** The findings indicated three themes: the participants' experiences of stress, the effects of stress caused by emotional abuse on the victim, and reasons for remaining in an abusive marriage, as well as eight sub-themes. Although married women experience stress in their marriages, findings revealed that poverty and love for their spouses make them remain in such abusive marriages. Married women in this study were unaware of the implications of emotional abuse. Cultural institutions that promote lobola undermine women, perpetuate violence, and give husbands power over their wives. Many women are taught from a young age to be submissive, subordinate and obedient to their male counterparts, and they are less valued than men. This increases stress on them which results in depression. The participants in the current study believed that men had the right to do anything they wanted with them because they had paid the bridal fee (lobola). As a result, it is critical to raise awareness of stress caused by emotional abuse among women by educating them about their rights through numerous channels. Women should be educated on strategies to handle stress to prevent the development of depression.

THE ORBITOFRONTAL CORTEX DETERMINES THE SPECIFICITY OF MODEL-BASED LEARNING. KM Costa, R Scholz, K Lloyd, P Moreno-Castilla, MPH Gardner, P Dayan, G Schoenbaum, National Institute on Drug Abuse Intramural Research Program, National Institute on Aging Intramural Research Program, Baltimore; University of Alabama at Birmingham, Birmingham, USA; Max Planck Institute for Biological Cybernetics, Tübingen, Germany; Concordia University, Montreal, Quebec, Canada. **INTRODUCTION:** Animals, including humans, use mental models of the world to guide behavior, but little is known about how these "cognitive maps" are created. The orbitofrontal cortex (OFC) is typically thought to access these maps to support model-based decision-making, but recent evidence suggests that it may instead integrate novel information into existing and new maps. We tested these two alternatives using a theory-inspired task, high-potency chemogenetics, and computational modelling. **METHODS:** Rats transfected with either hM4d (inhibitory DREADD receptor) or mCherry (control) in the OFC, first underwent conditioning, in which two different auditory cues (A and B) predicted the delivery of either banana- or bacon-flavored pellets. During this phase, rats were injected i.p. with 0.2 mg/kg JHU37160 dihydrochloride, a new-generation DREADD agonist, to inactivate OFC neurons in the hM4d group. Rats were subsequently subjected to conditioned taste aversion training, in which the pellet associated with B was paired with aversive LiCl injections. Finally, rats were given a probe test in which the cues were presented in extinction. **RESULTS AND DISCUSSION***:* Rats in both groups learned the cue-reward associations during conditioning, and both groups also reduced consumption of the devalued pellet after conditioned taste aversion training. During the probe, the control group reduced responding to cue B in relation to A, demonstrating an ability to perform model-based decision-making, but this was abolished in the hM4d group, confirming a role for the OFC in creating new maps. However, OFC inactivation surprisingly led to generalized devaluation (instead of no devaluation at all), defying traditional assumptions about model-based learning. We applied a novel reinforcement learning framework to model this behavioral pattern and found that the OFC inactivation effect is best explained by a circumscribed deficit in defining credit assignment precision during model construction. Our results suggest that the OFC defines the specificity of associations that comprise internal models of the world. We are now currently running studies in which we apply this computational framework to model associative learning in human decision-making behavior in health and disease. **RESEARCH SUPPORT:** National Institute on Drug Abuse Intramural Research Program, German Federal Ministry of Education and Research, Humboldt Foundation, German Research Foundation grant MA 8509/1-1.

CAREGIVER BURDEN AND FAMILY SUPPORT ON CLINICAL RECOVERY IN PATIENTS WITH SCHIZOPHRENIA: A LONGITUDINAL STUDY. A Caqueo-Urízar, Universidad de Tarapacá, Arica, Chile. **INTRODUCTION:** Recovery in schizophrenia is an important goal of mental health services. Factors involved in patients' recovery are related to individual characteristics, but also to environmental elements such as social support, family support and caregiver burden. **AIM:** To analyze the influence of caregiver burden and family support on clinical recovery of patients with schizophrenia during a one-year follow-up period. **METHODS:** Latent profile analysis (LCA) was used to identify recovery profiles in patients diagnosed with Schizophrenia by estimating a model of up to a total of 4 classes to identify the model with the best fit. A latent transition analysis (LTA) was used as a longitudinal extension of the LCA to analyze changes in the latent class at 12-month follow-up. For covariate analysis using the 3-step method to explore the relationships between the latent class variable and the predictor variables. **RESULTS:** LCA findings showed that a 3 latent class model was adequate to classify patients into three recovery profiles: low, medium and high. LTA results showed that the medium recovery profile was highly stable; on the other hand, the most significant latent transitions were observed between high and low recovery profiles after 12 months. During baseline caregiver burden was a significant predictor of class membership, however after 12-month longitudinal follow-up perceived family support significantly predicted class membership in low recovery profiles. **DISCUSSION:** The results are a significant source of information in the process of designing and developing interventions based on family and patient context. **RESEARCH SUPPORT:** Agencia Nacional de Investigación y Desarrollo de Chile ANID through FONDECYT 1200785.

VOLUNTARY PHYSICAL ACTIVITY DECREASES DEPRESSION-LIKE SYMPTOMS VIA INTERLEUKINE-1β RECEPTORS IN STRESSED MICE. Z Sudani, HA Mahdirejei, Ali-Akbar Salari, Salari Institute of Cognitive and Behavioral Disorders (SICBD), Karaj, Alborz, Iran. **INTRODUCTION:** Inflammatory cytokines, such as interleukin-1 (IL-1) β, have been associated with major depressive disorder. Recent clinical and animal studies have demonstrated that blocking IL-1β receptors can alleviate depression-related symptoms, indicating its potential as a therapeutic target. Conversely, increased physical activity has been shown to enhance quality of life by reducing stress-related symptoms and fortifying the immune system. Furthermore, exercise has been found to mitigate stress-

related disorders, encompassing anxiety, depression, and inflammatory responses. However, the interplay between physical activity and IL-1β in depression has remained unexplored. This study aimed to ascertain whether heightened physical activity could alleviate depression-related symptoms by influencing IL-1β receptors in stressed mice. **METHODS:** To investigate this, animals were subjected to a chronic stress protocol, followed by exposure to running wheels to boost their physical activity levels. Concurrently, animals received an IL-1β antagonist and agonist, and their depression-related behaviors were assessed through the sucrose preference test, tail suspension test, social behavior, and forced swim test. **RESULTS AND DISCUSSION:** The results revealed that blocking IL-1β receptors enhanced the antidepressant effects of increased physical activity, while agonist treatment counteracted the antidepressant impact of exercise in stressed mice. In conclusion, these findings suggest that heightened physical activity can alleviate depression-related symptoms by modulating IL-1β receptors under conditions of stress in mice. **RESEARCH SUPPORT:** Salari Institute of Cognitive and Behavioral Disorders (SICBD), Karaj, Alborz, Iran.

EFFECT OF PRENATAL HYPERHOMOCYSTEINEMIA ON THE STRUCTURE AND FUNCTIONING OF THE CIRCULAR SYSTEM OF THE RAT PLACENTA. DS Vasilev, NL Tumanova, AN Kadenov, AV Mikhel, IV Zalozniaia, YP Milyutina, AV Arutjunyan, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, DO Ott Research Institute of Obstetrics, Gynecology and Reproductive Medicine, St. Petersburg, Russia. **NTRODUCTION:** Pathologic influences affecting the functional state of the placenta during pregnancy can lead to negative changes in the fetus. One of such toxic factors is maternal hyperhomocysteinemia (HHC). It has been shown that a high level of homocysteine in the mother's body causes disruption of trophoblast invasion, affects uteroplacental and fetal-placental blood flow, and may cause placental detachment, leading to the development of oxidative stress in the fetal brain. However, there are few works devoted to the study of the placental structure pathogenesis in prenatal HHC. **METHODS:** HHC was induced in female rats by *per os* administration of 0.15% aqueous methionine solution (0.10-0.15 g per animal) in the period of days 4-21 of pregnancy. The females were injected with Evans blue dye into the bloodstream on 20th pregnant day. The dye content in the brain tissue and placenta of the offspring was investigated 3 h after dye injection. Placenta tissue was taken on the 20th day of pregnancy, fixed in 10% neutral formalin, sectioned on a freezing microtome-cryostat and stained with hematoxylin and eosin. The total area of microthrombi of lacunae and capillaries of the placenta were determined. Electron microscopy was also performed. **RESULTS AND DISCUSSION:** The dye content in the brain tissue of HHC embryos was higher than in controls, indicating increased permeability of the placental barrier for proteins. Electron microscopy showed more fenestra in endothelial layer and disintegration of syncytiotrophoblast. Also, microthrombosis of vessels in the placenta was detected in HHC animals, and an increase in the area of microthrombi in the labyrinthine layer of the placenta was shown. The microthrombosis in the placental tissue of HHC animals may impede the transplacental transfer of nutrients, trophic factors and oxygen, affecting fetal development. In the HHC group, pathological changes of placental trophoblast cells were observed, as well as pathological accumulation of lipid granules, electron-dense bodies and collagen fibers in their cytoplasm. The results obtained may indicate the presence of pathologic changes and the development of microthrombosis in the rat placenta during HHC. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00393.

DYNAMIC CHANGES IN NEUROVASCULAR CONNECTIVITY IN PATIENTS WITH CHRONIC CEREBRAL CIRCULATORY DISORDERS: A STUDY OF RESTING-STATE FMRI AND CEREBRAL PERFUSION. VD Abramova, International Tomography Center SB RAS, Novosibirsk State University, Novosibirsk, Russia. The neurovascular coupling is a model of the interaction between the neuronal activation and cerebral blood flow, which is the basis of the functional MRI (fMRI) method. Impaired neurovascular coupling in cerebrovascular diseases leads to a mismatch between the metabolic needs of neurons and blood supply, which can lead to an erroneous interpretation of the results of fMRI studies in this group of subjects. The application of a personalized approach that takes into account individual perfusion characteristics will improve the sensitivity of the assessment of cognitive functions using fMRI. This will help to get closer to understanding the violation of neurovascular communication in this group of subjects. The main purpose of this study was to study the dynamic changes in neurovascular coupling in patients with a history of stroke at different stages of disease development after a stroke in comparison with healthy subjects. This was done by combining regional fALFF maps (fractional amplitude of low-frequency fluctuations) obtained using fMRI at rest and cerebral perfusion maps obtained using ASL (arterial spin labeling). We also evaluated the activity of the default mode network (DMN). The work was carried out using an Ingenia 3.0 T MR tomograph, Philips. The study involved 20 healthy subjects (7 women, average age 23) and 17 subjects with a history of stroke (11 women, average age 61). For subjects with a history of stroke, 8 people attended all three sessions, 3

people two sessions, and 6 people one session. Functional and perfusion data were collected using echo-planar sequences (TE=16 ms for ASL and TE=35 ms for fMRI). Data preprocessing was carried out using the SPM software package, fALFF — CONN mapping, and FSL perfusion mapping. To determine the values of the neurovascular coupling, we used the correlation coefficients of the region-averaged (AAl-2 atlas) fALFF data and the values of cerebral perfusion. Functional differences in DMN were observed between healthy and post-stroke subjects in the acute, subacute and chronic periods. Statistically significant differences in neurovascular coupling in gray matter and in brain regions were also found when comparing healthy volunteers and patients after stroke. At the same time, no changes in the neurovascular coupling between periods of stroke were found, in line with known pathophysiological data for chronic cerebrovascular diseases.

NEW TRANSCRIPTOMIC BRAIN PATTERNS FOR AUTISM SPECTRUM DISORDERS PATIENTS. AD Shevlyakov, AN Ikrin, TO Kolesnikova, LG Danilov, KA Demin, AV Kalueff, Sirius University of Science and Technology, Sochi, St. Petersburg State University, Almazov National Medical Research Centre, St. Petersburg, Russia. **INTRODUCTION:** Autism spectrum disorders (ASD) is a group of neurodevelopmental diseases characterized by a high heterogeneity, complication of causes and lack appropriate treatments. Also, the exact biological pathways for target therapy are not yet determined. In this study, we applied transcriptome data analysis to assess the molecular pathway activity in the cerebral cortex of ASD patients. **METHODS:** Gene expression ASD data were downloaded from gene expression omnibus (GEO). GSE178206 included 13 ASD patient cerebral cortex tissue samples and 9 normal cerebral cortex tissue samples as control. The row reads were processed by Trimmomatic software (version 0.39) to remove adapters and cut low quality sequences. The unsatisfactory quality had only reverse reads, which were processed as a single end read type. The purified reads were mapped to the human GRCh37 reference transcriptome and quantified by salmon (version 1.10.0) pseudoalignment software. The differential expression (DE) analysis was performed with the DESeq2 v. 40.2 Bioconductor package. P-value and false discovery rate (FDR) were set at 0.05. Identified differentially expressed genes (DEGs) were eclipsed by ASD-associated genes loaded from the SFARI database (accessed Feb 2024). Gene set enrichment analysis (GSEA) was used to identify significant biological pathways. For this study the generally applicable gene set enrichment (GAGE) analysis was chosen as a more powerful subset of GSEA. The KEGG and GO pathway enrichment analyses were performed on normalized and log2-transformed counts by the gage function in R (version 4.3.1) Bioconductor package v. 2.50.0. FDR cut-off was set at 0.05 for the KEGG pathways and 0.01 for the GO pathways. **RESULTS AND DISCUSSION:** A total of 376 DEGs (306 upregulated and 70 downregulated) were identified after gene expression analysis. 34 upregulated genes from the DEGs group were associated with ASD. There genes were divided into four main functional clusters, which were related to the methylation process (*TET3, KDM4B, KDM6B, PHF2, SETD1B, SRCAP*), transcription regulation and chromatin remodeling (*ZBTB20, INTS1, SRRM2, SRCAP, CIC, LZTR1, ZC3H4, PHF12, PER1, BICRA, NFIX*), synaptic/neuron organization, vesicle formation and cytoskeleton activity (*FLNA, LRP1, MYH9, RAB43, PLXNB1, MTSS2, CLIP2*) and others (*SBF1, PREX1, MDGA2, ABCA7, DMPK, SKI, PACS2, PC, SLC38A10, SLC7A5, C12orf57*). The GAGE pathway analysis showed a significant increase in the enrichment of upregulated pathways: immune regulation, cell differentiation and morphogenesis, translation process, cytoskeleton activity and cellular mobility. The downregulated pathways also included autophagy, oxidative phosphorylation and mitochondrial activity, ubiquitination process, synaptic vesicle cycle and organization. Overall, we suppose that increased activity of these pathways can play a role in ASD pathogenesis. **CONCLUSIONS:** Thus, development of new methods for ASD-treatment based on correction these molecular pathways, can help prevent the development of the disease and be a useful tool for future ASD therapies and diagnostics. **RESEARCH SUPPORT:** Sirius University of Science and Technology Project ID NRB-RND-2116. KAD was supported by St. Petersburg State University Project 93020614.

EEG ASSOCIATION WITH BLOOD INDICES IN HEALTHY AGING. I Mikheev, I Polikanova, O Martynova, School of Psychology, HSE University, Federal Scientific Center for Psychological and Interdisciplinary Research, Institute of Higher Nervous Activity and Neurophysiology RAS, Moscow, Russia. The relationship between age and blood levels of hemoglobin and cholesterol has been extensively studied. Specifically, hematocrit may reflect certain biochemical changes occurring in various health conditions, including both aging and vascular-dependent cognitive impairment. Patterns of electroencephalography (EEG) have also shown age-dependent dynamics. While altered blood markers of hematocrit and cholesterol have been observed in different health conditions, there are few studies focusing on their association with brain changes during aging. To address this gap, we employed regression modeling of EEG features associated with blood index data. **METHODS:** We utilized resting-state EEG and blood index data from the elderly group in the Max Planck Institute

Leipzig Mind-Brain-Body Dataset (Lemon) (N=74, 67.6±4.7 years, range 59–77, 37 female). Preprocessing was performed using the MNE-BIDS-Pipeline. For feature extraction, we employed Source Power Comodulation (SPoC) to identify neural activity patterns associated with blood indices of hematocrit and low-density lipoprotein cholesterol (LDL-C), Alpha Peak Frequency (APF), and Riemannian Decomposition of EEG covariance matrices, followed by linear regression. To evaluate model quality, we conducted 5-fold cross-validation and used the adjusted R2 metric. **RESULTS:** The adjusted R2 metrics for predicting hematocrit index were 0.58±0.03, 0.71±0.04, and 0.73±0.02 for APF, SPoC, and Riemannian Decomposition, respectively. For predicting blood concentrations of LDL-Cl, the adjusted R2 metrics were 0.63±0.01, 0.66±0.01 and 0.71±0.01 for APF, SPoC and Riemannian Decomposition, respectively. **CONCLUSIONS:** Hematocrit declined with age, while increased LDL-C is directly related to atherosclerosis. Our results show a relatively strong predictive power of EEG in detecting changes in hematocrit and LDL-C, and suggest that resting-state EEG may display age-dependent brain changes influenced by the physiological state of the body as a whole.

MOLECULAR NEUROSCIENCE SYMPOSIUM OF THE INSTITUTE OF MOLECULAR BIOLOGY NAS RA (Chair AA Arekelyan)

TEMPORAL CHANGES OF GENE EXPRESSION IN HEALTH AND MENTAL DISORDERS. AA Arakelyan, S Avagyan, A Kurnosov, T Mkrtchyan, G Mkrtchyan, R Zakharyan, KR Mayilyan, H Binder, Institute of Molecular Biology NAS RA, Armenian Bioinformatics Institute, Yerevan, Armenia; Interdisciplinary Center for Bioinformatics, Leipzig University, Leipzig, Germany. Schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD), are complex and heterogeneous conditions thought to arise from an interplay of diverse genetic and environmental factors. The molecular events contributing to disease development, manifestation, and course are known to be distributed through embryonic life to the elderly. However, due to the age of onset, clinical samples are always thresholded to relatively older age, and little is known about early dynamics in gene expression in these diseases. We performed a secondary analysis of microarray datasets of post-mortem prefrontal cortex of control brains and patients with SCZ, BD, and MDD available in Gene Expression Omnibus and the Stanley Medical Research Institute Online Genomics Database. We used self-organized maps machine learning to dissect brain transcriptome into functional gene modules associated with aging and diseases and Gaussian Process Regression to detect time-perturbation points of disease-associated functional points characteristics to mental disorders. Finally, we performed eQTL enrichment of genes in time-perturbed functional modules. Our results indicate that mental disorders are characterized by early, mid, and late deregulation of identified functional spots. The results align with the hypothesis that two or more 'hits' are required over the lifespan rather than only one early-life event for disease manifestation. Time-perturbed functional spots were enriched with eQTL genes implicating the contribution of genetic components in the gene expression dynamics and development of the disease phenotype.

CAVITY CONSTRICTION OF KCNQ CHANNELS IMPEDES K+ CONDUCTION. V Vardanyan, Institute of Molecular Biology NAS RA, Yerevan, Armenia. KCNQ1 potassium channels play a pivotal role in the physiology of several human excitable and epithelial tissues. The latest cryo-EM structures provide new insights into channel function and pharmacology, opening avenues for novel therapeutic strategies against human diseases associated with KCNQ1 mutations. However, these structures also raise important questions that should be addressed in order to better appreciate the scientific and clinical relevance of the findings. Cryo-EM structures thought to represent the open state of the channel feature a cavity region not wide enough for accommodation of hydrated K+. To understand how K+ passes through the cavity constriction, we utilized microsecond-scale molecular dynamics (MD) simulations using the KCNQ1/KCNE3 cryo-EM structure, characterized mutants at the G345 residue situated at the narrowest point of the cavity, and recorded single channels. The findings indicate that ions become partially dehydrated at the constriction, which enables permeation. MD simulations demonstrate that the constriction can impede the flow of ions through the channel's pore, a finding that is corroborated by mutational screening and single channel recordings. The narrowing of constriction leading to decreased channel conductance is the main reason of the pathologies associated with KCNQ mutations at or near the constricted site.

THE COMPLEMENT SYSTEM: A CNS AND IMMUNITY WAYPOINT IN THE PATHOGENESIS OF PSYCHIATRIC ILLNESSES. KR Mayilyan, AF Soghoyan, RB Sim, Institute of Molecular Biology NAS RA, Yerevan, Armenia; MRC Immunochemistry Unit, Department of Biochemistry, Oxford University,

Oxford, UK; Department of Therapeutics, Faculty of General Medicine, University of Traditional Medicine, Department of Psychiatry, Yerevan State Medical University, Health Ministry of Armenia, Psychosocial Recovery Center, Yerevan, Armenia. The complement system is a crucial component of innate immunity, primarily known for its role in defending against infections and clearing pathogens, as well as altered self-components. However, emerging research suggests that the complement system may also play a role in the pathogenesis of psychiatric illnesses, particularly those involving neuroinflammation and synaptic dysfunction. In the context of the CNS, the complement system is involved in synaptic pruning, a process crucial for brain development and plasticity. Excessive or dysregulated synaptic pruning has been implicated in various psychiatric disorders, including schizophrenia and autism spectrum disorders (ASD). For instance, studies have shown abnormal complement protein expression in postmortem brains of individuals with schizophrenia, as well as in animal models of the disorder. Moreover, neuroinflammation, characterized by the activation of immune cells and the release of pro-inflammatory cytokines in the CNS, has been increasingly recognized as a contributing factor to psychiatric disorders. The complement system can be activated as part of the neuroinflammatory response, leading to the recruitment of immune cells and amplification of inflammation within the brain. Chronic neuroinflammation has been associated with mood disorders such as depression and bipolar disorder, as well as neurodegenerative diseases like Alzheimer's disease. Furthermore, recent studies have identified genetic variants in complement genes that are associated with an increased risk of developing certain psychiatric disorders. These findings further support the notion that dysregulation of the complement system may contribute to the pathogenesis of these illnesses. Preclinical studies targeting components of the complement system have shown promise in ameliorating symptoms of psychiatric disorders in animal models. For example, inhibition of complement activation has been shown to reduce neuroinflammation and improve behavioral outcomes in rodent models of schizophrenia and depression. Overall, while much of the research on the complement system's involvement in psychiatric illnesses is still in its early stages, there is growing evidence supporting its role as a potential CNS and immunity waypoint along the path of these disorders. Further investigations into the complex interplay between the complement system, neuroinflammation, and synaptic function may uncover novel therapeutic targets for psychiatric conditions.

ISBS TALK: PROSPECTS FOR PREVENTION OF POST-STRESS DISORDERS BASED ON RESTORING THE INTEGRITY OF THE INTESTINAL BARRIER. IN Abdurasulova, AV Matsulevich, VA Nikitina, NN Matsulevich, NM Grefner, Institute of Experimental Medicine, St. Petersburg, Russia. **INTRODUCTION:** One of the manifestations of the reaction to severe psychogenic trauma in humans may be a violation of the intestinal barrier function due to increased permeability (“leaky gut”). The microbiota, primarily species that produce short-chain fatty acids (SCFAs), is involved in maintaining the integrity of the intestinal barrier function. Under stress, the number of these bacteria decreases, hence weakening of the barrier function. Replenishment of the SCFA pool may be a rapid and effective way to restore and maintain the integrity of the intestinal barrier until the abundance of indigenous bacteria that produce these SCFAs is restored. One of the markers of increased intestinal permeability is the level of the protein zonulin, which regulates the expression of tight junction proteins. **AIM:** To evaluate the relationship of increased levels of fecal zonulin with the composition of the intestinal microbiome and the level of SCFAs and to test the effects of a course of sodium butyrate administration on the restoration of the integrity of the intestinal barrier and the structure and function of the intestinal microbiota. **METHODS:** The study involved 30 patients who experienced a stressful event, assessed for their psycho-emotional status and level of perception of stress, within 2 groups, with high and normal zonulin levels. The composition of the intestinal microbiota was determined by PCR using the Colonoflor-premium kit (“Alfalab”, Russia) and the 16S RNA gene sequencing method on the Illumina platform. The level of fecal zonulin was determined by ELISA, and short-chain fatty acids by HPLC. Correction of zonulin levels was carried out using a drug based on sodium butyrate for 30 days. **RESULTS:** When determining the composition of the intestinal microbiota using PCR in patients with high and normal zonulin levels, the following differences were revealed: the level of *Roseburia inulinivorans, Akkermansia muciniphila* and *Methanobrevibacter smithii* was higher in subjects with normal zonulin, while *Eubacterium rectale* was higher in subjects with high zonulin. Similar results were obtained when determining the composition of the intestinal microbiome using 16S RNA gene sequencing: in the group with normal zonulin levels, there was a greater representation of g_*Akkermansia* and g_*Methanobrevibacter*. When assessing levels of various short-chain fatty acids, higher amounts of acetate were observed in patients with normal zonulin levels, while the isovaleric/valeric acid ratio was increased in the high zonulin group. Interestingly, there was a correlation between the relative levels of acetic (C2) and propionic (C3) acids with the abundance of *Methanobrevibacter smithii* (r = 0.41) and *Prevotella spp*. (r=0.47), respectively, the level of butyric

(C4) acid correlated with the abundance of *Roseburia inulinivorans* (r=0.52), and the isovaleric/valeric acid ratio negatively correlated with the level of *Bacteroides thetaiotaomicron* (r = -0.46). Course (30 days) use of butyrate preparations normalized the level of zonulin and manifestations of intestinal dysbiosis. **CONCLUSIONS:** Increased permeability of the intestinal barrier was accompanied by changes in the taxonomic composition and spectrum of SCFAs produced, which may underlie post-stress disorders and their complications. Restoring intestinal barrier function may represent a promising strategy for preventing the development of post-stress and stress-related disorders. **RESEARCH SUPPORT:** ASR – FGWG-2023-0004.

ISBS PLENARY LECTURE: ZEBRAFISH MODELS OF COMPLEX BRAIN DISORDERS. AV Kaluev, AD Volgin, Department of Biological Sciences, Suzhou Key Laboratory of Neurobiology and Cell Signaling, School of Science, Xi'an Jiaotong-Liverpool University, Suzhou, China; International Zebrafish Neuroscience Research Consortium (ZNRC) Global HQ, Slidell, USA. Zebrafish have become a valuable and widely used animal model in biomedical research due to their high genetic and physiological homology to humans. They have a complex nervous system and exhibit a wide range of behaviors that are relevant to human psychiatric disorders and drug responses. Zebrafish have also emerged as a promising model organism for studying anxiety, stress, depression, addiction, and central nervous system (CNS) drugs. One of the major advantages of using zebrafish in research is their high reproducibility and low cost compared to other animal models. They are also relatively easy to maintain and have a rapid development, allowing for fast generation of results, making them ideal for large-scale screening and drug discovery studies. Zebrafish also share many physiological and molecular pathways with humans, making them an excellent model for studying the underlying mechanisms of psychiatric disorders. For example, they possess a similar hypothalamic-pituitary-interrenal (HPI) axis, involved in the body's response to stress. This talk will discuss recent findings from my laboratory on molecular underpinning of chronic stress, with a focus on 1) neurogenomic profiling of telencephalic samples, 2) recent advances of modeling traumatic brain injury (TBI) evoked by laser ablation of telencephalon and/or olfactory bulbs, as well as 3) recent data on the role of CNS Integrated Stress Response (ISR) signaling pathways in chronic stress and TBI model induced in zebrafish by needle damage to the telencephalon. **RESEARCH SUPPORT:** XJTLU research funding and Suzhou Key Laboratory of Neurobiology and Cell Signaling.

COGNITIVE FUNCTIONING, PSYCHOLOGICAL WELL-BEING, AND PROFESSIONAL MOTIVATION IN OLDER ACADEMIC WORKERS. EN Romanova, PA Manukyan, Research Institute for Brain Development and Peak Performance, RUDN, Moscow, Russia. **INTRODUCTION:** Higher education traditionally has high proportion of older employees. It is characterized by high cognitive demands and significant levels of psychological stress imposed on working individuals. Older academics represent an extremely valuable resource of grounding knowledge that serves as a foundation of contemporary research. Consequently, the topic of maintaining professional productivity and well-being of older academics has become one of the key concerns for psychologists, especially in the light of the successful ageing paradigm. Cognitive function has been demonstrated to be closely related to psychological state. Thus, to remain professionally productive and motivated, it is essential to maintain cognitive health and a positive psycho-emotional state. **AIM:** To evaluate cognitive and psychological functioning in senior academic staff to gain insight into their effects on proxies of professional productivity in academia, and to examine the interrelationships between cognitive functioning, psychological well-being, and professional motivation in older academics. **MATERIALS AND METHODS:** The sample included 25 academics aged 60.1±5.52 (28% male, 36% Ph.D., 36% D.Sc., 28% no degree). A battery of computerized tests including 2N-Back (2NB), Digit Span Forward (DSF) and Backwards (DSB), Go/No-Go (GnG), Task Switching (TS), Reaction Time (RT) tasks and the Stroop Test, was used to assess cognitive functioning. The psycho-emotional domain was assessed using adapted versions of the Hospital Anxiety and Depression Scale (HADS), the Positive and Negative Affect Schedule (PANAS), the Satisfaction with Life Scale (SWLS) and the Mental Health Continuum (MHC-SF). Professional motivation was evaluated via the Professional Motivation Questionnaire (PMQ). **RESULTS AND DISCUSSION:** Our analyses revealed significant associations of moderate to strong power among all domains examined. There are negative correlations between average rt and scores on the MHC-SF (r=-0.53, p=0.010), meaning that lower levels of emotional well-being are associated with poorer performance on cognitive tests; lower scores on measures of memory and attention are correlated with extrinsic motivation (e.g., DSB x introjected motivation: r =-0.44, p=0.042), and, finally, the indicators of professional motivation and psychological well-being are also interrelated (e.g., SWLS x internal motivation: r=0.45, p=0.03). Due to the limited sample size, the results cannot be generalized to the entire population of older academics, but nevertheless

emphasize the importance of maintaining psychological well-being to ensure cognitive health, professional productivity and motivation. **RESEARCH SUPPORT:** RUDN University Scientific Projects Grant System, project 212101-2-000.

EFFECTS OF DYNAMIC ENVIRONMENTAL STRUCTURE ON HUMAN SPATIAL NAVIGATION IN A VIRTUAL MAZE. PA Manukyan, VV Tolchennikova, EN Romanova, Research Institute for Brain Development and Peak Performance, RUDN University, Biological Faculty, Lomonosov Moscow State University, Moscow, Russia. **INTRODUCTION:** Spatial navigation is a complex cognitive process that allows organisms to determine their position in relation to objects, landmarks and goals, and to move efficiently within their surroundings. It relies on the ability to construct and update internal maps and adapt behavior in response to changes in the environment. Spatial navigation is generally investigated using specific testing procedures and mazes of various configurations. It is of significance to note that in real-world conditions humans live and navigate in a dynamically changing environment and constantly choose from a large number of equally possible alternatives. Therefore, such an experimental procedure should allow for the assessment of the human ability to organize their behavior in a multi-alternative dynamic context, when the behavioral response is not predetermined but is unfolding during problem solving. **AIM:** To investigate the behavioral effects of a changing environmental structure on human spatial navigation during solving the problem in a virtual nonlinear multi-alternative maze. **METHODS:** A total of 28 participants aged 18-22 recruited for the study were divided into two groups: exposed to a stable maze structure (n=14, M_{age}=19.6), and exposed to a changing maze structure (n=14, M_{age}=19.5), involving partitions in several sections of the maze during the first trials. The objective of the task was to navigate through the maze and collect coins. A hidden rule was to be identified to successfully complete the task: the coins appeared in the same locations if participants exited and re-entered the maze area. Hence, the task solution was considered optimal if participants managed to form a four-element tactical sequence (*optimal tactic*): entrance-coin1-coin2-exit. Once the task had been completed, participants were required to draw the structure of the maze. **RESULTS AND DISCUSSION:** In the stable maze structure, participants demonstrated significantly higher drawing accuracy ($U=60.0$, $p<0.05$), a greater percentage of using the optimal tactic ($U=50.0$, $p<.05$), and a faster learning rate of the optimal tactic ($U=35.5$, $p<0.01$). Notably, 50% of the experimental group showed a tendency to reproduce irrational routes to reach coins. These findings suggest that spatial structure instability impeded adequate spatial representations, which led to irrational route stereotyping and difficulty in forming the optimal tactic. **RESEARCH SUPPORT:** RUDN University Scientific Projects Grant System project 212200-2-000.

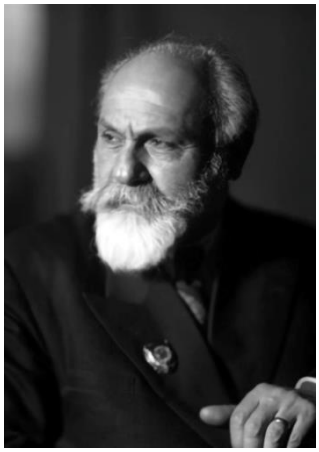
IMMUNE FUNCTION, GUT ULTRASTRUCTURE, AND MICROBIOTA COMPOSITION MODULATION BY *ENTEROCOCCUS FAECIUM* L-3 ADMINISTRATION REDUCES DISEASE SEVERITY IN EAE MODEL IN RATS. AN Trofimov, EA Tarasova, AV Matsulevich, NM Grefner, MK Serebryakova, IV Kudryavtsev, EI Ermolenko, IN Abdurasulova, Institute of Experimental Medicine, St. Petersburg, Russia. **INTRODUCTION:** Experimental autoimmune encephalomyelitis (EAE) serves as a laboratory model for multiple sclerosis (MS), an autoimmune disease characterized by chronic inflammation in the central nervous system, leading to demyelination and neurological disorders. Dysbiosis of the gut microbiota is a risk factor for MS. The introduction of probiotic strains to modulate the microbiota composition is considered a therapeutic approach for MS. This study aimed to explore the therapeutic potential of *Enterococcus faecium* L-3, a probiotic strain, in modulating gut microbiota, intestinal morphology, and immune responses within an EAE rat model. **METHODS:** The study was conducted on 70 female Wistar rats. EAE was induced by injection of an encephalitogenic mixture. On days 2-16 post-induction, rats received saline (control) or *E. faecium* L-3 orogastrically. Disease severity was assessed by clinical indices. Gut microbiota composition was studied by PCR and sequencing, intestinal ultrastructure via electron microscopy, immune cell profiling by flow cytometry, and cytokine levels through ELISA and RT-qPCR, $p<0.05$. **RESULTS AND DISCUSSION:** Rats receiving *E. faecium* L-3 showed reduced disease duration and severity, accompanied by significant microbiota shifts at the phylum level during EAE peak, including increased *Bacteroidota* in treated rats and decreased, then normalized, *Bacillota* (*Firmicutes*), without affecting other phyla. Additionally, *E. faecium* L-3 treated rats exhibited better intestinal epithelium recovery, evidenced by fewer damaged microvilli areas compared to the control. Investigation into immune cell phenotypes and cytokine levels revealed modifications in circulating immune cells, with an increase in B cells and dynamic changes in T cell subsets in *E. faecium* L-3 treated rats, as well as increased anti-inflammatory response in *E. faecium* L-3 treated animals indicating a potential immune modulation mechanism behind the observed EAE attenuation. Thus, a 15-day administration of probiotic strain *E. faecium* L-3 alleviates the severity of neurological symptoms and reduces the duration of EAE in rats, due to its

immunomodulatory effect, reduced enterocyte damage, and positive impact on the composition of gut microbiota. **RESEARCH SUPPORT:** Government-funded research project FGWG-2022-0008.

Day 4, May 19, 2024

Venue – LA Orbeli Institute of Physiology NAS RA

ORBELI SYMPOSIUM ON PHYSIOLOGY (Chairs NM Ayvazyan, LM Firsov)



ISBS TALK: NEUROBIOLOGY AND THERAPEUTIC UTILITY OF NATURAL NEUROTOXINS TARGETING PRE- AND POSTSYNAPTIC MECHANISMS OF NEUROMUSCULAR TRANSMISSION. NM Ayvazyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia.
Synaptic transmission serves as a vital process in neuroscience, facilitating the exchange of signals among neurons and between neurons and other cellular effectors. The intricate molecular workings of the synaptic vesicle cycle and the release of neurotransmitters have developed over time to enable swift responses to external stimuli during the course of evolution. Alongside this evolution, a diverse array of biomolecules and neuroactive peptides has emerged, each targeting specific components of the neurotransmitter release pathway to either inhibit natural competitors or neutralize prey. Recent neuropharmacology and quantitative biology advancements have led to growing interest in neurotoxins that selectively disrupt pre- and postsynaptic transmission processes, with potential applications in both research and medical contexts. This exploration delves into the mechanisms by which well-known animal toxins affect the secretory machinery of synapses, examining their cellular basis, molecular potency, and selectivity across various neural functions. Additionally, it reviews emerging preclinical and clinical evidence supporting the therapeutic potential of neurotoxins in molecular medicine, paving the way for the development of restorative therapies.

CORRELATION OF SYNAPTIC PROCESSES IN THE PERIAQUEDUCTAL GRAY MATTER OF THE BRAIN IN A MODEL OF PARKINSON'S DISEASE WITH HYDROCORTISONE PROTECTION. MV Poghosyan, ME Hovsepyan, MH Danielyan, AL Minasian, HY Stepanyan, KV Karapetyan, RSh Sargsyan, JS Sarkissian, LA Orbeli Institute of Physiology NAS RA, M Heratsi Yerevan State Medical University, University of Traditional Medicine, Yerevan, Armenia. **INTRODUCTION**: In neurodegenerative diseases, especially Parkinson's disease (PD), antinociceptive centers are affected, which is accompanied by chronic pain. **AIM:** In 3 series of experiments on 15 Albino rats, an analysis of impulse activity was carried out 241 single neurons of Periaqueductal gray matter (PAG) under high-frequency stimulation (HFS) of Nucleus Raphe magnus (RMG) in norm, on rotenone model of PD and with protection by hydrocortisone. **RESULTS:** Based on programmed mathematical analysis of severity of pre- and post-stimulus frequency of activity, excitatory and depressor post-stimulus tetanic effects has been identified. Analysis of the pre-stimulus frequency of activation of PAG neurons at HFS RMG, on the model of PD with protection by hydrocortisone, led to the conclusion of 53.82-, 53.20- and 38.35-, 38,25-fold decrease, in comparison with the PD model without protection, with approximation to the norm. Post-stimulus frequency of activation of PAG neurons in condition of protection, compared to one without it, in depressor tetanic effects was 81.50- and 105.37-fold reduced, a post-stimulus activation frequency, in an excitatory post-stimulus effects reached 26.72- and 29.01-fold reductions, with a real approximation to the norm. **CONCLUSIONS:** Given the protective destination of depressor reactions that we have identified in previous studies, we note a generally more than successful counteraction of hydrocortisone to excitotoxicity.

DIABETIC STRESS AND SPINAL CORD INJURY: BEHAVIORAL, MORPHOLOGICAL, AND ELECTROPHYSIOLOGICAL CORRELATES. KV Simonyan, MH Danielyan, AS Isoyan, RA Avetisyan, LG Avetisyan, KA Nebogova, VA Chavushyan, Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** Neural plasticity following traumatic spinal cord injury (SCI) is

crucial for recovery of motor and sensory function. The effects of diabetes mellitus on neuronal recovery after SCI are not well studied. The purpose of this study was to assess morphofunctional recovery, as well as the short-term plasticity of lumbar spinal cord motoneurons in lateral hemisection (SCI), fructose-induced diabetes (D), and diabetes associated with hemisection (D+SCI). **METHODS:** The present study used a fructose-induced diabetic rat model (50% fructose solution instead of drinking water) for 8 weeks. We performed a lateral hemisection of the spinal cord (SCI) at the L2-L3 level. Four weeks later, we recorded extracellular spike activity of motoneurons in the SCI area and studied the morphological changes using toluidine blue staining and histochemical assay for the activity of Ca2+-dependent acid phosphatase. Behavioral indices of motor and sensory recovery were assessed 1-4 weeks post-injury. **RESULTS AND DISCUSSION:** The evaluation of the degree of sensory (flexor reflex test) and motor function (open field test and static sciatic index) did not reveal recovery by the 4th week post-injury in SCI and D+ SCI groups. By week 4, a more pronounced connective tissue scar had formed in the D+SCI group compared to the SCI group. We found that for SCI, D, and D+SCI groups, the ratio of the percentage share of excitatory and inhibitory combinations of motoneuron responses to high-frequency stimulation of the sciatic nerve is multidirectional. In SCI and D+SCI groups, the cumulative changes in generalized baseline frequencies decreased significantly. When we compared the cumulative changes in the intensity of excitatory and inhibitory responses relative to baseline during high-frequency stimulation (tetanization epoch), we found a significant intensification in tetanic potentiation in D + SCI group compared to D and D+SCI groups vs. SCI group. Thus, in conditions of traumatic injury and metabolic disorder, inhibitory inputs were impaired. On the lesioned side, important ascending/descending tracts and modulatory fiber systems were interrupted by the lesion. Following SCI, defects in axon guidance and neurochemical imbalance affect neuronal circuit rebuilding, and these integral changes likely shape postsynaptic short-term plasticity in the spinal motor network. **RESEARCH SUPPORT:** Higher Education and Science Committee of MESCS RA, Research project 19YR-1F010**.**

CHANGES IN CENTRAL BLOOD FLOW UNDER THE INFLUENCE OF SPELEOCLIMATE AND RHEOGRAM PARAMETERS. VA Semiletova**,** Department of Normal Physiology, Voronezh State Medical University, Voronezh, Russia. The purpose of the work is to study changes in central blood flow in an adult healthy person under the influence of speleoclimate according to rheogram parameters. **MATERIALS AND METHODS:** The study involved 75 volunteers from among 1st-2nd year students of Burdenko VSMU. The speleotherapy course consisted of ten 60-min ‘caving’ sessions. Before the start of speleotherapy, after the 3rd and the 10th session at rest, a central rheogram was recorded using "Encephalan-SA" through polygraphic channels in conjunction with EEG signals. **RESULTS:** Under speleoclimate, the amplitude of rapid blood filling significantly decreased after the third speleotherapy session and remained significantly reduced after the tenth session. The end-diastolic phase amplitude also decreased significantly after the third and remained significantly reduced after the tenth speleotherapy session vs. the baseline level. The power indices of individual delta-, theta-, alpha- and beta- rhythms increased by speleoclimate. The alpha/theta ratio increased slightly after the third session, and decreased significantly after the tenth session. The dynamics of significant correlations showed more significant correlations between the examined rheogram parameters after the 3rd session, and after the 10th session vs. resting state after caving (17-21-15). **CONCLUSIONS:** Under the influence of the speleoclimate, the tone of large and medium-sized vessels changes significantly, reflected in lower amplitude of rapid blood filling and the diastolic index of the rheogram, and reduced amplitude of the end-diastolic phase. The power of individual rheogram rhythms increased following speleotherapy, and the alpha/theta index, increasing after the 3rd session, significantly decreases after the 10th speleotherapy session.

THE NEUROIMMUNE-INFLAMMATORY MODEL OF CHRONIC STRESS, DISTRESS, AND DEPRESSION. MV Komelkova, AP Sarapultsev, EY Gusev, South Ural State University, Chelyabinsk, Russia. **INTRODUCTION:** The neuroimmune-inflammatory (NIIS) model delineates an understanding of the mechanisms underpinning chronic stress, distress, and depression triggered by psychogenic stress. It articulates the interaction between neurotransmitter dysfunctions, homeostatic alterations in neurons and glial cells, and morpho-functional changes across various brain regions, rooted in cellular and tissue pro-inflammatory processes. This model emphasizes that the escalation of such processes leads to low-grade neuroinflammation, fostering neurodegenerative changes and a complex pathological cycle that intertwines local brain inflammation with systemic chronic low-grade inflammation, thereby establishing a persistent allostatic state. **DISCUSSION**: Central to this model are the physiological mechanisms predisposing nervous tissue to damage and programmed death due to inherent characteristics such as receptor effects of neurotransmitters on electrolyte balance,

high energy consumption for ATP production, reliance on endoplasmic reticulum for protein biosynthesis, and vulnerability to oxidative stress. When chronic, cellular stress turns dysfunctional, exacerbating cellular damage, especially through oxidative stress, while the brain's regulatory mechanisms, such as the blood-brain barrier and specific metabolic pathways, serve to limit pro-inflammatory cellular stress. The pathological shift towards neuroinflammation in chronic stress and depression is marked by neuronal dysfunction, damage, and death leading to neurodegeneration. This process is significantly influenced by cytokines and inflammation mediators, emphasizing the role of microglial cells' pro-inflammatory transformation and the progression of oxidative stress in neuronal dysfunction. Furthermore, the NIIS model extends its relevance to clinical practice and experimental research, illustrating the developmental pathologies in individuals exposed to various stressors from early life and those identified as at-risk due to metabolic syndrome, obesity, and chronic systemic diseases. It situates chronic stress and depression within a framework of low-grade systemic inflammation and significant mental health alterations, providing insights into conditions like long COVID. **CONCLUSIONS**: The NIIS model offers a nuanced perspective on the neuroimmune-inflammatory bases of chronic stress and depression, highlighting the critical balance between physiological stress responses and pathological outcomes. This model not only enhances our understanding of the intricate mechanisms involved but also underscores the importance of a comprehensive approach to addressing the multifaceted nature of psychogenic stress-induced pathologies.

PSYCHONEUROIMMUNOMODULATORY EFFECTS OF IMMUNE CELLS IN DEPRESSION-LIKE STATE. EV Markova, MA Knyazheva. Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia. **INTRODUCTION:** Depression is a serious medical and social problem due to its high prevalence throughout the world, the involvement of people of working age and the lack of highly effective therapy. Cell technologies actively used in the treatment of many diseases; they are based on manipulating the patient's cells outside the body, as a result of which cells acquire a higher therapeutic potential. No doubt the essential role of immune cells and their biologically active products in the pathogenesis of depression, which allows to view the *ex vivo* modulated immune cells as model objects for developing new approaches to immunotherapy for depression. **METHODS: (**CBAxC57Bl/6) F1 depressive-like male mice, developed under the long-term social stress, were undergoing the transplantation of syngeneic splenocytes with *ex vivo* caffeine-modulated functional activity. Recipient’s behavior, parameters of nervous and immune systems functional activities were studied. **RESULTS AND DISCUSSION:** We first demonstrated that immune cells isolated from depressive-like mice and treated *in vitro* with caffeine change their properties and after intravenous administration to syngeneic depressive-like recipients have a significant positive psycho- and neuroimmunomodulatory influence, affecting the main pathogenetic mechanisms of depression: behavioral editing (reduction of anhedonia, stimulation of exploratory behavior and activity in the forced swimming test); stimulating neuroplasticity processes (increasing the density of pyramidal neurons in the CA1 and CA3 hippocampal zones against the background of BDNF level increasing in the hippocampus and prefrontal cortex); changes in the content of cytokines pathogenetically significant for depression (IL-1β, IL-6, INF-γ, TNFα, IL-4, IL-10) in brain structures (hippocampus, hypothalamus, prefrontal cortex, striatum), indicating a decrease in neuroinflammation (Markova et al. Patent RU 2675111 C1); and also modulating the immune system functional activity (stimulation of antibody formation, proliferative activity of splenocytes, against the background of suppression of the pro-inflammatory activity of these cells and reduction of tryptophan catabolism in the spleen). Taking into account the fact that hippocampal neurogenesis, BDNF reduction and neuroinflammation may serve as targets for the treatment of depressive disorders, immune cells with *ex vivo* caffeine modulated functional activity can be considered as a potential therapeutic agent with a pronounced antidepressant effect, which is manifested in the above-mentioned positive changes in the central nervous system and the immune system. **RESEARCH SUPPORT:** Russian Federal Budget for basic scientific research at the Scientific Research Institute of Fundamental and Clinical Immunology.

A SPIKE IS A SPIKE: ON THE UNIVERSALITY OF ITS FREQUENCY CHARACTERISTICS IN FIVE EPILEPSY MODELS. A Sargsyan, PM Casillas-Espinosa, D Melkonian, TJ O'Brien, G van Luijtelaar, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia; Department of Neuroscience, Central Clinical School, Monash University, Melbourne, Victoria, Kaoskey Pty Ltd, Sydney, New South Wales, Australia; Donders Centre for Cognition, Radboud University, Nijmegen, Netherlands. **INTRODUCTION:** Frequency properties of the EEG characteristics of different seizure types including spike-wave discharges (SWD) have been described for various rodent models of epilepsy. However, little attention has been paid to the frequency properties of individual spike-wave complexes (SWC) constituting these electrographic seizures. Knowledge of these properties is important for

understanding the mechanisms underlying seizure generation. Besides, these properties may be used for identification of epileptiform activity and seizure detection. Here we compared the frequency properties of SWCs in different models of epilepsy. **METHODS:** A software package was designed and used for extraction and frequency analysis of SWCs from long-term EEG of four spontaneously seizing, chronic epilepsy models: post-status epilepticus model of temporal lobe epilepsy; lateral fluid percussion injury model of post-traumatic epilepsy; and two genetic models of absence epilepsy – GAERS and rats of the WAG/Rij strain. The SWCs were separated into fast (three-phasic spike) and slow (mostly containing the wave) components. Eight different animals from each model were used (32 recordings, 108362 SWCs in total). In addition, we compared the amplitude spectra (AS) of experimental SWCs with AS of SWCs generated by a computer model of a cortical neuronal population. **RESULTS AND DISCUSSION:** We found that the three-phasic spike component was similar in all animal models both in time and frequency domains, their AS showed a single expressed peak at 18-20Hz. The AS of the SWC generated by computer model resembled the shape and peak frequency of experimental AS. The slow component showed larger variability across rat models. The similarity of the spike component and the differences in the slow components of the SWCs between the animal models allows us to hypothesize that at least two systems participate in generation of SWCs. One is common and similar for all cortical locations, animals and epilepsy models/types, while the other shows certain differences that might be the consequence of diverse epileptogenesis and ictiogenesis processes between the models.

EMOTIONAL ABNORMALITIES AS EARLY BEHAVIORAL SYMPTOMS OF ALZHEIMER'S DISEASE IN APP/PS1 MUTANT MICE TO CORRELATE WITH PLAQUE FORMATION. K Sitdikova, A Gorlova, S Morozov, Z Nefedova, K Chaprov, T Strekalova, Institute of General Pathology and Pathophysiology, Sechenov First Moscow State Medical University, Moscow, Institute of Physiologically Active Compounds RAS, Chernogolovka, Belgorod State National Research University, Belgorod, Russia. **INTRODUCTION**: There is a high societal need in the development of pharmacotherapy of Alzheimer's disease (AD). However, high costs that are associated with the use of aged animals is a serious limitation in pre-clinical studies on the AD. Therefore, accurate determination of early hallmarks of AD-like pathology in mutants can be of great help in this field of research. The goal of this study was to investigate how behavioral symptoms displayed by 5-month-old APP/PS1 mice, well-established model of AD correlate with amyloid plaque formation in the brain of this animals - a histological hallmark of the disease. **METHODS:** APP/PS1 mice (APPswe/PS1dE9 line with the Swedish mutation (K670N/M671L) in the *App* gene and deletion of exon 9 in the *PSEN1* gene) were investigated at the age of 5 months for behavioral tests for emotionality and cognition. The amyloid plaque aggregation in the cortex, hippocampus and thalamus was performed using Congo staining and the staining with 6E10 anti-amyloid antibody. Their density of the amyloid plaques was evaluated by the means of confocal microscopy. **RESULTS AND DISCUSSION**: 5-month-old APP/PS1 mice demonstrate higher measures of anxiety in and impaired associative memory in conditioned aversion test, and unaltered locomotion in the open field. Correlation analysis showed that negative association between thalamic amyloid plaque density and scores of associative memory. There was positive correlation between the amyloid plaque density in the cortex or in the hippocampus on one hand, and anxiety scores, on another hand. Thus, 5-month-old APP/PS1 mice can serve a good model of AD-like pathology and be employed in pre-clinical studies on the AD that is much age, at which these mutants are usually used. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation grant 075-15-2022-310.

THE EFFECTS OF COMPETITIVE STRESS ON THE COMPONENTS OF EVENT RELATED POTENTIALS DURING JOINT VERBAL PROBLEM SOLVING. NV Shemyakina, ZhV Nagornova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia. Brain activity changes significantly under various conditions of social interaction. However, the impact of the context of social interactions on neurophysiological correlates of cognitive and creative activity per se has not been sufficiently addressed. Two polar types of interactions can be distinguished when solving tasks, cooperation or competition. Task solving in a group (or in a dyad), on the one hand, can be a source of anxiety and stress, e.g., under conditions of negative feedback; on the other hand, it can raise motivation and increase engagement in joint activities. **AIM:** To assess the impact of competitive conditions on the amplitudes of event-related potentials (ERPs) when solving creative task taking into account the factor of trait anxiety. The subjects (26 males, 18 females) performed creative task individually or in dyads (male-male, female-female): to think up unusual uses of a simple everyday objects. ERPs were compared during competitive (dyadic) versus individual performance. Before participation in psychophysiological study, the subjects underwent the State-Trait Anxiety Inventory for Adults (STAI), self-evaluation questionnaire (Spielberger, Russian adaptation by Khanin). According

to level of trait anxiety, the group of participants was divided into subgroups with low and medium (24 subjects, MAL group) and high anxiety levels (16 subjects, HAL group) to assess behavioral and physiological effects of anxiety during task performance. To calculate ERPs, the artifact-free trials, in which subjects found a response and clicked the button, were analyzed from 300 ms prior to stimulus presentation through 2000 ms after it. For each ERP component amplitudes were compared between the conditions of individual and competitive task performance with ANXIETY LEVEL intergroup factor. There were no differences in the number of answers to creative task between the MAL vs the HAL groups during both individual and competitive task performance. Significant effect of the factor ANXIETY LEVEL on ERP amplitudes during creative task performance was observer only in time interval of the P2 (136-240 and 240-320 ms) component: $F(1, 38) = 4.8$, $p<0.05$. Both in competitive and individual task performance, ERP amplitude was higher in HAL vs. MAL groups. An increased amplitude of the early ERP components in individuals with high anxiety is associated with more attention to disturbing stimulation. Here, factor ANXIETY LEVEL influenced amplitudes of early components of ERP not only in the competition conditions, but also in the individual task performance, suggesting that competition conditions were not an intense stressful factor for the subjects. **RESEARCH SUPPORT:** Russian Science Foundation grant 24-28-01797.

MOTOR EVOKED POTENTIALS CHANGE UNDER CONDITIONS OF VARIOUS DOPAMINERGIC CONTROL IN THE DAT-KO RAT MODEL. DS Kalinina, OV Gorsky, RR Gainetdinov, PE Musienko, Department of Neuroscience, Sirius University of Science and Technology, Sirius, Institute of Translational Biomedicine, St. Petersburg State University, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Pavlov Institute of Physiology RAS, St. Petersburg, Life Improvement by Future Technologies Center “LIFT”, Moscow, Russia. **INTRODUCTION:** Dopamine (DA) is closely involved in the formation of intended behavior and motivation processes and participates in the control of the integral operation of movement. The main regulator of DA levels is the DA transporter (DAT), which provides its reuptake and plays a decisive role in the balance of the intracellular and extracellular levels of the DA. Previously it was shown that inhibition of tyrosine hydroxylase by alpha-methyl-p-tyrosine (AMPT) leads to block catecholamine synthesis and mild decline of DA level in normal while in DAT-KO mice observed almost lack of DA (Sotnikova et al., 2005). The aim of the study was to investigate dopamine-dependent changes in conductivity and excitability in DAT-KO and WT rats. **METHODS:** Dopamine transporter knockout (DAT-KO, n=4) and wild type (WT, n=4) male rats 3–5 months old were used. The cortex soft and flexible electrode arrays were implanted (Isoflurane 1,5%) epidurally on left hindlimb motor area. Reference electrode was positioned epidurally over the cerebellum 1 mm caudal to the lambda. For record of electromyogram (EMG) signals the stainless-steel wire electrodes were implanted into the left and right hindlimb gastrocnemius medialis muscles (L_GM, R_GM). Motor evoked potentials were induced by electrical stimulation (A-M Systems) of the hindlimb motor cortex area (0.5 ms biphasic pulse, 300 Hz, 15 ms, 0.6–1.9 mA). **RESULTS AND DISCUSSION:** MEP registered here represent polysynaptic potentials. The conduction velocities of directly stimulated corticospinal neurons ranges from 5 to 19 m/s (Mediratta and Nicoll, 1983), that corresponds to our results. The mean latency in control conditions was unaltered (23.42±0.52 ms in WT and 22.34±0.52 ms in DAT-KO rats). Block of catecholamine synthesis by AMPT not affected on latency in WT (24.39±0.38 ms) but reduced it in DAT-KO (19.63±0.46 ms) rats. MEP amplitude intensity in wild type rats has a high peak in the 5-25 bins while in DAT-KO rats an activity was distributed across all bins with a slight increase in the 5-35 bins. However, after AMPT-injection, amplitude distribution changed: in WT maximum was on 10-25 bins, in DAT-KO - on 5-20 bins. MEP amplitude increased vs. base condition without drug in the first 15 bins in DAT-KO rats while in WT it decreased. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation, Agreement 075-10-2021-093, Project NRB-RND-2115.

ISBS ONLINE TALK. AN INTERDISCIPLINARY BIOLOGICAL MODEL OF PSYCHOPHARMAPHYSIOLOGICAL FUNCTION QUANTITATIVELY VISUALIZED BY MOLECULAR AND BODY TEMPERATURE INDICATORS IN THE ELDERLY. M Koshiba, Yamaguchi University, Yamaguchi, Tohoku University, Tohoku, Saitama Medical University, Saitama, Japan. Body may indicate super-complex output states with overlapping mechanisms of different modalities, such as the metabolic and thermal states, as well as sensory-motor interactions with the environment. To evaluate such physiological mechanisms, we explored explanatory variables of statistical significance by designing multiple high impact predictive conditions. The influencing factors were specifically set for two different modalities. First involved a randomized double-blind comparative study of the pharmacological effects of ubiquinol, and second applied whole-body exercise in social environmental settings, which may promote improved psychosomatic status, and on cellular energy production based on redox potentials. To examine the multiple heterogeneous impacts, we performed

multivariate correlation analyses with depression and anxiety scales, blood-psychophysiology-related molecules, and variables measured by infrared sensors that capture body temperature physiology in a non-contact manner. Overall, ubiquinol intake or more temperature fluctuations (which may be influenced by vasopressin) correlate significantly with positivity on anxiety rather than on the depression scale, although the two mechanisms might be of different structure. It may be important to establish human cognitive functions to understand complex models of psychosomatic dynamics in a three-dimensional manner (see doi.org/10.3390/app14062366 for details).

ANALYSIS OF THE EEG RHYTHMS POWER DURING VIEWING AN EMOTIONAL VIDEO AS A BIOMARKER OF A PERSON'S PSYCHO-EMOTIONAL STATE. ED Blagovechtchenski, MM Koriakina, KV Bartseva, UR Nikishina, MU Lukov, DA Fomicheva, VV Moiseeva, AN Shestakova, National Research University HSE, Moscow, St Petersburg State University, St Petersburg, Yaroslav-the-Wise Novgorod State University, Novgorod, Russia. **INTRODUCTION:** To test a person's psycho-emotional state, various methods are used, one of which is a reaction to an emotional video sequence. Such a reaction can make it possible to assess the degree of a person's involvement in certain emotional events. However, now there are few developed methods to make objectively assess psycho-emotional status. One of the sensitive markers is the analysis of a subject's electroencephalogram (EEG), requiring appropriate videos and EEG analyses. Here, a unique video sequence was chosen that evokes positive emotions in the first third, and empathy in the final part. We compared the main EEG characteristics during viewing of the first and last part of the video sequence. **METHODS:** 24 subjects (12 men, average age 21+-3) watched a 12-min video sequence, a 1969 "Penguins" cartoon. The focus group rated this video as emotional (10 points on a 12-point scale) with a clear expression of empathy in the second part. During viewing, EEG was recorded using a 52-channel LiveAmp EEG setup (BrainProducts, Germany), sampling frequency 500 Hz. The recording was divided into equal intervals of 4 min. A comparison was made between the first and last interval. The powers of the main EEG rhythms were assessed in the alpha (8-12 Hz), beta (15-20 Hz), theta (5-8 Hz) and gamma (35-45 Hz) ranges. The neurodynamic performance of the long-range temporal correlations (LRTC) in these ranges was also assessed, using the paired Wilcoxon test with Bonferroni correction for multiple comparisons. **RESULTS AND DISCUSSION:** A significant difference was obtained between the first and last interval in the beta (pval=0.0012) and gamma (pval=0.0029) ranges. No differences could be found in LRTC. Thus, the proposed video sequence, together with EEG correlates, can be an objective assessment of a person's emotional involvement (psycho-emotional status). The proposed method can be an objective biomarker for assessing human emotions. **RESEARCH SUPPORT:** Basic Research Program at the National Research University Higher School of Economics (HSE University). The project utilized the HSE Automated system of non-invasive brain stimulation with the possibility of synchronous registration of brain activity and registration of eye movements. The study was conducted within the project "Mirror Laboratories" of HSE University.

CONTINUOUS MEASURMENT OF ELRCTRODERMAL ACTIVITY AS AN INDICATOR OF STRESS LEVELS EXCITABILITY: A PILOT STUDY. MY Lukov, ES Zemnukhov, St. Petersburg State University, St. Petersburg, Novgorod State University, Velikiy Novgorod, Russia. **INTRODUCTION:** Electrodermal activity (EDA) is a reliable indicator of excitation/inhibition mechanisms of the central nervous system. This parameter is widely used in both basic and applied psychophysiological research. Stress is usually accompanied by strong emotional reactions and is significantly manifested in the indices of the autonomic nervous system and especially in EDA. The greatest amount of research has been devoted to the laboratory study of stress. In our study we decided to investigate how the EDA would manifest itself when measured over a long period of time in everyday life, including stressful situations. **METHODS**: Two male subjects (26 and 36 years) had EDA readings taken during 24-h monitoring for 12 months. The data were taken using a wearable bracelet from the inner surface of the wrist using the exosomatic method. During data processing, we evaluated indices such as skin conductance level (SCL) as well as the number of phasic responses per unit time (SCR, SSCR). Self-report data on the general psycho-emotional state of the subjects were also recorded. At the initial stages, we encountered difficulties in assessing the baseline EDA indices. Since even for one person, they depend on many parameters, such as: cognitive, emotional, physical load, temperature and humidity of the environment. However, as the data accumulated (about 2-3 weeks), we were able to determine typical values for a particular subject. The most informative (and less influenced by the environment) in assessing the level of stress were SCR, SSCR indices, which grew in proportion to increasing stress of any (cognitive, emotional, physical) origin. Interestingly, during prolonged periods of stress, EDA indices initially increased, but in the absence of necessary rest phases, EDA indices began to decrease sharply (below the individual norm), which

was accompanied by a general decrease in tone and mood in both subjects. After the necessary recovery period, the indices also returned to normal. Thus, EDA in the long-term can be not only a marker of stress, but also a good indicator of the onset of the phase of maladaptation and exhaustion of the organism because of distress. **RESULTS AND DISCUSSION**: Although the present study cannot be called sufficient, its duration is a significant advantage. We believe that the data obtained are a good foundation for further research on the possibility of diagnosing and controlling stress in everyday life. These data may help future users to reduce psycho-emotional load in time, thus preventing negative consequences of distress. **RESEARCH SUPPORT**: Novgorod State University.

PAIN AND BEHAVIOR. AV Voskanyan, AV Moghrovyan, LM Parseghyan, SS Poghosyan, AA Darbinyan, LA Orbeli Institute of Physiology NAS RA, M Heratsi Yerevan State Medical University, Armenia, Yerevan. Pain and behavior are intricately connected. Pain can impact behavior. Dealing with pain can be stressful. It often leads to withdrawal from activities that might exacerbate the pain. People might instinctively guard or protect the painful area. Pain can make a person more irritable or easily frustrated. It demands attention, causes sleep disturbances, and so on. In the case of pain, animals respond to it on multiple behavioral levels – the behavior of organism, organs, and systems, cell and molecular behavior, or metabolic changes. The study was aimed at investigating of analgesic and anti-inflammatory properties of combined preparation, based on small doses of snake venom (*Macrovipera lebetina obtusa*) and essential oil (*Origanum vulgare*). In experiments, pain was induced through various methods, such as inflammatory pain modeled using formalin and carrageenan. Analgesic preparations were studied through formalin hot plate tests and open-field methods. Rats exhibited observable behaviors in response to pain, including hind paw licking/biting; changes in gait or posture; and decreased exploratory behavior. In pharmacological studies, the analgesic and anti-inflammatory effects of combined preparation were tested. As golden standards, morphine, sodium diclofenac, and sodium metamizole were used. The opioid receptor (OR) blocker naloxone and cannabinoid receptor (CB2R) inverse agonist SR144528 were used to estimate the role of opioid and cannabinoid receptors and participation in anti-pain behavior. Microglial cells (MGCs) behavior, their activation, and transformation were investigated in histo-chemical studies. Behavioral experiments showed an analgesic effect with 64% participation of the opioid and 71% of the cannabinoid antinociceptive systems, which is evidence of consistent activation of these two systems. Open-field tests did not show any significant changes in the locomotive activity of mice. Microglial cell activation reflects the modulatory role of sole usage of *O. vulgare* essential oil. The analgesic action of *M. l. obtusa* was correlated with phospholipase A2 enzymatic activity, which was inhibited by bromphenacyl bromide. The possible mechanism of venom analgesic activity is related to potassium voltage-gated channels blocking and activation of sodium voltage-gated channels of afferent nociceptive neurons. It is proposed that in the case of high doses of venom, the analgesic effect of it is masked with pain-like behavior. Overall, venom toxicity increases when combined with essential oil in an injective form of preparation, while ointment was highly effective, was not toxic, and did not irritate the skin.

THE RELATIONSHIP OF EXCITATORY AND DEPRESSOR SYNAPTIC PROCESSES IN ANTINOCICEPTIVE RAPHE MAGNUS NUCLEUS ON THE MODEL OF PARKINSON'S DISEASE UNDER CONDITIONS OF PROTECTION WITH *NAJA NAJA OXIANA* (NNO) VENOM POISONING. HY Stepanyan, AL Minasyan, MV Poghosyan, TK Harutyunyan, KV Tsakanyan, HG Vahradyan, ZA Avetisyan, JS Sarkissian, LA Orbeli Institute of Physiology NAS RA, University of Traditional Medicine, Yerevan Haybusak University, Yerevan, Armenia. **INTRODUCTION** In neurodegenerative diseases, more often in Parkinson's disease (PD), antinociceptive centers are involved in neurodegeneration, which is accompanied by constant pain that is not relieved by drugs. **AIM:** In 3 series of experiments on 12 Albino rats, an analysis of the impulse activity of 431 single neurons of the Raphe magnus nucleus (RMG) was carried out under high-frequency stimulation (HFS) of Periaqueductal gray matter (PAG) in normal conditions, on the rotenone model of PD and with protection by NNO venom. **RESULTS:** Based on a software mathematical analysis of the average degree of frequency severity of post-stimulus depressor and excitatory synaptic effects on the PD model, a sharp excess of tetanic and post-tetanic excitatory effects was revealed. At the same time, the number of neurons responding with similar depressor reactions decreased many times over, with an increase in those responding with excitatory reactions. This is the result of excitotoxicity, indicating neurodegenerative damage of RMG neurons. In pathology, compared with the norm, the pre-stimulus frequency of activity preceding depressive post-stimulus effects increased and decreased by 2.45- and 1.71-fold. Under conditions of protection with NNO venom, in comparison with pathology without protection and the norm, there was a 1.60-fold decrease in the pre-stimulus frequency preceded by depressive post-stimulus manifestations of activity approaching the norm (17.92 vs. 28.54 and 11.63, respectively), in the absence of such frequency preceded by excitatory ones. In pathology, compared with the norm, the

post-stimulus frequency of activity of RMG neurons, accompanied by depressive reactions, exceeded the norm 2.05 times, and decreased 1.61 times, and was much higher (7.46- and 10.50-fold), accompanied by excitatory effects. In the case of protection, the post-stimulus excitatory frequency of activity disappeared, which reliably indicates in favor of protection with NNO poison, which is more than successfully manageable with excitotoxicity. **CONCLUSIONS:** Given the protective purpose of depressive reactions identified in previous studies, the effect of NNO venom becomes clear.

SLEEP DISTURBANCES IN PATIENTS AS A RESULT OF STRESS FACTOR DUE TO HEADACHE ATTACKS. IV Fokin, Moscow Central House of Sciences, Moscow, Russia. **INTRODUCTION:** Evaluation of clinical features of headaches during sleep-wake cycles in patients with cluster headache (CH) and migraine and improvement of medical care for headache patients with sleep disorders. CH and migraine-related headache depends on patient's baseline condition during the sleep-wake cycle. CH and migraine are significantly impairing patient's physical performance and cause nocturnal sleep disturbances. **MATERIALS AND METHODS:** 38 patients (20 CH and 18 migraine patients) and 22 healthy reference subjects were examined using clinical, psychological, neurophysiologic methods of sleep studies, and questionnaires. **RESULTS:** CH patients presented severe disorders of sleep architecture with absence of REM- sleep before and after the headache attack with shift of the delta sleep stage with its prolongation in the morning after attacks. During the remission their sleep architecture was almost normal. In migraine patients we found the following sleep disturbances during the pain attack and in remission: absence of REM- sleep before and after pain episode, absence of the delta sleep, difficulty of falling in to sleep, increased nocturnal wakefulness; frequent movements during the sleep, and prevalence of superficial sleep. The time of the episode onset significantly affects the severity of headache attacks: CH and migraine episodes were more severe during sleep, than during wakefulness. **DISCUSSION:** Our study demonstrated different relations between headache attacks and sleep disturbances in migraine and CH patients. It depends of chronobiological clock-wise mechanisms of pain and sleep regulations lying in hypothalamus and brain stem structures. Headaches attacks serves as stress factors for brain that impairs normal sleep structure in these patients.

MODERATED POSTER SESSION 2

ERP AMPLITUDES TO "EDIBLE" VS "INEDIBLE" NOUNS CHANGE DEPENDING ON GLUCOSE LEVEL IN HUMAN BLOOD (A PILOT STUDY). EI Galperina, VA Ivanov, YA Chiligina, OV Kruchinina, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Herzen Russian State Pedagogical University, St. Petersburg, Russia. **INTRODUCTION:** The relationship between peripheral blood glucose levels and cognitive function, such as RT, number of errors in switching tasks, and a decrease in working memory, has been shown in diabetic patients (Sastre et al., 2017; Nilsson et al. 2019). The neurophysiological mechanisms of the peripheral blood glucose levels that influence on the event-related potentials (ERPs) during cognitive performance in healthy subjects are poorly understood. Our objectives were to investigate the brain ERPs during the decision in a double categorical choice task under conditions of low glucose in peripheral blood (fasting) and after glucose solution administration. **METHODS:** Eleven healthy adults (n=11, 3 males, age 23.1± 3.7) participated in the study. EEG was recorded twice: on an empty stomach (early morning) and after glucose solution administration (0.5 g/kg) during the test for categorization of written nouns denoting "edible" or "inedible". Peripheral blood glucose levels were measured. Behavioral data were compared in 2 conditions using the Wilcoxon criterion for related samples. The mean amplitudes of ERP components were compared between conditions using the t-criterion for related samples. **RESULTS AND DISCUSSION:** No significant differences were found in behavioral data (RT, number of errors, omissions, false alarms) between the fasting and post-glucose states. The ERP's amplitudes differences to "edible-inedible" regardless of the glucose level (both on an empty stomach and after taking a glucose solution), were found in the frontal and central sites of the left hemisphere and along the central line ($p<0.01$), as well as in the parietal regions of both hemispheres at the 700-800 ms interval, with higher amplitude of the positive component to "edible" ($p<0.01$). Sensitivity to glucose level in peripheral blood (on an empty stomach or after taking glucose solution) was regardless of the stimulus ("edible-inedible") in frontal and central sites of both hemispheres at early components with latency of 100-200 ms. A specific response was revealed only for "edible", presenting in pairwise comparison of the two registrations: in the central line sites (Fz, Cz) the amplitude of the ERP was higher on an empty stomach at 100-200 ms, and in the right sites the ERP was higher after the glucose consumption (F4 and C4 by 100-200 ms, and P4 by 700-800 ms).

1-DEAMINO-8-D-ARGININE-VASOPRESSIN IMPLEMENTS ITS ANALGESIC EFFECTS IN ELECTROCUTANEOUS PAW STIMULATION TEST IN RATS BY MODULATING THE ACTIVITY OF MONOAMINES IN THE BRAIN. AA Nikitina, SG Belokoskova, SG Tsikunov, Institute of Experimental Medicine, St. Petersburg, Russia. **INTRODUCTION:** The role of the neuroendocrine system in the mechanisms of pain remains poorly understood. The analgesic properties of arginine vasopressin (AVP) are known for various pain effects in rodents. However, the neurochemical mechanisms of these effects have been little studied. **AIM:** To evaluate the effect of the V2R agonist, 1-deamino-8-D-arginine-vasopressin, DDAVP, on pain sensitivity, serum corticosterone levels, levels of norepinephrine (NE), serotonin (5-HT), dopamine (DA) and their metabolites, brain neurotrophic factor (BDNF) in the parietal cortex and spinal cord in electrocutaneous paw stimulation test in rats. **METHODS:** The study was conducted on male Wistar rats. The animals were divided into 4 groups: intact rats, saline treated rats, 10 rats receiving DDAVP at 20 ng/day, 100 ng/course, and 10 rats receiving DDAVP at 2 mcg/day, 10 mcg/course. DDAVP was administered intranasally once a day for 5 days. The saline solution was administered according to the peptide application scheme. The content of corticosterone in blood serum was determined using enzyme immunoassay. The content of NE, 5-HT, DA and their metabolites in the brain was determined using HPLC; BDNF levels were determined using EIA. Electrocutaneous stimulation of the paws in animals was performed using single pulses of electric current with a current strength of 0.1 mA with a frequency of 40 Hz, with a duration of 0.5 s, uniformly increasing the current strength by 0.01 mA. In order to prevent vocalization, stimulation was stopped when the current reached 0.6 mA. **RESULTS AND DISCUSSION:** DDAVP at different doses reduced pain sensitivity in rats, and more pronounced when administered in large doses. The peptide in small doses in the parietal cortex increased the content of DA and reduced the levels of 5-HIAA, a metabolite of 5-HT; in the spinal cord, it reduced the content of 5-NIAA. DDAVP in high doses in the parietal cortex increased the content of DA and reduced the levels of 5-HIAA; in the spinal cord — reduced 5-HT and DOPAC (DA metabolite), increased NE and HVA (DA metabolite). The peptide did not affect the content of corticosterone in the blood and BDNF in the brain of rats. Thus, regardless of the doses administered, peptide—induced anesthesia was associated with the involvement of the dopaminergic and serotonergic systems at the supraspinal level; the serotonergic system at the spinal cord level. More pronounced analgesia with the administration of DDAVP at high doses was due to the additional involvement of spinal dopaminergic and noradrenergic systems.

THETA OSCILLATIONS MAY INTERFERE WITH ALPHA AND BETA DESYNCHRONISATION OF SUBTHALAMIC NEURONS DURING MOVEMENTS IN PARKINSON'S DISEASE PATIENTS. AA Nezvinskiy, EM Belova, AA Gamaleya, AA Tomskiy, AS Sedov, Semenov Research Center for Chemical Physics RAS, NN Burdenko National Medical Research Center of Neurosurgery, Moscow, Russia. **INTRODUCTION:** Movement-related neural activity in basal ganglia of Parkinson's disease (PD) patients is excessively studied for deep brain stimulation (DBS) improvement. In this study we examined associations between voluntary movement induced desynchronization and spontaneous rhythmic activity of the subthalamic (STN) neurons in patients with PD. We anticipated the desynchronization of alpha (7-12 Hz) rhythmic activity starting about 2 seconds before the first movement in a series and the desynchronization of low-beta (12-20 Hz) oscillations in the STN starting 500 ms ahead of the subsequent movements. **METHODS:** We studied multiunit (entire spiking) activity recorded during DBS electrode implantation for mixed and akinetic-rigid Parkinson's disease patients. Intraoperative motor tests were performed by patients on each recording site with rhythmic neural activity. Movement paradigm consisted of about 15 seconds of rest (spontaneous activity) and then a series of externally-driven contralateral hand clenching and unclenching. Power spectral densities (%PSD) of neural activity in 96 recording sites with movement tests of 13 patients was studied. We compared alpha band oscillations in three time periods of 2 s before, during and after the first movement execution in a series and %PSD of low-beta band in 500 ms time periods around the start of the subsequent movements. Recordings from each site, which satisfy both alpha desynchronization during the first movement and low-beta desynchronization related to all the following movements were marked as "responsive". Recording sites with other types of responses were marked as "nonresponsive". We then used statistical analysis to find the difference in spontaneous activity between the groups. **RESULTS AND DISCUSSION:** We found reduced alpha and low-beta oscillation during movement executions in "responsive" group (57 recording sites) and no desynchronization in the same time periods in "nonresponsive" group (39 recording sites). The main difference in spontaneous activity involves theta frequency (3-7 Hz, KW-H=11.22, $p<0.001$). We assume that theta oscillations may represent resting tremor episodes of PD patients, which could alter movement realization and neuronal movement-related activity changes in subthalamic nucleus. **RESEARCH SUPPORT:** Russian Science Foundation (22-15-00344).

THE ROLE OF DIET AND DRINKING WATER IN EMOTIONAL RESPONSES: AN INSIGHT FROM ANIMAL MODELS. A Burova, A Gorlova, G Somlyai, K Chaprov, K Sitdikova, A Litavrin, E Svirin, J de Munter, T Strekalova, Neuroplast BV, Department of Psychiatry and Neuropsychology, Maastricht University, Maastricht, Netherlands; Institute of General Pathology and Pathophysiology, Sechenov First Moscow State Medical University, Moscow, Russia; HYD Pharma Inc., Budapest, Hungary. **INTRODUCTION:** Environmental factors such as consumed diet and water can be risk factors of many disorders and affect mental health. Dietary choices and deviant standards in drinking water are a leading global cause of health problems and environmental degradation. To better identify the multifaceted health and environmental impacts of these factors, we employed mouse paradigms in which aberrant behaviors can be attributed to the most common psychiatric conditions. **METHODS:** Mice were exposed to so-called “emotional stress model” using the ultrasound stress (US) of variable frequencies. In another study, a paradigm of “Western diet” (WD) - highly caloric diet enriched with sugar and saturated fat was used. Subgroups of these challenged animals received various treatments improving insulin receptor mediated signaling, such as dicholine succinate, folic acid, edimox or omega-3 dietary supplement. Mice were studied for their emotionality, cognition and numerous physiological read-outs. In a separate study, groups of US- and WD-challenged mice were housed on water depleted for deuterium (DDW) – a major inhibitor of mitochondrial activity. Therefore, we additionally studied how housing on water with increased level of deuterium can affect emotional responses and other read-outs in these models. **RESULTS AND DISCUSSION:** We found that exposure to the WD in mice was associated with elevated signs anxiety, hyperactivity and signs of attention deficit hyperactivity disorder (ADHD) that were overall improved by the use pharmaca increasing mitochondrial processes, as well as by DDW. On the contrary, even a short exposure of mice to water with increased levels of deuterium that corresponded with natural values, has induced anxiety-like and anhedonic (depressive-like) behaviors. In the US-exposed mice, beneficial effects of omega-3 containing diet were reported. Together, our studies show that adult health can be highly susceptible to environmental impacts, whose role might be underestimated. At the same time, modifying diets and drinking water can be a powerful tool in decreasing morbidity. This point to a necessity of further mechanistic studies addressing the role of diet and drinking water in global and mental health, in which the use of animal models is not to be replaced. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation grant 075-15-2022-310.

AGING-RELATED IMPAIRMENT OF GLUCOSE TOLERANCE: THE EFFECTS OF THE WESTERN DIET AND DRINKING WATER WITH ALTERED DEUTERIUM CONTENT. Z Nefedova, A Burova, E Svirin, J de Munter, E Kochina, A Gorlova, G Somlyai, T Strekalova, A Umriukhin, Neuroplast BV, Maastricht, Netherlands; RUDN University, Department of Normal Physiology, Sechenov Moscow State Medical University, Institute of General Pathology and Pathophysiology, Moscow, Russia; HYD Pharma Inc., Budapest, Hungary. **INTRODUCTION:** Aging is associated with a decline of mitochondrial functions and ensuing metabolic abnormalities, such as diabetes type two, metabolic syndrome and others. This necessitates the studies addressing better understanding the mechanisms of environmental risks of these conditions helping to increase prevention measures in seniors. First, given rising societal preference for highly caloric “comfortable food”, “fast food” and “cafeteria-type diets” that are enriched with unsaturated fat and sugars, it is important to understand the role of this type of diet in metabolic dysregulation during aging. Second, levels of deuterium in drinking water can influence mitochondrial functions and thus contribute to metabolic processes in aged people. **METHODS:** We used previously established mouse model of “Western-type diet”, which is based on a heightened intake of unsaturated fat and sugar, and housed eleven-month-old C57BL6 female mice on this diet for 3 weeks. Subgroups of mice were housed on drinking water with highest (180 ppm) or lowest (90 ppm) natural content of deuterium, or on a regular water with common deuterium concentration (145 ppm). Glucose tolerance test, behavioral assessment and other methods were applied. In addition, the effect of a reduced content of the deuterium in the incubation medium on calcium influx in a primary neuroglial culture obtained from rat pups was studied. **RESULTS AND CONCLUSIONS:** Our study showed that consumption of “Western diet”, as well as of drinking water with variable content of deuterium can alter parameters of locomotion, exploration, cognition and anxiety. There was a complex interplay between these conditions suggesting that not only a diet, but also drinking water can be major environmental factors affecting mitochondrial functions during ageing. Finally, altered deuterium concentrations affected the level of intracellular calcium in the cortical neurons. These mechanisms can underlie environmental effects of deuterium on human health in a context of metabolic conditions associated with aging. In conclusion, environmental factors such as consumed diet and water can be risk factors of metabolic dysfunction associated with aging.

RESEARCH SUPPORT: Ministry of Science and Higher Education of Russian Federation grant 075-15-2022-310.

THE ZEBRAFISH VERTICAL 100-500-ML CYLINDER TEST AS A SIMPLE AND FAST METHOD FOR MEASURING FISH STRESS AND ANXIETY. L Yang, Y Zhang, Y Lin, J Cui, Y Qin, C Zhao, AV Kaluev, Department of Biological Sciences, Suzhou Key Laboratory of Neurobiology and Cell Signaling, School of Science, Xi'an Jiaotong-Liverpool University, Suzhou, China. Zebrafish (Danio rerio) have become increasingly popular as a model organism for studying CNS diseases, including anxiety and depression. Because zebrafish move horizontally in the novel tank (measuring anxiety-related geotaxis), horizontal movement may have an impact on the results. In order to examine this problem, we compared fish behavior in a 500 ml glass cylinder (5 cm wide, 24.5 cm long) to the conventional 1.5-L plastic novel tank (bottom 22 cm, high 12 cm, top 26 cm, wide 5 cm). For this, we tested fish that had been chronically stressed for 10 days and a normal control group (n=20-25 per group). Each fish was recorded for 5 min scoring the number and time of entries to top area. Both the cylinder and the regular novel tank tests efficiently detected higher anxiety–like behaviors in chronically stressed fish vs. naïve control fish. Thus, limiting horizontal movements of zebrafish ensures reliable testing for their geotaxis-like anxiety. In separate study, we used a smaller 100-ml cylinder, assessing top 30 ml as top zone and reducing the test duration to 3 min. Our pilot data show that chronically stressed fish differ markedly from intact controls, significantly reducing top entries and time. In control fish, top duration endpoint in this test also showed robust within-trial habituation, similar to the novel tank behavior. In general, the vertical cylinder test can well measure anxiety-like behavior in zebrafish, is simple to operate, and can be run as multiple units simultaneously, thereby increasing potential through-put of CNS drug screening in this aquatic model species. The express-version of this protocol (the 3-min 100-ml cylinder test) can be an efficient modification of this assay that enables rapid, fast and simplified testing of stress-modulating drugs and experimental manipulations. **RESEARCH SUPPORT:** XJTLU research funding, Suzhou Key Laboratory of Neurobiology and Cell Signaling.

ANTIDEPRESSANT AND ANXIOLYTIC EFFECTS OF SMALL DOSES OF ANTIPSYCHOTIC DRUG SULPIRIDE IN ZEBRAFISH. AS Lebedev, DS Galstyan, TO Kolesnikova, MS Papulova, DK Saklakova, AV Kalueff. St. Petersburg State University, St. Petersburg, Russia. **INTRODUCTION:** Sulpiride is an atypical (according to some data, typical) antipsychotic that has an antipsychotic effect on the central nervous system. These neurotropic effects of sulpiride are thought to be due to its stronger binding to dopamine D2 receptors compared to D1 receptors. By blocking the activation of presynaptic D2 receptors, which normally reduces dopamine release, sulpiride can increase dopamine levels in the synaptic cleft. Higher doses of sulpiride may result in inactivation of postsynaptic D1 receptors, resulting in decreased dopamine-related behavioral responses and potentially leading to a more depressive behavioral profile. **AIM:** To study antidepressant and anxiolytic effects of low (non-antipsychotic) doses of sulpiride in a zebrafish model using specialized behavioral tests. **METHODS:** A total of 80 adult short-finned wild-type zebrafish were used for this study. All fish were divided into 4 groups: 50, 100 and 200 mg/l sulpiride and control group. Before testing, zebrafish were placed in a 0.25 L plastic beaker containing drug for 20 min. Sulpiride was previously dissolved in 1 ml of dimethyl sulfoxide (DMSO, also given to control group). Behavior was recorded between 11.00 and 17.00 h, using novel tank test (NTT) and zebrafish tail immobilization (ZTI) test. Behavioral parameters such as frequency, duration of being in the top, distance traveled were calculated using the Noldus EthoVision XT11.5 software. Statistical data were analyzed using the Kruskal-Wallis (MW) test. Statistical significance between the considered parameters was set at p<0.05 in all tests. **RESULTS AND DISCUSSION:** The experiments revealed that the most significant reduction in anxiety in NTT was observed with a dose of 100 mg/l, as this dose displayed statistical variance from the control group that manifests itself in an increase in the distance traveled by the fish, as well as in an increase in the total time spent in the top of the tank. The 200 mg/l dose also exhibited a mild anxiolytic effect, although it was not statistically significant (total distance traveled and the total time spent in the top of the tank were not increased enough). Conversely, the 50 mg/l dose did not demonstrate any discernible impact. In the ZTI test, only the 200 mg/l dose showed a statistically significant antidepressant-like effect that was expressed in an increase in the distance traveled by the fish, as well as an increase in the overall speed of the fish, while the other doses did not produce this effect. The results of the study showed that wild-type zebrafish show dose-dependent sensitivity to the action of sulpiride, which is expressed in an increase in activity in the NTT (100 mg/l) and ZTI (200 mg/l). **RESEARCH SUPPORT:** Russian Science Foundation grant 23-25-00412.

EFFECTS OF CHRONIC NITROGLYCERINE ADMINISTRATION ON MECHANICAL SENSITIVITY OF RATS. VD Ilyushichev, AA Kochneva, NO Fokeeva, PE Musienko, EV Gerasimova, Sirius University of Science and Technology, Sochi, Russia**. INTRODUCTION:** Migraine is the most common neurological disorder with a 1-year prevalence of 11.2% worldwide. Most migraine attacks are characterized by sensory abnormalities: photophobia, phonophobia, osmophobia and tactile allodynia. Here, we investigate changes in cutaneous mechanoreception in a model of chronic migraine without aura induced by nitroglycerin (NTG) administration. **METHODS:** Experiments were performed in male Wistar rats (n=5). Skin sensitivity thresholds were measured in 5 animals as controls. Migraine was modeled by intraperitoneal injection of NTG. Injections were given every other day for 5 days. Prior to NTG injection, the animals' cutaneous sensitivity thresholds were measured using an electronic von Frey device (Ugo Basil, Italy), pressure was applied to the plantar areas of the hind paws, 5 measurements were taken for each paw, and the threshold was considered to be reached when the animal withdrew the paw. Cutaneous sensitivity thresholds on the first day of NTG administration (acute migraine) were measured for 1, 2, 3 h. Thresholds on subsequent days were measured on days 3 and 5 (2nd and 3rd injections of NTG) at 1, 2, 3 h and on Day 9 (5th injection of NTG) at 1, 2 h. Statistical analysis was based on the nonparametric Wilcoxon (paired samples). Signed rank sum test with the significance level set at $p<0.05$. Results are given as means ± SD. **RESULTS**: Mechanical sensitivity was measured before NTG injection (32.2± 8.9 g/mm²) and compared to results obtained during NTG administration: 3 h on the third day (28.1±8.5; 26.5±9.3; 29.6±11 g/mm²), 3 h on Day 5 (26.8±9.2; 24.5±8.7; 23.2±7 g/mm²), 2 h on Day 9 (29.1±9.9; 26.6±9.2 g/mm²). Significant differences were found between the control measures and the second hour of Day 3 ($p \leq 0.05$), the second and third hours of Day 5 ($p<0.001$) and the second hour of Day 9 ($p \leq 0.05$). One of the symptoms of migraine is mechanical allodynia, which occurs not only in the area innervated by the trigeminal nerve in the head, but also in other parts of the body. We found that acute administration of NTG did reduce mechanical thresholds, but chronic administration of NTG reduced the thresholds of the hind paws, evoking allodynia in rats. **RESEARCH SUPPORT:** The Neurobiology Program (NRB-RND-2115) and the Graduate Program in Genetics and Genetic Technologies, Center of Genetics and Life Sciences, Sirius University of Science and Technology.

EFFECT OF NITROGLYCERIN ON MAST CELL DEGRANULATION IN A MODEL OF CHRONIC MIGRAINE IN RATS. NO Fokeeva, VD Ilyushichev, AA Kochneva, PE Musienko, EV Gerasimova, Sirius University of Science and Technology, Sochi, Russia. **INTRODUCTION**: Mast cells, which belong to the group of immune cells, can be a source of inflammatory mediators during a migraine attack (Levy et al., 2007). In the dura mater, mast cells are predominantly located in the dura mater, where they are close to blood vessels. Infusion of nitroglycerin, a migraine inducer, may mediate the induction of dural mast cell degranulation. **METHODS**: A model of chronic migraine in male Wistar rats was used in our study. Animals were injected intraperitoneally with nitroglycerin at a concentration of 10 mg/kg on days 1, 3, 5, 7, 9 of the experiment. There were 7 animals in the control group and 5 in the experimental group. One day after the last injection of nitroglycerin, the animals were perfused with physiological solution followed by 4% paraformaldehyde solution. The isolated membranes were fixed on a microscope slide. Staining with 0.1% toluidine blue, was performed for 10 min, then the fixed preparations were washed with distilled water and dehydrated with 95% ethyl alcohol. The degree of mast cell degranulation was analyzed visually using a Zeiss Primo Star microscope at 10x magnification. The degranulation index was calculated as: Degranulation index = (A*0 + B*1 +B*2 + G*3)/n, where A, B, C, D - Degree of cell degranulation, where A - inactive mast cells, B - cells with a low degree of degranulation, C - cells with a moderate degree of degranulation, D - strongly degranulating mast cells, n - total number of cells. The minimum number of cells for each preparation was 100. Normality of sample data was assessed using the Shapiro-Wilk test, and statistical significance was calculated using t-test. **RESULTS AND DISCUSSION:** The total degranulation index in the control group was 0.31±0.35 (n=7). The mast cell degranulation index in the meningeal membranes of rats following nitroglycerin administration was higher than in the control group and was 1.06±0.04 ($p<0.05$, n=5). Overall, during nitroglycerin-induced migraine, there is a change in the activity of mast cells, which increases the degree of their degranulation and the production of various substances (cytokines) that play an important role in the development of neuroinflammation. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-15-00328.

COMPARISON OF PAIN SENSITIVITY THRESHOLDS IN RATS WITH DIFFERENT DOPAMINE LEVELS USING THE ELECTRONIC VON FREY SYSTEM. AA Kochneva, VD Ilyushichev, NO Fokeeva, PEM Musienko, EV Gerasimova, Center for Genetics and Life Science, Sirius University of Science and Technology, Sochi, Russia. **INTRODUCTION:** Multiple pathologies in humans, including one of the most common neurological diseases, migraine, are accompanied by allodynia, when pain

is caused by stimuli that do not normally cause it, and hyperalgesia, when sensitivity to painful stimuli is increased. In addition to the extensive role of the serotonin and opioid systems in pain perception, there is evidence of dopamine involvement in pain syndromes, fibromyalgia, neuropathies, and altered sensory sensitivity in Parkinson's disease. In 2018, Leo et al. created a line of the dopamine transporter (DAT) knockout rats with elevated levels of dopamine in the synaptic cleft and behavioral phenotype similar to ADHD (increased spontaneous locomotor activity). Here, we studied the baseline values of pain sensitivity thresholds of rats with different dopamine levels. **METHODS:** Male rats aged 6 months of wild-type (WT, n=4), homozygous (DAT-KO, n=4) and heterozygous (DAT-HET, n=7) lines with dopamine transporter gene knockout were used. The animals were placed in small boxes with a mesh floor, left to adapt for 10 min and then tested the plantar zone of the hind paws by applying the Electronic von Frey system (Ugo Basil, Italy), 5 times on both paws alternately, with an interval of 5-10 s, until the moment of paw retraction or licking it. For all measurements, the same rate of increase of the force was used (30 gf/s). Statistical analyses were performed in GraphPad Prism**. RESULTS:** The pain thresholds of rats were unaltered: WT 37.7±6.8, DAT-HET 40±4.5 and DAT-KO 31.5±7.3 gf ($p>0.05$). Thus, despite varying dopamine levels, they did not affect the processing of pain signals elicited by tactile stimulation. **RESEARCH SUPPORT:** Russian Science Foundation grant 23-15-00328.

PATTERNS OF ELECTRICAL BRAIN ACTIVITY FOLLOWING ACUTE NITROGLYCERIN EXPOSURE IN ADULT ZEBRAFISH, AND THEIR RELEVANCE TO MODELING MIGRAINE. VD Riga, TO Kolesnikova, DS Kalinina, EV Gerasimova, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** Nitroglycerin is one of potent inducers of migraine and is frequently utilized to model this condition experimentally in rodents. While nitroglycerin-induced migraine is associated with specific markers on electroencephalography (EEG), migraine-like patterns of EEG in zebrafish remain poorly understood. **AIM:** To characterize patterns of electrical activity in zebrafish brain following acute nitroglycerin exposure. **METHODS:** Zebrafish (n = 22) were anesthetized in ice water, and a fragment of the right temporal skull bone was removed to access the area above the optic tectum, where the active electrode was then inserted. A reference electrode was positioned 2 mm medially from the recording electrode, and the grounding electrode was placed in the water. The adapted adult zebrafish EEG recording system was connected to a biosignal acquisition system on the portable Neuron-Spectrum-65 electroencephalograph. After a 3-min acclimation, the registration of background EEG commenced for a duration of 7 min, followed by the administration of nitroglycerin until a concentration of 10 mg/L was reached, and flowed by 20-min EEG recording session, analyzing 5-s artifact-free epochs by the Neuron-Spectrum.NET electroencephalograph software. **RESULTS AND DISCUSSION:** We recorded lower mean amplitude of the delta range ($p<0.01$) in fish following nitroglycerin administration vs. baseline values. The mean, total, and maximum power decreased compared to the baseline recording ($p<0.05$). One interictal and four ictal events were also recorded, which accounts for 18% of the entire sample. The latent period ranged from 3 to 9 min. Ictal signals had an amplitude from peak to peak of approximately 30-400 μV and a duration of about 20 s. Postictal mortality affected 2 fish (9%). Overall, these results confirm the sensitivity of zebrafish CNS to nitroglycerin and indicate brain deficits upon its acute administration. Since clinical EEG data from migraine patients also report spike activity and reduced amplitude of background activity, there may be evolutionarily conserved mechanisms underlying migraine pathogenesis. This finding may be valuable for understanding the pathophysiology of migraine and identifying new biomarkers of this serious neurological condition. **RESEARCH SUPPORT:** Sirius University of Science and Technology project NRB-RND-2116.

THE NARROW 5-ML VERTICAL CYLINDER TEST AS A POTENTIAL RAPID ASSAY FOR ZEBRAFISH STRESS-EVOKED 'DESPAIR'-LIKE BEHAVIOR. L Yang, Y Zhang, Y Lin, C Zhao, Y Qin, J Cui, AV Kaluev, Department of Biological Sciences, Suzhou Key Laboratory of Neurobiology and Cell Signaling, School of Science, Xi'an Jiaotong-Liverpool University, Suzhou, Jiangsu, China. **INTRODUCTION:** Zebrafish (*Danio rerio*) are a popular a model organism for studying various CNS diseases, including depression. Similar to the behavioral testing in rodents, a set of behavioral assays has also been developed for zebrafish. For example, similar to the 'learned helplessness' ('despair'-like) behavior in mice, the rodent Tail Suspension Test (TST) has recently been adapted (as the Zebrafish Tail Immobilization, ZTI test) for adult zebrafish. However, because this model represents an invasive procedure related to immobilizing tail of the fish, which can be harmful to zebrafish, this may non-specifically affect the accuracy of the experimental data. **AIM:** To improve this aquatic paradigm, here we developed a novel assay to mimic the learned helplessness/despair-like behavior in zebrafish. **METHODS:** For this, we used a narrow 5-ml glass transparent measuring cylinder (1 cm diameter, 10 cm high) to test this behavior. During the testing, we placed zebrafish vertically (head

down) into the measuring cylinder, and then recorded the fish despair-like immobility time and frequency for 5 min, also recording the number of times the fish would reach the top 20% of the cylinder, and the duration there, as measures likely reflecting fish 'struggling' activity. To validate this method, we compared the fish that had been chronically stressed for 15 days, with the normal control group. **RESULTS AND CONCLUSIONS:** Overall, the immobility time in the narrow vertical cylinder assay was significantly higher in stressed vs. control group, resembling similar findings obtained using traditional ZTI testing protocol in fish, and conceptually paralleling the mouse TST findings. The duration, but not frequency, in top was also significantly reduced in the stress group, suggesting less struggling activity and, hence, more despair-like behavior in these fish. In summary, this non-invasive and sensitive to stress protocol can greatly improve the existing testing methods for zebrafish despair-like behavior. **RESEARCH SUPPORT:** XJTLU research funding, Suzhou Key Laboratory of Neurobiology and Cell Signaling.

THE EFFECT OF LASER BEAMS ON BEHAVIOR OF ADULT ZEBRAFISH: TOP, SIDE OR BOTTOM LASER HAS NO EFFECT ON FISH ANXIETY. KV Apukhtin, VS Nikitin, TO Kolesnikova, AV Kalueff, Sirius University of Science and Technology, Sochi, Russia. **INTRODUCTION:** The zebrafish (*Danio rario*) is a useful and convenient translational model for studying stress, anxiety, depression and other common affective disorders. Bright light has long been used in acute and chronic stress modeling protocols in zebrafish. They are also able to distinguish the size and shape of objects, and swim towards small laser dots (taking them for food) but avoid laser dots larger than 4 mm. **AIM:** To evaluate the effects of a multi-beam laser pointer as a stressor, on adult zebrafish behavior. We hypothesized that laser exposure can be anxiogenic in fish, and that some unusual laser source location (e.g., from the bottom or side of the tank) can be more stressful since it would be unnatural for zebrafish in the wild to have bright light at the bottom or side of their natural habitat (as compared to sun or stars visible from the top). **METHODS:** A total of 192 wild type short-fin outbred zebrafish (~50:50 male:female ratio) were tested in the standard 2-L novel tank test (NTT) for 5 min, following a brief exposure to laser beams in a glass container. NTT endpoints included total distance moved, the latency (s) and number of top entries, time spent in top, duration and frequency of freezing, mobility and immobility behaviors, assessed by Noldus EthoVision XT11.5 software. For laser beam exposure, the fish were placed in a cubical glass tank (25 height, length width, cm) and shined upon for 30 or 60 s using a green multi-beam laser pointer (~530 nm) positioned 67 cm away from the tank from the top, bottom, or side. **RESULTS AND CONCLUSIONS:** Overall, 30-s or 60-s multi-beam laser exposure from the top, bottom or side of the tank, did not alter fish anxiety and activity endpoints in the NTT. Thus, contrary to our original working hypothesis, acute exposure to laser beams for both durations was not stressful for zebrafish regardless of the light source location (from top, bottom or side). **RESEARCH SUPPORT:** Sirius University of Science and Technology.

THE IMPACT OF DIFFERENT CONCENTRATIONS OF BACTERIAL MELANIN ON THE BEHAVIOR, MORPHO-FUNCTIONAL STATE OF THE BRAIN, AND BONE MARROW IN A RAT MODEL OF PARKINSON'S DISEASE. KV Karapetyan, KA Nebogova, AG Karapetyan, AM Dallakyan, MV Pogosyan, ZA Avetisyan, MH Danielyan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** Parkinson's disease (PD) is a common neurodegenerative disease of the central nervous system, characterized by selective death of neurons in the substantia nigra (SN), manifested by motor disorders. An important aspect in the development of the pathological process during the progression of PD is disturbances in brain trophism, which arise at the level of the microcirculatory bed. **AIM:** To comparatively investigate the behavior and morphofunctional state of the SN in rats using the rotenone model of PD and subsequent administration of different concentrations of bacterial melanin (BM). Additionally, we aimed to analyze cytogenetic data from the bone marrow of rats to examine the factors determining the development or alleviation of PD. **METHODS:** The research was conducted on the SN of intact rats, on the PD model after 4 weeks of rotenone injection, and on the PD model with BM administration (i.p. 0.17 g/kg) for 4 weeks. The detection of the microcirculatory bed was conducted following Chilingarian's method. The morphometric measurements of the diameter of the SN capillaries of the rat brain were carried out. Cytogenetic parameters were studied using the Ford-Wollam method, which determined the mitotic index (MI) and the percentage of polyploid cells (PPC) in the bone marrow cells of the femur (counting 1000 cells in each group). Data analysis was performed using Statsoft and SPSS-10.0. Behavioral tests were conducted using cylinder and rotarod tests. **RESULTS AND DISCUSSION:** Overall, compared to intact rats, experimental animals with rotenone intoxication exhibited an increase in the diameter of capillaries and a total reduction of the capillary network. Under the influence of BM at all concentrations, there is a tendency to approach the diameter of the capillaries to norm, and the capillary network is restored. Behavioral tests showed that animals after rotenone intoxication

demonstrate behaviors typical of PD rats (freezing, immobility, apathy), confirming the development of an experimental model of PD in rats. Under the influence of BM, animal behavioral indices were close to norm. Analysis of cytogenetic indices showed that PD animals had higher PPC and lesser MI, indicative of inflammatory processes and accompanied by inhibition of bone marrow hematopoiesis. Higher MI and lower PPC can be genetic risk factors for the development of PD. Under the influence of BM, there was a tendency to normalize MI, and a significant decrease in the percentage of PPC was observed, which may indicate its beneficial effect. This indicates angioprotective effect of BM on SN capillaries in rat brain with rotenone intoxication, associated with improved microcirculation and brain tissue trophism. This results from the normalization of vascular lumen and the opening of new capillary branches, ensuring nerve cell preservation. Behavioral tests confirm PD-like state in rats corrected by BM. The resulting cytogenetic disorders (changes in MI and the percentage of PPC in the bone marrow) may reflect these changes. Thus, BM can be used as a therapeutic agent in complex PD therapy. **RESEARCH SUPPORT:** Science Committee of Armenia research project 21T-1F282.

THE IMPACT OF HYDROPONIC *SUTHERLANDIA FRUTESCENS* ON HIPPOCAMPAL NEURONAL ACTIVITY IN A RAT MODEL OF PARKINSON'S DISEASE. LP Manukyan, LE Hambardzumyan, VH Sarkisian, KV Simonyan, LE Hovhannisyan, LV Darbinyan, Sensorimotor Integration Lab, Neuroendocrine Relationships Lab, Orbeli Institute of Physiology NAS RA, GS Davtyan Institute of Hydroponics Problems NAS RA, Yerevan, Armenia. **INTRODUCTION:** Parkinson's disease (PD) is an age-related neurodegenerative disorder characterized by the selective degeneration of dopaminergic neurons in the Substantia nigra, leading to motor symptoms. Rotenone exposure for an extended period of time causes PD-like symptoms in humans. When administered to rats in vivo, rotenone causes neurological and behavioral changes that lead to PD. *Sutherlandia frutescens* (SF) is widely used in South Africa for various health conditions. SF contains various biologically active compounds, including GABA, L-canavanine, and D-pinitol. These compounds have been reported to have potential antioxidant, anti-inflammatory, and anticarcinogenic effects**. METHODS:** Here, we used in vivo electrophysiological recordings from the hippocampus and conducted an open field test to assess motor behavior. **RESULTS AND DISCUSSION:** We investigated the impact of rotenone (2.0 mg/kg) on hippocampal neuron activity and evaluated the potential protective effects of hydroponically grown SF. Rats treated with SF exhibited significantly higher activity levels compared to both the control and rotenone groups. Conversely, the rotenone group showed lower activity levels and exploration, suggesting a suppressive effect of rotenone. Our results suggest that SF may modulate the activity of hippocampal neurons, indicating a potential neuroprotective effect. **RESEARCH SUPPORT:** Armenian National Science and Education Fund project 23AN:NS-biochem-2925.

PROTECTIVE EFFECTS OF L-THYROXINE ON HIPPOCAMPAL VASCULAR MORPHOLOGY AND ELECTRICAL ACTIVITY IN THYROIDECTOMIZED RATS. LV Darbinyan, KV Simonyan, LG Avetisyan, LE Hambardzumyan, LP Manukyan, KV Karapetyan, MH Danielyan, Orbeli Institute of Physiology NAS RA**,** Yerevan, Armenia. **INTRODUCTION:** Thyroid hormones play a pivotal role in influencing learning and memory, yet limited electrophysiological evidence exists to support these effects. This study, conducted on adult male Wistar rats, aimed to investigate the impact of L-thyroxine on the hippocampus in thyroidectomized (TX) rats, addressing the limited electrophysiological evidence in the existing literature. **METHODS:** Rats were randomly assigned to the TX, TX+ L-thyroxine injection (10 µg/100 g/day, i.p. administered one week after surgery for 4 weeks), and vehicle-control groups. To record the spike activity flow of single neurons in hippocampal neurons, a stimulating electrode was inserted according to stereotaxic coordinates into the ipsilateral entorhinal cortex (AP –9, L ±3.5, DV +4). A glass recording electrode (1-2 µm tip in diameter) filled with 3 M KCl was repeatedly submerged into the hippocampus (coordinates AP −3.3; L ± 1.5-3.5; DV+3-4). We used morphometric analysis based on ImageJ to visualize and quantify individual hippocampal capillaries and to define changes in response to disease progression in rat models of TX and after L-thyroxine treatment. **RESULTS AND DISCUSSION:** We found significant alterations in hippocampal electrophysiological activity in L-thyroxine-treated rats, providing clear in vivo evidence for the action of L-thyroxine in the hippocampus of TX rats. Morphological data, along with electrophysiological findings, contribute to a comprehensive understanding of the complex relationship between thyroid hormones and hippocampal function. These findings have potential implications for cognitive and memory-related complaints reported by hyperthyroid patients. **RESEARCH SUPPORT:** Higher Education and Science Committee of MESCS RA Research project 22YR-1F003.

NEW THERAPIES AND THERAPEUTIC DIET PROTOTYPE: PROMISING EFFECTS IN FEMALE APP/PS1 MICE, A MODEL OF ALZHEIMER DISEASE. K Sitdikova, J de Munter, K Chaprov, A Tsoy,

A Gorlova, Z Nefedova, E Svirin, A Kassenova, L Ohanyan, N Ayvazyan, K Lebedeva, M Kuznetsova, T Veremeyko, ED Ponomarev, S Askarova, T Strekalova, Institute of General Pathology and Pathophysiology, Sechenov First Moscow State Medical University, Moscow, Russia; Neuroplast BV, Maastricht, Netherlands; Astana National Laboratory, Department of Biology, School of Sciences and Humanities, Nazarbayev University, Astana, Kazakhstan; LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia; Biomedical Sciences Department, City University of Hong Kong, Hong Kong, China. **INTRODUCTION:** Our project aimed to study potential beneficial effects of anti-oxidants, as well as of 'Neuro-Cells' (NC), or dietary extract containing sialic acid-binding *Wheat Germ Agglutinin* (WGA) in comparison with the effects of recently FDA-approved lecanemab in transgenic model of Alzheimer's disorder (AD), APP/PS1 mice, NC- unmanipulated human stem cell preparation of Mesenchimal stem cells (MSC) and Hemopoetic stem cells (HSC). **METHODS:** 12 months old female APP/PS1 mice and their wild-type (WT) littermates were subjected either to (a) chronic dosing with thiamine, fullerenol-based drugs and insulin receptor sensitizer compounds via drinking water; (b) WGA containing drinking solution; (c) single administration of 500 000 NC to cysterna magna; (d) i.v. injections of lecanemab with 2-week interval, (e) a combination of NC and lecanemab treatment, or (f) no treatment. Behavioral measures of locomotion, anxiety, and learning were investigated. Brains from NC-treated groups of mice were harvested for amyloid beta Congo staining, 6E10 antibody, DAPI and GFAP in the cortex, hippocampus and thalamus and compared against non-treated and lecanemab-treated groups. Gene expression of the markers of neurons, astroglia and inflammation were studied in the hippocampus and prefrontal cortex. Deep learning methods were applied to study the density of amyloid plaques of various sizes. **RESULTS AND DISCUSSION:** We found profound cognitive deficits of APP/PS1 mice and increased anxiety accompanied by massive plaque formation in the brain. Histological, behavioral and cognitive hallmarks of AD were ameliorated by the use of NC; WGA treatment was found to be effective in reducing emotional abnormalities. Our study identified new correlates of AD-like pathology in APP/PS1 mice, and proposes the use of fullerenol and NC transplantational therapy as potential new treatment of AD. **RESEARCH SUPPORT:** Neuroplast BV, RF grant 075-15-2022-310 and EU Marie-Curie Skłodowska 'PhytoApp' 0101007642.

NEONATAL INFLAMMATION DOES NOT LEAD TO DELAYED EFFECTS ON THE GLUTAMATERGIC SYSTEM AND BRAIN NEUROPLASTICITY: CHARACTERISTICS OF MICE WITH AUTISM-LIKE PHENOTYPE. EV Mezhlumyan, KA Ayriyants, AS Mutovina, MM Kolesnikova, NP Bondar, Novosibirsk State University, Institute of Cytology and Genetics, Novosibirsk, Russia. **INTRODUCTION:** Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and restricted or repetitive behaviors. Patients with idiopathic ASD often have aberrant immune response. There are also signs of chronic neuroinflammation in postmortem brain samples, suggesting that inflammation can play a role in disorder development. On the other hand, ASD is accompanied by neurochemical abnormalities (e.g., impaired synaptic pruning and dysregulation in the glutamatergic system), suggesting that neurochemical deficits may be associated with observed immune alterations via glial cells. The role of early-postnatal inflammatory induction is still unclear. We used BTBR T+Itpr3tf/J strain of mice (BTBR), a well-validated model for studying ASD, to analyze how early-postnatal inflammatory stress alters the expression of genes associated with activation of neurons and glia, as well as the glutamatergic system, in the frontal cortex and hypothalamus of BTBR mice. **METHODS:** Male BTBR and C57Bl/6 mice were injected with bacterial (lipopolysaccharide, 50 mcg/kg) and viral (polyinosinic:polycytidylic acid, 10 mcg/kg) mimetics, or their combination, on postnatal days 3 and 5. We analyzed the expression of genes associated with neuronal activation (*Fos*), astroglia and microglia activation (*Gfap*, *Aif1*), anti-inflammatory response (*Serpina3*, *Trem2*) and glutamate transmission (*Grin2b*, *Gls1*) in the frontal cortex and hypothalamus on 24th day of life by real-time PCR. **RESULTS AND DISCUSSION:** Overall, we found no effects of inflammatory induction on the gene expression in BTBR and C57Bl6 mice in both structures ($p>0.05$). However, we revealed inter-strain expression differences in genes associated with neuronal and glial activation, anti-inflammatory response and glutamate neurotransmission: the frontal cortex expression of the *Aif1*, *Fos*, *Trem2* and *Gls1* genes in the BTBR mice was lower, while *Gfap* and *Serpina3* higher, vs. C57Bl6 mice ($p<0.01$ for all genes). There were no differences in *Grin2b* expression in the frontal cortex. In hypothalamus, *Gfap, Serpina3, Gls1* and *Grin2b* had higher expression in BTBR than C57Bl6 mice, while *Trem2* expression was lower. Thus, BTBR mice with an autism-like phenotype display altered expression (vs. C57Bl6 mice) of genes associated with neural and glial activation, anti-inflammatory response and glutamatergic system. However, effects of early-postnatal inflammation were not found in both strains. **RESEARCH SUPPORT:** State Budget project FWNR-2022-0016.

COPPER COMPLEXES Cu (L^{CF3})$_2$ AND Cu(L^{cur})$_2H_2O$ AS RADIOPROTECTIVE COMPOUNDS. AG Karapetyan, VS Grigoryan, AM Dallakyan, LA Orbeli Institute of Physiology NAS RA, University of Traditional Medicine of Armenia, Yerevan, Armenia. One of the first and direct signs of the impact of ionizing radiation (IR) on a cell is the destabilization of chromosomes. Radiation-induced damage to the karyotype is an important indicator both for biological indication of the severity of radiation injuries and for predicting the development of long-term adverse effects of IR. The search for new, effective radioprotective compounds is a priority task of modern radiobiology. In this area, organometallic complexes with high antioxidant activity are of particular interest. The purpose of this work is to determine the possible radioprotective properties of the **Cu** (L^{CF3})$_2$ and Cu(L^{cur})$_2H_2O$ complexes. Determined survival, life expectancy and cytogenetic parameters: mitotic index, chromosome aberrations and % of polyploid cells in the bone marrow cells of the femur (count in 1000 cells in each preparation). Group I included intact animals; Group II consisted of animals exposed to the radioisotope technetium, group III consisted of animals that were intraperitoneally injected with copper complex Cu (L^{CF3})$_2$ at a dose of 50 mg/kg in a volume of 2 ml 1 h before the administration of the Tc isotope ("irradiation + copper compound Cu (L^{CF3})$_2$ (complex 1). Group IV included animals that received the compound Cu(L^{cur})$_2H_2O$ (complex2) before irradiation. The groups with the injection of Cu(L^{CF3})$_2$ complex had the highest survival. In terms of indicators: chromosomal aberrations and the number of polyploid cells, a significant difference was found in those irradiated compared with the "irradiation + Cu (L^{CF3})$_2$" group (both after 15 and after 30 days), which indicates the radioprotective property of the compound. In terms of the mitotic index, a tendency towards normalization was noted after 15 days and a significant difference between groups 2 and 3 by the end of the study (after 30 days), which also proves the beneficial effect of this compound. Analysis of survival, changes in cytogenetic parameters, multiregression analysis using 2 complexes confirms the greatest efficiency of Cu (L^{CF3})$_2$ relative to Cu(L^{cur})$_2H_2O$, because when using Cu(L^{cur})$_2H_2O$ in group IV and comparing it with "pure irradiation," only a tendency toward normalization of cytogenetic parameters was observed. Multiregression analysis of cytogenetic parameters also confirmed the highest efficiency of the Cu(L^{CF3})$_2$ compound relative to Cu(L^{cur})$_2H_2O$. The results of the research indicate the need to continue work in the direction of searching for agents that have a therapeutic effect in radiation injuries.

COMPARATIVE ELECTROPHYSIOLOGICAL STUDY OF THE ACTIVITY OF VESTIBULO- AND RETICULOSPINAL NEURONS IN FROG. LR Manvelyan, DO Terzyan, ML Grigoryan, LR Ohanyan, Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** The motor activity of the body is a result of a complex interaction between the motor structures of the brain and spinal cord. The vestibular and reticular neurons, as a part of the ancient descending pathways, play the key role in the interaction between integration and execution of movements as these areas of medulla oblongata affect the motoneurons of the spinal cord. The neurons of two main pathways (vestibulo-spinal and reticulo-spinal) are closely interconnected and this relationship directly affects body movements. It is especially interesting to study the effect of motor structures on amphibians' motoneurons, since they are the least differentiated. In this work are presented the comparative results of an electrophysiological study of the activation features of the vestibulo- and reticulospinal neurons on stimulation of the cervical and lumbar spinal cord in frog. **METHODS:** The experiments were performed on frogs (*Rana ridibunda*) of both sexes using the isolated brain perfusion. The animals were anesthetized with a 0.1% solution of MS-222 (0.2 g/kg). Electrical stimulation of the anterior branch of the VIII nerve was carried out by single DC shocks with silver suction electrode. Bipolar tungsten electrodes were applied to the ventral cord at the cervical (II pair of spinal nerves, C) and lumbar (VIII-X pairs, L) thickenings of the spinal cord. The same current parameters were used as for the anterior branch of the VIII nerve. For intracellular recording of the electrical activity of the VNC and MRF neurons, were used glass microelectrodes filled with a 2M KCL solution. Computer analysis of the data was performed. **RESULTS AND DISCUSSION:** VNC and MRF neurons were identified based on excitatory postsynaptic potentials (EPSP) arising in response to stimulation of the ipsilateral vestibular nerve and their activation by stimulation of the cervical and lumbar spinal cord. Neurons that activated only upon stimulation of the cervical spinal cord were designated C neurons, and neurons that are also activated to stimulation of the lumbar spinal cord were designated L-neurons. Monosynaptic EPSPs arose during the intracellular recording of the electrical activity of vestibular and reticular neurons in response to nerve stimulation with a latent period of 1.5-2.96 and 2.22-6.82 ms, respectively. In response to cervical and lumbar spinal cord stimulation, antidromic action potentials with a short and fixed latent period arose at different stimulation intensities. They were distinguished by their short refractoriness and the ability to reproduce high-frequency stimulation. The latent period of vestibular and reticular C neurons was 0.57-3.6 and 0.37-1.66 ms, respectively. The latent period of the vestibular and reticular L neurons was 1.3-3.89 and 0.51-1.8 ms, respectively. Vestibulo- and reticulospinal neurons are activated antidromically by stimulation of the cervical and lumbar spinal cord. In vestibulospinal neurons, the distance between the sites of irritation

of the C and L was 7-13 mm (9.55±9.66 mm; n=97) and in reticulospinal neurons 5-14 mm (9.84±1.44; n=55). The distance between the place where the microelectrode was inserted into the brain and the place of stimulation of the cervical spinal cord for vestibulospinal neurons was 3.8-9.9 mm (6.22±6.34 mm; n=125). The corresponding parameter in the case of reticulospinal neurons was 3-6.9 mm (4.63±0.7; n=211). Based on the velocities of axonal conduction, vestibular and reticular neurons were subdivided into slow (up to 14 m/s) and fast (15 m/s or higher). Slow and fast vestibular and reticular C- and L-neurons were recorded in all areas of the VNC and MRF. Overall, there were more slow than fast C-neurons. **CONCLUSIONS.** The axons of the vestibulo- and reticulospinal neurons of the frog monosynaptically contact the motor neurons of the cervical and lumbar thickenings. It was released that the neurons of two studied pathways showed the similar data during the spinal cord stimulation. This proves that although reticular neurons localized in small groups, compared with vestibular ones, they significantly affect body movements. Collectively, these data indicate the important role of these neurons in mediating vestibular and reticular influences on spinal motor mechanisms.

IMPLEMENTATION OF STIMULATION OF SOME LIMBIC BRAIN STRUCTURES ON IDENTIFIED VAGAL NEURONS OF THE SOLITARY TRACT NUCLEUS. EA Avetisyan, AA Petrosyan, SA Shogeryan, NA Sahakyan, VH Sarkisian, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. Elucidation of the mechanisms of regulation and control of autonomic reactions (cardiovascular, vasomotor, respiratory, etc.) by the structures of the limbic brain is important for the correct diagnosis of diseases, associated with the pathology of the aforesaid systems. The limbic system, receiving afferent signals from almost all internal organs, itself affects the neurons of the solitary tract (NST), which is the terminal zone of the laryngeal, tracheobronchial, pulmonary, cardiac and gastrointestinal afferent fibers of the vagus nerve. In order to clarify all these issues, we selected the structures of the limbic brain - the paraventricular nucleus of the hypothalamus (PVN), the corticomedial nucleus (CMN) of the amygdala and the dorsal limbic cortex (DLC), which not only have direct access to the studied vagosolitary neurons, but also take an active part in the cardiovascular reactions. In vivo electrophysiological experiments were performed on anesthetized albino Wistar rats (220-240 g). The experimental protocol corresponded to the conditions of the European Communities Council Directive (2010/63/UE). Functional identification of input vagosensitive neurons was carried out with stimulation of the vagus nerve in the cervical region. 42 NST neurons were recorded, of which 25 (59.5%) units responded to a single stimulation of the PVN by initial excitation and of which 15 responded with a short latency (4-8 ms), 8 with average values (10-20ms) and two neurons with 30-40ms. The remaining 17 vagal units were non-responding. The recovery cycle of test responses for the majority of neurons (55%) is >20ms, 17% up to 20ms and 28% up to 10ms. For stimulating CMN, a wide range of latentcies of phase-excitatory reactions was revealed: 5-10ms (35.7%), 11-19ms (46.4%), 20-40ms (17.9%), showing the presence of various stages of amygdalo-fugal discharges. A strong blocking effect of DLK on the input "vagal" NST neurons was found, starting from 10-600 ms. Thus, the studied brain structures play a significant role in the mechanisms of control of the activity of vago-sensitive NST neurons and provides not only the implementation of vago-vagal reflexes, but also take an active part in the mechanism of central regulation of the activity of the body. visceral systems.

INVESTIGATION OF THE ROLE OF TRACE AMINE-ASSOCIATED RECEPTOR 5 (TAAR 5) IN THE RESTORATION OF SENSORIMOTOR FUNCTIONS AFTER SPINAL CORD INJURY. AD Buglinina, DS Kalinina, EA Romanyuk, PE Musienko, Department of Neuroscience, Sirius University of Science and Technology, Sirius, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg, Life Improvement by Future Technologies Center “LIFT”, Moscow, Russia. **INTRODUCTION**: Trace amine-associated receptors type 5 (TAAR5) has been shown to be involved in the regulating of motor functions and may participate in adult neurogenesis. **AIM:** To evaluate the TAAR5 involvement in the restoration of sensorimotor functions after spinal cord injury (SCI). **METHODS**: Mice with knock-out of the gene encoding TAAR5 (TAAR5-KO) and wild-type mice (WT) were used as a model object. All experiments were performed on mature male TAAR5-KO (n=11) and WT (n=10) mice. For modeling SCI, a left-sided lateral hemisection between the 7th and 8th vertebrae was used (Isoflurane 1.5%). Exploratory activity and anxiety were evaluated using the Open Field and the Elevated Plus Maze (EPM) tests. Sensorimotor function was assessed using the Footprint test and the modified BBB (Toyama Mouse Score, TMS) test. For the Footprint test, step length and distance between pairs of limbs were estimated. Recovery of sensorimotor function after SCI including limb functioning, body support and coordination, were evaluated during walking on a flat surface by a TMS scale from 0 to 30 points. Data were analyzed using RealTimer, Noldus EthoVision XT17 and GraphPad Prism 9. **RESULTS AND DISCUSSION:** In the Open field test, there were no significant differences in average and maximum speed, distance traveled, or time spent in the center or on the periphery between the TAAR5-WT and

TAAR5-KO groups. However, the average self-grooming time for TAAR5-KO mice was found to be higher than for TAAR5-WT mice (TAAR5-KO: 10.05; WT: 6.1; P=0.035). The EPM and Footprint tests showed no significant differences between TAAR5-KO and WT groups. TMS showed only a tendency to improved recovery in TAAR-KO. Overall, TAAR5 has minor effect on motor function recovery, but may play a role in de-aurosal and stress behavior, controlled by the amygdala and other limbic structures where TAAR5 is expressed. Further research is needed to determine TAAR5 involvement in recovery after injury. **RESEARCH SUPPORT:** Russian Science Foundation grant 24-15-20036.

AUTOPHAGOLYSOSOMES FORMATION IN BRAIN TISSUE OF RAT FETUSES SUBJECTED TO PRENATAL HYPERHOMOCYSTEINEMIA. AV Alov, NL Tumanova, AV Mikhel, IV Zalozniaia, YP Milyutina, DS Vasilev, AV Arutjunyan, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Ott Research Institute of Obstetrics, Gynecology and Reproductive Medicine, St. Petersburg, Russia. **INTRODUCTION:** Prenatal hyperhomocysteinemia (pHHC) is associated with increased level of the toxic amino acid homocysteine in fetal tissues, and impairs brain development accompanied by neuronal death in postnatal ontogenesis. In the brain cortex and hippocampus of rat offspring exposed to experimentally induced pHHC, the features of developmental delay and neurodegenerative changes were previously shown. However, the molecular mechanisms of cell death involved in the development of pHHC are poorly understood. The autophagosomes presence in the neurons of pHHC rats was previously revealed in postnatal period using electron microscopy, which suggests the activation of autophagy. We investigated the distribution of authophagosomes and authophagolysosomes in the brain tissue during embryonic and postnatal periods of pHHC rat ontogenesis. **METHODS:** Hyperhomocysteinemia was induced by oral administration of 0.15% aqueous solution of L-methionine to pregnant rats daily, from Day 4 of gestation until birth. The investigation of the fetal brain tissue was performed on day 20 (E20) of prenatal development when there was an increased level of homocysteine in the brain, or in postnatal period (P5 and P20) when it was normalized. Cortical and hippocampal brain tissue of the offspring were analyzed using electron microscopy and immunochemical method. In order to verify the formation of autophagolysosomes in the pHHC fetal brain, the localization of autophagosome (LC3B-II) and lysosome (Lamp2) marker proteins was studied by immunofluorescence staining and Proximity Ligation Assay (PLA) method. **RESULTS AND DISCUSSION:** The appearance of the numerous autophagosomes in both parietal cortex and hippocampus of pHHC offspring was detected on E20, P5 and P20. The fluorescence signal corresponding to Lamp-2 was localized in the whole volume of cytoplasm of the majority of cells in the in both pHHC and control embryonic brain, which corresponds to the natural distribution of this protein. LC3B-II fluorescence signal was detected in brain cells more frequently in pHHC embryos than in controls. Using the Duolink® PLA kit, co-localization of LC3B-II and Lamp-2 marker protein signals was demonstrated, suggesting the possibility of autophagy activation. In combination with observations of autophagosomes by electron microscopy in both fetal pHHC brains and in P5-P20 pups, it is possible to assume the activation of autophagy cell death caused by homocysteine action. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-15-00393.

THE PRACTICAL CHALLENGES AND LIMITATIONS OF DETECTING MOTOR UNITS FROM SURFACE ELECTROMYOGRAPHY. GV Iskarevsky, AD Buglinina, AE Pozdnyakova, AA Pekonidi, DA Onishchenko, AM Beknazarova, YR Bravyy, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** High-density surface electromyography (HD sEMG) is increasingly used in neuroscience to study early diagnosis of neurodegenerative diseases. Several parameters of motor unit (MU) activity, such as motor unit action potential, firing rate, and recruitment threshold, can be estimated from HD sEMG recordings. Recording accuracy is critical for early diagnosis of neurodegenerative diseases. Recording quality depends on electrode placement, skin conductivity and sweat, which may affect the accuracy of motor unit decomposition. The aim of this study was to identify the limiting factors of HD sEMG recording. **METHODS:** One group of subjects (female, n = 3) performed 4 x 15-min runs at a speed of 3 km/h on a treadmill (h/p cosmos). HD sEMG (Delsys Trigno Galileo) was recorded on the following muscles: m. tibialis anterior, m. gastrocnemius lateralis of the right leg, and m. erector spinae on both the right and left sides. Decomposition of the HD sEMG signal was performed using commercial software (Delsys Neuromap). The research was approved by the Ethics Committee of Sirius University. **RESULTS AND DISCUSSION:** 23 recordings were classified as low quality after analysis of the entire 47 HD sEMG recordings. Participants with thicker skinfolds and weaker muscles had lower quality decomposition, and conversely, participants with thinner skinfolds and stronger back muscles had better quality decomposition. High sweat rates decrease the quality of the recordings, and low-quality results in missing numbers of identified motor units and incorrect decomposition results. In order to improve the quality of signal decomposition, it is important to have the sensors in the correct position as recommended in an atlas of muscle innervation zones and to consider the influence of sweat rate, skinfold thickness, muscle strength and exercise

duration. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation, Agreement 075-10-2021-093, Project ISR-RND-2252.

IS ARTIFICIAL INTELLIGENCE AN EFFECTIVE TOOL FOR PROVIDING THERAPY ADVICE IN NEUROREHABILITATION? AM Beknazarova, NO Prokhorenko, GV Iskarevsky, AA Pekonidi, YR Braviy, DA Onishchenko, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION.** Neurodegenerative diseases are a group of diseases caused by the gradual death of nerve cells. Currently, more than 40 million people worldwide are affected by various neurodegenerative diseases, including younger individuals. Recent years have seen a significant increase in people's reliance on internet resources for their own health. Increasingly, the population is turning to the internet to find answers to questions about their condition. Issues of early diagnosis of neurodegenerative diseases are becoming more relevant every year. In this regard, we hypothesized that artificial intelligence could be a good tool to provide guidance in the field of rehabilitation and therapy of neurodegenerative disorders. **METHODS:** We compiled a list of 9 questions on 3 neurodegenerative diseases (Alzheimer's, Parkinson's and consequences of stroke) and asked these questions to OpenAI ChatGPT-3.5 and OpenAI ChatGPT-4 (20 March 2024). Evaluation was performed by specialists in neuroscience and medicine (rehabilitation and neurology). The scores from experts have been averaged. **RESULTS AND DISCUSSION:** A comparative analysis of the responses by independent qualified experts revealed that the version of answers from ChatGPT- 3.5 and ChatGPT-4 are in general similar. Answers from both versions contain some inaccuracies. The answers related to PD were most inaccurate compared to the answers related to AD and stroke. According to the scores from experts, the most complete and accurate were the answers on the topic of post-stroke rehabilitation. This may be due to the fact that at present this area is the most studied out of the three we selected. Thus, it is possible to offer advice by OpenAI ChatGPT-3.5 and there is no need to purchase ChatGPT-4. It is still very early to talk about replacing real medical consultations by artificial intelligence. Chatbots have the huge potential to become a successful assistant for doctors. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation, Agreement 075-10-2021-093, Project ISR-RND-2252.

EFFECT OF BLOOD FLOW RESTRICTION ON RECRUITMENT THRESHOLD AND AMPLITUDE-FREQUENCY CHARACTERISTICS OF MOTOR UNITS DURING EXERCISE. AA Pekonidi, GV Iskarevsky, AE Pozdnyakova, AM Beknazarova, AS Kirsanov, DA Onishchenko, YR Bravyy, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** Insulin-like growth factor, brain-derived neurotrophic factor, growth hormone and blood lactate play key roles in promoting neuroplasticity, significantly enhancing rehabilitation outcomes for patients with neurodegenerative diseases. These biomolecules are released during low-intensity (LI) exercises with blood flow restriction (BFR), which are as effective as high-intensity strength training in developing strength and muscle hypertrophy. It is suggested that LI exercises with BFR activate high-threshold motor units (MUs), although the amplitude-frequency characteristics and recruitment patterns of these units under such conditions are not well understood. This study aims to explore the effects of acute LI BFR-exercises on MU recruitment dynamics and amplitude-frequency characteristics, informing the development of targeted rehabilitation protocols for neurodegeneration and muscle atrophy. MU activity will be non-invasively evaluated through decomposition analysis of high-density surface electromyography (HD sEMG). **METHODS:** A group of subjects (n = 8) performed controlled workload exercises on an isokinetic dynamometer (Isomed 2000), with continuous recording of force, muscle oxygenation (Moxy monitor), and HD sEMG (Delsys Trigno Galileo). HD sEMG signal was decomposed using software (Delsys Neuromap). Exercises were conducted in isometric mode for the wrist flexors, alternating between contraction and rest stages at 40% of maximum voluntary contraction. BFR was applied on the most proximal portion of the arm at 230 mmHg just before starting exercise. Protocols with and without BFR were executed in random order. The research has been approved by the ethics committee of Sirius University. **RESULTS AND DISCUSSION:** Comparing MU characteristics under free-flow and BFR conditions showed lower muscle oxygenation and a shift in MU recruitment strategy with BFR, featuring earlier engagement of high-threshold MUs at a lower discharge rate. These findings may help clarify the mechanisms behind hypertrophy observed with LI training with BFR. Further investigation of how LI BFR-exercises affect bioactive molecule release and impact neuroplasticity may lead to more effective rehabilitation methods for a broad patient range. **RESEARCH SUPPORT:** Ministry of Science and Higher Education of Russian Federation, Agreement 075-10-2021-093, Project ISR-RND-2252.

RAPID CORTICAL PLASTICITY: DISSOCIATING THE EFFECTS OF ACTIVE AND PASSIVE ATTENTION IN AUDITORY PROCESSING. G Kopytin, A Kondratenko, M Ivanova, A Gorin, A

Shestakova, V Moiseeva, National Research University Higher School of Economics, Moscow, Russia. Neuroscientific research has highlighted the capacity for rapid cortical plasticity, showing dissociable effects of plasticity induced by active and passive attention. While these effects are observed after memory consolidation, less is known about more rapid plasticity effects. We used magnetoencephalography (MEG) to record the brain responses of 30 healthy participants to passively presented auditory stimuli (roving oddball paradigm; two sessions) and to a monetary reward learning task, in which these stimuli were partly used as reward-associated cues, between two oddball sessions. The auditory stimuli consisted of ten pure tones. Thus, while participants attended to one part of the auditory cues both passively (oddball) and actively (reward learning task), attention to the other part was only passive (oddball only), which allows to dissociate effects of plasticity induced by active and passive attention. Mismatch negativity responses were computed for all presented tones and showed a significant increase in P3a amplitude in the post-learning oddball responses in both passive and active conditions. However, there was no difference in P3a amplitude between conditions. Thus, while previous research shows dissociable effects of active and passive attention on cortical plasticity observed after memory consolidation, in our study we observed similar plasticity effects in all conditions, regardless of whether the cues were presented actively or passively. This suggests faster, passively attended induced plasticity, while suggesting slower, delayed plasticity effects induced by active attention. **RESEARCH SUPPORT:** Russian Science Foundation grant 22-18-00660.

REGULATION OF CHARACTERISTICS OF ELECTRICAL RHYTHMOGENESIS IN THE REPRODUCTIVE SYSTEM. AV Mkrtchyan, NG Hunanyan, RG Chibukhchyan, TA Piliposyan, HH Mkrtchyan, YY Trofimova, KV Kazaryan, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia. **INTRODUCTION:** Spontaneous electrical activity of the uterus and fallopian tubes provides their contractile activity and underlies the reproductive function. In non-pregnant rats, in norm, irregular bursts of electrical activity occur in specific regions of the myometrium and are the result of cyclic depolarization of the membrane potential. These bursts of myogenic activity are recorded both in the uterine corpus and in the ovarian and cervical ends of the fallopian tubes, with each of these bursts triggering a sequential contractile response. In the uterus of a non-pregnant rat, the propagation of electrical impulses occurs only within a few millimeters, which is explained by the presence of weak electrical interactions between smooth muscle cells. Thus, the activity occurring in the pacemaker regions of the myometrium cannot be the result of an impulse wave propagating along the myometrium. Based on previous studies, myometrial pacemakers are not located in specific regions and each individual cell is capable of generating pacemaker activity. Therefore, the cell with the highest excitability can generate an action potential and become the source of the pacemaker activity of the given region of the myometrium. However, the need for a clear direction of electric wave propagation indicates that, along with the above-mentioned labile pacemakers, there are also other sources of rhythmogenesis. Numerous studies have confirmed the specific localization of pacemaker regions in the myometrium of different animals, which determines the direction of propagation of the excitation wave. **AIM:** To resolve these problems through electrophysiological studies, as well as through a comparative analysis of activity indicators. **METHODS:** Experiments were performed in situ on female rats weighing 200-250 g. The abdominal cavity was opened by performing a medial incision of the abdominal wall and the fallopian tubes with the uterine corpus were exposed. The uterus was denervated by transection of the nerves plexus hypogastricus, uterinus, uterovaginalis. The relationship between the spontaneous electrical activities of paired fallopian tubes, and, accordingly, each of them with the uterine corpus, was studied by stepwise transections. Spontaneous electrical activity was registered by bipolar electrodes. The amplitude (A), mean rise - rate (V), rise-time (T/2 – action potential duration of upgoing phase) and half width (t – action potential duration forming the upper half of its amplitude) of peaks of action potentials (AP) were determined. Recordings were done by a 4-channel device developed at Orbeli Institute of Physiology NAS RA. Signal registration was performed using the Lab View-V 2018 software. Subsequent statistical analysis of recorded signals utilized Origin-8.5 and Sigma Plot 11.0 with t-test. **RESULTS AND DISCUSSION:** Spontaneous bursts of action potentials occurring in the ovarian and cervical horn areas as well as in uterine corpus were investigated in non-pregnant rats. The ovarian horn area generates high-amplitude spikes that significantly exceed the magnitude of spikes in two other areas. There are small differences between the frequency values in the above- mentioned rhythmogenic areas. The peak rise-rates are the greatest in the ovarian horn area. On the contrary, the peak rise-times and the peak half-widths had small values here. We found a significant difference between the values of activity parameters in the ovarian horn area and two other pacemaker areas localized rather close to each other.

ACUTE BEHAVIORAL EFFECTS OF NOVEL N-BENZYL-2-PHENYLETHYLAMINE DERIVATIVES IN ZEBRAFISH LARVAE. DD Martynov, DS Galstyan, NP Ilyin, NI Golushko, AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg State Pediatric Medical University, Institute of Experimental Medicine, Almazov National Medical Research Centre, St. Petersburg, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** Serotonergic psychedelics, such as compounds with 2C-X structures (phenylethylamines) or their N-methoxybenzyl analogues (NBOMes), activate the serotonin 2A receptor (5-HT2AR). Zebrafish larvae represent a popular model in psychopharmacology and neurobiology. The present study characterized acute behavioral effects of isomers 23H-NBOMe, 24H-NBOMe and 26H-NBOMe. **METHODS:** A total 132 10-day-old zebrafish larvae were used for behavior analysis in a 10-min open field test following acute (20-min) exposure to 0.3, 1.5 and 7.5 mg/L of 23H-NBOMe, 24H-NBOMe and 26H-NBOMe (as 26H-NBOMe was dissolved with 1% DMSO, a similar amount was added to the control group). The test scored the frequency and time of entries to central or peripheral zones and distance traveled/min, using a Zantiks MWP installation with 12-well plates (1 fish per well). Data were analyzed using the Kruskal-Wallis test (KW) and Dunn post-hoc test ($P < 0.05$). **RESULTS AND DISCUSSION:** 23H-NBOMe increased time spent near the walls of the well at all dosages, while the total distance traveled remained similar to controls. 24H-NBOMe also increased time near the walls and increased distance traveled at 0.3-1.5 mg/l but reduced it at 7.5 mg/L, whereas 26H-NBOMe evoked dose-dependent hypolocomotion without affecting center/periphery preference. Taken together, this suggests that acute effects of tested NBOMes may involve distinct anxiogenic and locomotor activity profiles. **RESEARCH SUPPORT:** Russian Science Foundation project 23-25-00412.

BEHAVIORAL EFFECTS OF TOFIZOPAM IN ZEBRAFISH NOVEL TANK AND TAIL IMMOBILIZATION TESTS. VV Tishkina, DS Galstyan, TO Kolesnikova, MS Papulova, AV Kalueff, Institute of Translational Biomedicine, St. Petersburg State University, St. Petersburg State Pediatric Medical University, Institute of Experimental Medicine, Almazov National Medical Research Centre, St. Petersburg, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** Tofisopam (Grandaxin) is an anxiolytic benzodiazepine derivative, whose exact mechanism of action is poorly understood. **AIM:** To evaluate the acute behavioral effects of tofisopam in adult zebrafish. **METHODS:** Adult 3-4-month-old short-fin wild-type zebrafish (female:male ratio 1:1) were divided into 3 groups depending on the dosage of tofisopam: 200, 100 mg/l and control group (15 fish per group) and tested in 5-min novel tank test (NTT) and the immobilization test zebrafish tail (ZTI) after an acute 20-min exposure to the drug pre-dissolved in 0.1% dimethyl sulfoxide (DMSO). Behavioral parameters such as frequency, duration of stay at the summit, distance traveled for NTT and activity parameters in ZTI were recorded using video tracking, processed by Noldus EthoVision XT11.5 software and analyzed by Kruskal-Wallis (KW) test followed by Dunn's post-hoc test ($p<0.05$). **RESULTS AND DISCUSSION:** A 20-min exposure to tofisopam demonstrated statistically significantly higher distance traveled ($p<0.05$) at 200 mg/l and frequency of swimming to the top at 200 and 100 mg/l ($p<0.01$-0.5) vs. control group. In ZTI test, fish exposed to 200 mg/l showed greater activity in distance parameters ($p=0.0151$). Thus, in the NTT, fish after a 20-min exposure to tofisopam demonstrated a hypolocomotor behavioral profile, whereas increased ZTI activity indicates a potential antidepressant-like effect, which is also consistent with previous experiments in rodents linking the drug effects to action via the serotonergic, opioidergic and other neurotransmitter systems. **RESEARCH SUPPORT:** Russian Science Foundation project 23-25-00412.

RHODOPSIN G-PROTEIN SPECIFICITY ADJUSTMENT FOR RETINA OPTOGENETIC PROSTHESIS. DA Meshalkina, SD Losev, ML Firsov, Sechenov Institute of Evolutional Physiology and Biochemistry RAS, St. Petersburg State University, St. Petersburg, Russia. Retinal degeneration (retinitis pigmentosa) is a leading cause of inherited blindness in the human population (affecting 1/4000 individuals) (Ferrari et al., 2011). Its pathogenesis involves the death of photoreceptor cells caused by one of more than 3100 mutations in different genes encoding the participants of the visual cascade. One of the approaches to restore function is optogenetic prosthesis, in which photo-sensitivity is conferred to the surviving retinal cells through the introduction of a genetic vector encoding a photosensitive GPCR. Targeting the vector to retinal bipolar cells allows the maximum number of information processing levels to be maintained in the retina. To shift the coupling of the prosthetic photosensitive GPCR from the transducin signaling cascade (characteristic of photoreceptor cells) to the Go signaling cascade (characteristic of retinal bipolar cells), the GPCR genes are usually chimerized with the GRM6 receptor, which normally functions in bipolar cells. However, according to the coupling studies, the GRM6 receptor is not the most effective interactor for

the Go protein complex, which allows us to propose two new candidates for this chimerization, MTR1A and HTR1B. Here, we designed and cloned rhodopsin chimeras with these genes and tested the obtained variants in our reporter system. The chimeric GPCRs included the light-sensitive part of rhodopsin and the intracellular loops of MTR1A or HTR1B. The reporter system was based on the Gs-protein chimera, including the core activating adenylyl cyclase from Gs-protein and the C-terminus interacting with GPCR from Go-protein. It also contained a transcriptional cAMP reporter that expressed the red fluorescent protein mRuby2 when cAMP levels were elevated. We found that HTR1B chimeras with rhodopsin demonstrated higher signal intensity in our reporter system with lower background activation and therefore a better signal-to-noise ratio compared to wild-type rhodopsin. Using the G-protein chimeras with different specificities (Gs, Gst and Gsi), we found that the HTR1B chimera Rh-H23C shifted the specificity from the Gst protein (characteristic of rhodopsin) to the Gso protein. This specificity was also found to be narrower than the specificity of the rhodopsin and GRM6 chimera tested, which interacted with both Gst and Gso with comparable intensities. The rhodopsin mutations that confer photocyclic properties to rhodopsin did not decrease Gso interaction in our model. RESEARCH SUPPORT: Ministry of Science and Higher Education of Russian Federation, agreement 075-15-2022-296 for the cutting-edge Pavlov Center “Integrative Physiology”.

THE STRUCTURE OF COURTSHIP BEHAVIOR IN DROSOPHILA MALES: BOUNDARIES OF PLASTICITY. SA Fedotov, AA Goncharova, NG Besedina, LV Danilenkova, EA Kamysheva, JV Bragina, Laboratory of Toxinology and Molecular Systematics, LA Orbeli Institute of Physiology NAS RA, Yerevan, Armenia; Laboratory of Comparative Behavioral Genetics, Pavlov Institute of Physiology RAS, St. Petersburg, Russia. *Drosophila* male courtship is an innate behavior that males perform in the presence of a female before copulation. Courtship provides information about the species, sex, and receptiveness of the flies. The male taps the female with a foreleg to sample her pheromones, starts to vibrate with one wing (courtship song) and pursuit her, afterwards licks the genitals and attempts to copulate. With a virgin female, an attempt is 90% successful, but with a mated or immature female, attempts do not lead to copulation, since non-receptive females prevent mating by their counteractions. After an unsuccessful attempt to copulate with a mated female, the male reduces the intensity of courtship within 1-3 h in repeated tests with the mated female. Courtship suppression has been used in many studies as a model to study memory mechanisms. However, the factors causing courtship suppression have not yet been revealed. The main reason for the suppression of courtship after a mating failure is considered to be increased sensitivity to the antiaphrodisiac 11-cis-vaccenyl acetate on the surface of the female’s body. However, in a recent study, we showed that unsuccessful courtship towards an immature female does not cause courtship suppression in a repeat test with another mated female. We hypothesized that perhaps differences in courtship patterns between mated and immature females could indicate factors influencing suppression. We calculated the duration and frequency of each component of courtship, as well as the frequency of transitions between individual components in naive males when courting virgin and mated females. Based on the results of the work, a new model of courtship behavior for a virgin female was proposed and structural differences were identified in the courtship of males for immature and mated females, which may be the reason for the different effectiveness of training and will help in the future to identify the factors that determine the development of courtship suppression. **RESEARCH SUPPORT:** State funding allocated to Pavlov Institute of Physiology RAS 1021062411629-7-3.1.4). Center for Collective Use, Biocollection of I. P. Pavlov Institute of Physiology, housed *Drosophila* lines for this study.

EFFECTS OF REPEATED EXPERIENCE OF AGGRESSION ON GENE EXPRESSION IN HYPOTHALAMUS IN MALE MICE. AA Sapronova, AS Mutovina, PE Kisaretova, R Salman, NP Bondar, Institute of Cytology and Genetics SB RAS, Novosibirsk State Research University, Novosibirsk, Russia. **INTRODUCTION:** Repeated positive fighting experience can lead to changes in the neurophysiology and behavior of animals and to the development of pathological aggression. Mechanisms of adaptation to repeated aggression are thought to be controlled through the hypothalamus and HPA axis. **AIM:** To evaluate the effect of a long-term experience of aggression and fighting deprivation on the expression of HPA axis genes in hypothalamus. **METHODS:** Two groups of male CD1 mice were studied using the sensory contact model: fighting experience (FE) group, with experience of winning 30 consecutive encounters, and fighting deprivation (FD) group with experience of winning 30 consecutive encounters and subsequent fighting deprivation for 30 days. The development of pathological aggression was assessed using encounters with immobilized (narcotized) male CD1 mice at two points: 30 days after FE and after FD. Gene expression in the hypothalamus in FE and FD groups was assessed using real-time PCR with fluorescently labeled probes 30 days after FE and after FD. We measured expression levels of the corticotropin-releasing hormone (CRH) gene *Crh*, the CRH receptor gene *Crhr1*, the gene of the CRH-binding protein *Crhbp*,

and the genes of the glucocorticoid receptor (GR) *Nr3c1* and its co-chaperone *Fkbp5*. **RESULTS AND DISCUSSION:** FE leads to the manifestation of inadequate, pathological aggression towards the narcotized male. FD does not reduce pathological aggression, but increases it even more. 30-days daily FE results in a slight increase (at the level of a trend) in the level of *Crh* in combination with a decrease in the level of inhibitors of CRH secretion (*Crhbp* and *Crhr1*). This may indicate an adaptation of CD1 mice to repeated aggression - an increase in the level of availability of CRH and an enhance the reactions it causes. 30 days of FD lead to decreased *Crh* expression compared with the A30 group. However, FD does not restore *Crhbp* expression, indicating that negative feedback is disrupted. The expression of *Nr3c1* and its co-chaperone *Fkbp5* did not depend on fighting experience. Thus, fighting experience alters HPA axis regulation, and fighting deprivation restores neither gene expression nor behavior. **RESEARCH SUPPORT:** Russian Science Foundation grant 24-25-00189.
BRIDGING SELF- AND SOCIAL GROOMING: COMPUTATIONAL ANALYSES OF RODENT BEHAVIOR AND BRAIN GENES. AM Moskalenko, AN Ikrin, AV Kozlova, TO Kolesnikova, AV Kalueff, Sirius University of Science and Technology, Sirius Federal Territory, Russia. **INTRODUCTION:** Grooming behavior is highly prevalent in rodents, conservatively patterned, and crucial for regulating various physiological functions. Complex and highly conserved nature makes self- and hetero- (social) grooming a valuable translational model for abnormal behaviors in clinical neuropsychiatric disorders. **METHODS:** We compiled two extensive datasets of mouse genes linked to genetic variations associated with rodent social behavior (43 genes) and self-grooming (227 genes). These datasets included interacting genes identified by the STRING database (mean confidence interval = 0.40). **AIM:** To establish robust protein-protein interaction (PPI) networks with significant clusters for rodent grooming behavior. The CytoHubba plugin of Cytoscape (version 3.9.1) was used to search the global PPI network for "hub" genes using the Betweenness, Stress, and BottleNeck methods. Subsequently, these networks were manually integrated to form a cohesive PPI network (188 genes out of summarized data from both networks) encompassing all interactions related to rodent grooming behavior. **RESULTS AND DISCUSSION:** We identified 9 clusters of self-grooming (NOS-mediated neurotransmission, Post-synaptic density, Neuronal differentiation, Neuronal cell cycle, Transcriptional factors, WNT-signaling, Microtubule regulation, Neurodevelopment regulation, Mitochondrial genes) and 4 clusters of hetero-grooming (Neuronal differentiation, WNT-signaling, Synapsinic genes, Cytoskeleton). By combining the self- and hetero-grooming clusters, we identified bridge graphs that connect these two large behavioral networks in rodents. Thus, clusters of Neuronal differentiation and WNT-signaling were shared between the two types of grooming. These clusters were linked to GSK3b via the ‘hub’ protein TRAF6 (hetero-grooming), and TRAF6 - to the neuronal cell cycle cluster via ITCH. We also merged the PPI network via TNF (self-grooming) via the interactor protein MAP3K7 (hetero-grooming), as well as with BRIC2, IKBKG and TAB2. The Cytoskeletal cluster linked to Microtubule regulation cluster via IMNA. Overall, for the first time we constructed a molecular genetic pathway that defines the potential operation of a complex behavioral phenomenon such as grooming in rodents. **RESEARCH SUPPORT:** Neurobiology Program (NRB-RND-2116) and Graduate Program in Genetics and Genetic Technologies (Center of Genetics and Life Sciences, Sirius University of Science and Technology).

May 20-21, 2024

Research visits to laboratories:

- ***Yerevan State Medical University***
- ***YSMU COBRAIN Center***
- ***LA Orbeli Institute of Physiology NAS RA***

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Xi'an Jiaotong-Liverpool University (XJTLU)

XJTLU is an international joint venture university founded by Xi'an Jiaotong University in China and the University of Liverpool in the UK in 2006.The University offers more than 100 degree programs in science, engineering, business, finance, architecture, urban planning, language, culture taught in English. XJTLU is located in Suzhou Industrial Park (SIP), China's equivalent of Silicon Valley and a hub of global innovation, houses a large cluster of Fortune 500 companies, transnational enterprises and R&D centers. Address: Xi'an Jiaotong-Liverpool University (XJTLU), School of Science Building (Building SA/SB, Dushu Lake Higher Education Town, Suzhou Industrial Park, 215123 Suzhou, Jiangsu).

www.xjtlu.edu.cn/en

The International Stress and Behavior Society (ISBS)

The International Stress and Behavior Society (ISBS) was founded in 2008, based on our experience with community-building and organizing over 10 Stress and Behavior Conferences, with the goal of promoting research and education on the relationship between stress and behavior. The society aims to bring together experts from various fields such as psychology, biology, medicine, and neuroscience to advance understanding of the effects of stress on behavior and provide evidence-based solutions for stress management. The roots of the ISBS can be traced back to the 1950s when the concept of stress was first introduced by Dr. Hans Selye, a Hungarian-Canadian endocrinologist. His groundbreaking and paradigm-shifting research on the physiological responses to stress laid the foundation for the study of stress and its impact on brain and behavior. In the following decades, the study of stress and behavior gained momentum, leading to the establishment of the ISBS in 2008. The society organizes annual international conferences where researchers and practitioners from different disciplines come together to present their findings and exchange ideas. These conferences have become a platform for the dissemination of cutting-edge research and the development of collaborations and partnerships. Over the years, ISBS members have also published several books that serve as valuable resources for academics and professionals in the field of stress and behavior.

Join ISBS and its events:

www.stressandbehavior.com