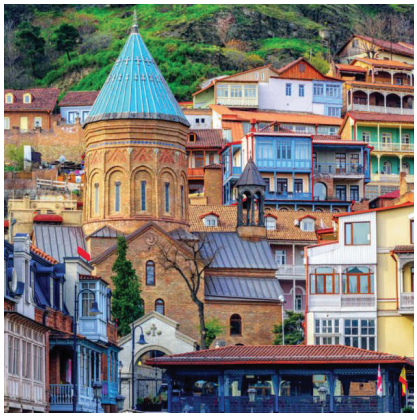
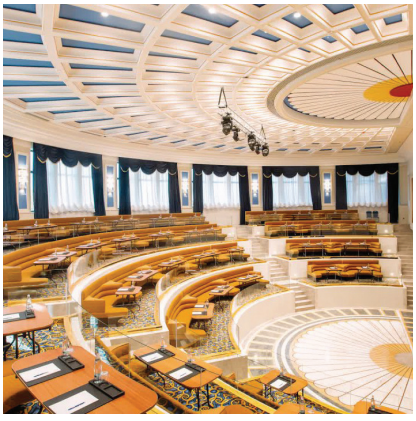
4th International Symposium and School of Young Scientists

"Brain & Neuroplasticity: Structural and Molecular Aspects"

May 1-7, 2019. Tbilisi, Georgia





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ABSTRACTS

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Ilia State University

I.Beritashvili Center of Experimental Biomedicine

Tbilisi, Georgia

CXCR4/UB METABOLIC PATHWAYS AND THEIR ROLE IN CANCER PROGRESSION (Review)

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CXCR-4 is Cell surface receptor for stromal-derived factor 1 (SDF-1 or CXCL12). Recent studies suggest that CXCR-4 has other ligands, including post-translational protein modifier inside the cell- Ubiquitin. The action of CXCR-4 receptor in our body is not fully studied yet. To date is known that HIV uses CXCR-4to infect CD4+ T cells. CXCR-4/CXCL12 is involvedin concentration of hematopoietic stem cells in the bone marrow and regulating of their passage into peripheral tissues upon injury or stress. Interaction of CXCR-4 receptor with CXCL12 ligand regulates tumor proliferation, invasion, lymph node homing and metastatic progression. Some studies have shown that high CXCR4 expression in colorectal cancer patients correlates with an advanced tumor stage, an increased risk for recurrence and distant metastasis and a poor overall survival. To date, extracellular ubiquitin is identified as an agonist of the G-protein-coupled chemokine receptor CXCR4. CXCR4 has been found in membrane of leukocytes, where it regulates intracellular Ca+2 ions flux during mitosis. In many instances CXCL12 and UB activate the same metabolic pathways via activation of the chemokine receptor CXCR4.

Meanwhile, functional consequences of CXCR4 activation with ubiquitin are poorly defined. Moreover, literature regarding the prognostic role of CXCR4-ubiquitin interaction in cancer is relatively vague. More insight into the metabolic pathways involving CXCR-4 receptor and ubiquitin and determination of its prognostic role in cancers of different origin may help us to introduce new biomarker for cancer progression and facilitate the structure based drug design for ubiquitin and CXCR4.

PATHOLOGY OF NEUROPIL ELEMENTS OF BRAIN CORTEX AT NEUROINFLAMMATION

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Objectives. The great impact of inflammation in several brain disorders that ultimately lead to neurodegeneration was widely accepted. Despite of that detailed descriptions of the brain neuropil at inflammatory reactions are required for accurate explanation of their morphologic neuropathology. We investigated the dendrites, axons and neuroglial processes in brain cortex after peripheral exposure to lypopolysacharide (LPS).

Methods. Systemic inflammation was induced by intravenous injection of LPS at a dose of 1,0 mg/kg. Semi thin and ultrathin tissue sections were examined by means of light and electron microscopy.

Results. Despite of swollen perivascular astrocytic endfeet (AEF) the brain parenchyma architecture was preserved around cortical capillaries. However, the destructive changes of neuropil elements as well as neuronal cell bodies were found in close vicinity of postcapillary venules of brain cortex. Along with disturbances in structural integrity of blood-brain barrier AEF around those vessels were not edematous as it should be expected. Instead, accumulation of edema fluid was detected in interstitial tissue of brain and morphometric analysis of microscopic slides showed increase in occupancy of interstitial space. Moreover, we observed degeneration of various degrees in myelinated nerve fibers with regions of myelin interruptions; osmiophilic, myelin-like bodies with irregular shape in interstitial spaces as well as inside of AEF. Swollen mitochondria with destructed cristae, condensation of cytoskeleton was detected in dendrites.

Conclusion. Systemic LPS caused brain inflammation with vasogenic brain edema and structural disturbances of brain parenchyma that ultimately may play a crucial role in subsequent neurodegeneration.

COMBINATION THERAPY OF EPILEPSY WITH ANTIEPILEPTIC DRUGS AND ELECTRIC-MAGNETIC STIMULATION

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BACKGROUND. Anti-epileptic drugs are prescribed to patients taking into account the etiology, age, type of epilepsy, but these drugs can cause disturbance of psychobiological processes. Although antiepileptic drugs which significantly suppress the frequency of seizures has side effects. Depression that accompany medications are more important than the frequency and intensity of seizures. In addition, it is impossible to distinguish what caused depression, the use of antiepileptic drugs or the development of epileptic seizures. The goal of experiment was to study combination therapy effects of electric-magnetic stimulation (EMS) and antiepileptic drugs on behaviour seizure activity.

METHODS. In implementation of the project the genetically epilepsy-prone rats (GEPR) (250-450 g) were used. For each task two groups of animal were conducted: experimental group (with EMS) and control group (without EMS). Antiepileptic drugs – Benzodiazepine (enhance inhibitory effect of GABA), Carbamazepine (enhance inhibition of glutamate) were injected intraperitoneally (3 mg/kg, 10 days), in both group of rats. Prior to antiepileptic drug injection, experimental group were stimulated by electric-magnetic field during 5 days (parameters: 10-15kHz, 1-1,5m/Tesla, duration 20 min). Behavioral manifestations of audiogenic seizure in response to a strong sound were tested after 30 minutes of reagents injection. Emotional-motivated behaviour of rats was tested in open field test.

RESULTS AND DISCUSSION. Low doses of carbamazepine and benzodiazepine, which could not cause inhibition of seizure activity, in the conditions of EMS caused a desired antiepileptic effect. Therefore, EMS combine with antidepressants enhanced anticonvulsive action. It did not change motivational-emotional behaviour of rats in open field test. Reduction of medication dosage is important to reduce side effects of antiepileptic drugs. The positive effect of combined therapy was maintained within 2 weeks compared to non- stimulated one's.

CONCLUSION. EMS can be selected independently or in combination with antiepileptic medicines for epilepsy treatment, which will reduce

negative side effects of antiepileptic drugs. Data obtained will contribute to reducing the use of the antiepileptic drugs for treatment of pharmaco-resistant epilepsy patients.

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HIPPOCAMPAL NEURON: ATOMIC FORCE MICROSCOPIC STUDY

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For the most usually used approaches in brain studies, it is difficult to reveal structural alterations that contribute to the development of neurodegenerative diseases. The structure of neuron is affected on nano scale level, by different parts of cytoskeleton, organelles and extracellular matrix interactions. Therefore, the application of various advanced techniques in the research of precise nanoarchitecture of neuron is of great importance. Atomic force microscopy is a one of the most advanced and informative tools for such studies. In the present atomic force microscopic research high-resolution detection of three-dimensional architecture of fixed hippocampal neuron was performed. The neuronal culture was prepared from newborn rats (P0 and P1-2). The cultured hippocampal neurons on polylyzine-coating glasses were fixed with 1% of glutaraldehyde on phosphate buffer and were evaluated under atomic force microscope Bioscope II (Veeco). Contact mode, the most common approach of atomic force microscope operation and the most useful for obtaining three-dimensional topography of nanostructured surface, was used. The three-dimensional topographic informations of samples with lateral resolution down to 0.3 nm and vertical resolution down to 0.1 nm were achieved. The images provide precise quantitative measurements of height, size, surface area and volume of cell at the nanoscale resolution. Various ridges, ‘spines” and extensions of the soma, growth cone and neuronal processes were revealed. The study may be considered as the

first step for the evaluation of neurodegenerative changes, which can be developed on nanoscale level of hippocampal neuron under various pathological conditions.

EFFECTS OF CHRONIC ADMINISTRATION OF MEMANTINE ON OKADAIC INDUCED SPATIAL SHORT-TERM MEMORY IMPAIRMENT

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Alzheimer's disease (AD) is a neurodegenerative disease that causes progressive cognitive and behavior impairment in the elderly. It is widely believed that changes in the cerebral activity of protein phosphatases have been implicated in the pathogenesis of AD. Okadaic acid (OA) is a potent and selective inhibitor of protein phosphatases.

OA induced memory deficit and elevation of Ca2+ was found to be correlated with neurotoxicity and N-methyl-D-aspartate (NMDA) receptor emerged as a plausible link .According to available data, the NMDA receptor antagonists (including memantin) have the potential to perform neuroprotective role in neurodegenerative processes caused by Ca2 + ionotoxicity.

In the present study, the possible beneficial effect of memantine on the Okadaic Acid (OA) induced spatial short-term memory impairment was examined in spatial alternation task. OA was dissolved in artificial cerebrospinal fluid (aCSF) and injected intracerebroventricularly (ICV) 200 ng in a volume of 10 µl bilaterally. Vehicle control received aCSF ICV bilaterally. Control and OA injected rats were divided into 2 subgroups injected i.p. with saline or memantine (5 mg/kg,) Memantine or saline were given daily for 13 days starting from the day of OA injection. Behavioral study showed that bilateral ICV microinjection of OA induced impairment in spatial short-term memory and chronic administration of memantine effectively attenuated OA induced spatial short-term memory impairment. Therefore, ICV injection of OA can be used as an experimental model to study mechanisms of neurodegeneration and define novel therapeutics targets for AD pathology.

THE EFFECTS OF METABOTROPIC GLUTAMATE RECEPTOR 5 (mGlur5) ON THE MBP CHARGE ISOMER FUNCTIONS

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OBJECTIVE. Myelin basic protein (MBP) is a major component of the myelin sheath surrounding the axons of the central nervous system. Alteration of MBP cationicity may represent a regulatory mechanism for normal myelin assembly. Among many endogenous and exogenous factors that regulate microglial and macrophage activation, secretary products of neurons, oligodendrocytes and vascular endothelium have been suggested to play a key role in the regulatory processes.

BACKGROUND. Previously we have shown that elevation of intracellular glutamate and expression of mGluR5 may initiate the metabolic rearrangement in macrophages. Also MBP isomers, depending on the intensity of the post-translational modification can be involved in the induction of inflammatory potential of macrophages and in differentiating the immunosuppressive phenotype. The main goal of our experiments was to investigate if the effects of MBP charge isomers on the macrophage plasticity are linked to the glutamatergic system of cells.

METHODS. We used mGlur5-transfected and non-transfected mouse RAW 264.7 macrophages; Western blot analysis, iNO-synthase and arginase-1 expression assays.

RESULTS. We have found that the amount of NO, secreted by action of C1 and C8 MBP isomers are increased in transfected cells; the amount of HMGB1 secreted by action of C1 and C8 MBP isomers are increased in transfected cells also. Besides mGlur5 transfection changes an effect of C1/C8 isomers on the expression of excitatory amino acid transporter-2 (EAAT2).

CONCLUSIONS. In summary, our results suggest that MBP charge isomers play an important role in the macrophage plasticity due to mGlur5.

ENZYME KINETIC AND P-TYPE ATP-ASES

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P-type ATPases are ion pumps that carry out many fundamental processes in biology and medicine, ranging from the production of membrane potential, to muscle contraction and the removal of toxic ions from the cells. Making use of the energy stored in ATP, they transport specific ions across the cell membrane against a concentration gradient. Our aim is to kinetically characterize these enzyme systems and formulate the kinetic singularities that they possess. P type ATPase appears to be a multi-sited enzyme system which does not obey the Michael-Menten theory. Its activity is described by kinetic curves of complicated geometric shapes that make analysis even harder. To decipher molecular mechanism of the P-type ATPases a method of kinetic analysis of multi-sited enzyme systems [Kometiani, 2007] were used.

As a result of this study, general kinetic features of P-type ATPases, which are necessary but insufficient conditions for the identification of these systems has been established: 1) Bell-like geometric shape of kinetic $V = f(x)$ curve (x referees to the transported ion concentration, V-velocity of the enzyme) is certainly specific for all p type-ATPases; 2) Numbers for essential activators and full inhibitors for transported ions are equal; 3) MgATP complex is Tr-ATPases substrate; 4) P type-ATPases are a multi-sited enzyme systems and their functional unit is minimum a dimmer; 5) in the process of reaction a phosphorylated intermediate is formed.

SPATIAL MEMORY IMPAIRMENT AND HIPPOCAMPAL CELL LOSS INDUCED BY OCADAIC ACID IN ADULT RATS

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BACKGROUND. Alzheimer's disease (AD) is a neurodegenerative disease that causes progressive cognitive and behavior impairment in the elderly. Okadaic acid (OA) induces characteristics that resemble AD –like symptoms, including cognitive impairment and hippocampal degeneration.

OBJECTIVES. The aim of experiment was to evaluate the effect of intracerebroventricular (ICV) and intrahippocampal bilateral microinjection of OA on spatial memory in adult male rats.

METHODS. Rats were divided into following groups: Control 1 – rats were injected ICV with artificial cerebrospinal fluid (aCSF); Control II - rats were injected intrahippocampally, with aCSF; Experimental Group I – rats were injected ICV with OA; Experimental Group II - rats were injected intrahippocampally with OA. Spatial memory was assessed in one-day water maze paradigm. Hippocampal structure was evaluated by Nissl staining.

RESULTS. Nissl staining showed significant pyramidal cell loss in Experimental Group II. Behavioral experiments revealed that both treatments with OA do not affect learning and short-term spatial memory, but induce impairment in spatial long-term memory, assessed in probe test performance 24 h after training.

CONCLUSIONS. ICV or bilateral microinjection of OA provokes the decrease of the number of pyramidal neurons in hippocampal CA1 and CA3 regions. Cell loss was the most pronounced in CA1 area. The injection OA to hippocampus produces more substantial cell loss than ICV injection. Both types of treatment result to significant impairments of long-term spatial memory. The results indicate that OA induces memory deficit and the changes in hippocampal architecture.

SLEEP-WAKE PATTERNS, SLEEP DISORDERS AND HEALTH RELATED QUALITY OF LIFE - RESULTS FROM THE GEORGIA SOMNUS STUDY

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OBJECTIVES. Sleep problems represent a worldwide health concern but their prevalence and the extent to which sleep disorders are associated with impairment of health-related quality of life (HRQoL) is poorly described in the developing world. We evaluated sleep-wake patterns, the prevalence and severity of various sleep disorders and their associations with HRQoL in an urban Georgian population.

METHODS. 395 volunteers (20–60 years) completed Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, STOP-Bang questionnaire, Insomnia Severity Index, Beck Depression Inventory-Short Form, and Short Form Health Survey (SF-12). Socio-demographic data and body mass index were obtained.

RESULTS. 43% of subjects had poor sleep quality. Further, 41% had low sleep efficiency, 27.4% slept less than 6 hours, 32.4% went to bed after midnight, 27.6% snored, 10.6% were taking sleep medication, and 26.8% had sleep maintenance problems. The economic status was the most significant predictor of sleep quality. All SF-12 components and physical and mental component summaries (PCS, MCS) were significantly lower in poor sleepers, subjects with daytime sleepiness, apnea risk, or insomnia. After controlling for potential confounding factors, sleep quality significantly increased model's predictive power with an R2 change by 3.5% for PCS and 2.9% for MCS; ESS, STOP-Bang, ISI scores, all exerted clear effects on PCS and MCS.

CONCLUSIONS. Poor sleep quality is strongly linked to the economic status. Our results on the relationship of sleep and HRQoL confirms and extend the findings of studies from Western societies. Intervention programs designed to strengthen sleep-related health care and thereof HRQoL is especially important in the developing world.

TARGETED DELIVERY OF QUERCETIN-LOADED MAGNETIC NANOPARTICLES INHIBITS KAINATE-INDUCED EPILEPTIFORM DISCHARGES

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OBJECTIVES. The purpose of our research was to use an external static magnetic field exposure (ESMFE) for targeted delivery of Quercetin-loaded magnetic nanoparticles (Q-MNPs) and to investigate the effects of Q-MNPS on epileptiform discharges caused by unilateral intrahippocampal application of kainic acid (KA).

BACKGROUND. 1% of world population suffers from epilepsy and in 35% cases epilepsy is resistant to drugs. In recent years, treatment strategies have been extensively focused on flavonoids. However poor bioavailability of flavonoids restricts it's usage in clinic. The nanoparticles have ability to conjunct the drugs, and thus enhance their permeability across the biological membranes.

METHODS. In ketamine-anesthetized rats electrodes were stereotaxically implanted into the CA1 of the hippocampus. For induction of epileptiform discharges unilateral KA applications (5x1mkl, 7.5mkg each times) were executed in the CA3 field. To evaluate the effect of Q-MNPs on epileptiform activity tail vein Q-MNPs injection was performed under ESMFE. The effects of Q-MNPs on the hippocampal background and evoked (electrical/pharmacological) responses were assessed. Registration/analyses were performed using software Chart5.5 (Ad instruments Co). Software PRIZM was used for statistical analysis.

RESULTS. Experiment showed that Q-MNPs/ESMFE alone did not change the mean amplitude and frequency of neuronal activity, however preliminary administration together of both factors statistically reliably reduced the frequency and amplitudes of the repetitive epileptiform discharges caused by intrahippocampal application of the KA. Quercetin-alone-treated group did not show any significant alteration.

CONCLUSIONS. ESMFE improves quality of delivery of Q-MNPs to the brain and avoids generation of repetitive epileptiform discharges induced by KA.

ACKNOWLEDGMENTS. Research was supported by Shota Rustaveli National Science Foundation of Georgia, grant FR17_629.

THE EFFECT OF QUERCETIN-LOADED MAGNETIC NANOPARTICLES ON EPILEPSY-INDUCED MEMORY DISTURBANCE IN RATS

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OBJECTIVES. The aim of our work was the usage of external static magnetic field (ESMF) for targeted-delivery of Quercetin-loaded magnetic nanoparticles (Q-MNPs) to the brain and investigation the effect of Q-MNPs on kainic acid-status epilepsy (KA-SE)-induced memory disturbance.

BACKGROUND. Epilepsy is a neurological disease characterized by recurrent seizures. In temporal lobe epilepsy, seizuregenic-circuits are located in memory-supporting brain regions, thereby the syndromes include memory disturbances. Flavonoids are extensively used against disorders of various genesis. Many effects of Quercetin are known, but the use has been limited due to it poor bioavailability. Nanoparticles are considered as the delivery system for drugs.

METHODS. Experiments were conducted on rats. KA-SE-model was used to define antiamnesic potency of Q-MNPs. In ketamine-anesthetized control and KA-SE-animals Q-MNPs were injected in the tail vena under ESMF-exposure of the brain. Behavioral experiments were performed in the open field and T-maze. Prussian blue stain was used to determine the Fe content in the brain. For statistical analyses PRIZM was used.

RESULTS. Experiments demonstrated that ESMF/MNPs alone do not change the behavior of animals. Quercetin/Q-MNPs facilitate the learning of the control rats. Only Q-MNPs targeted by ESMF showed statistically significant improvement of KA-SE-induced memory impairment. Quercetin alone/Q-MNPs without ESMF was ineffective against epilepsy-induced memory disturbance. Morphological experiments revealed that the number of Fe inserts are significantly higher in the site of ESMF-exposure with comparison the untreated site, suggesting that the ESMF improves targeted-delivery of the Q-MNPs to the brain.

CONCLUSIONS. Targeted-delivery of Q-MNPs effectively abolish memory impairment induced by KA-SE.

ACKNOWLEDGMENTS. Research was supported by Shota Rustaveli National Science Foundation of Georgia, grant FR17_629.

CL ACTIVATED ATP-ASE

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Plasma membranes of cells contain Cl– -activated Mg2+-ATPase, the enzyme with the basal Mg2+-ATPase activity inducible by Cl– ions. Biochemical investigations of Cl– -activated Mg2+-ATPase and ATP-dependent Cl– transport in different membrane systems suggest that this enzyme is an ATP-dependent Cl– pump involved in active Cl– transport against the electrochemical gradient.

The goal of the present work is to study Cl-ATPases molecular mechanism. The reaction velocity of the Cl-ATPase enzyme system is a function of at least three physiological ligands, Mg-ATP, Mgf2+ and ATPf, each of which may exert an activating or inhibiting action on the enzyme. To analyze the initial velocity of an enzymatic reaction, it is required to obtain V = f([Mg-ATP], [ATP] [Mgf2+]) as a function of one variable, where the values of other ligands are constant. In the Cl-ATPase study we applied method of kinetic analysis of multi-sited enzyme systems [Kometiani, 2007] which is a single method used from kinetic investigation of multi-sited enzyme systems.

Kinetic study has shown: (1) the [Mg-ATP] complex constitutes the substrate of the enzymic reaction; (2) the V = f(Cl−) dependence-reflecting curve is bell-shaped; (3) the number for essential activators and full inhibitors for anion is equal; (4) in the process of reaction a phosphorylated intermediate is formed.

MODERN APPROACHES OF ELECTRON MICROSCOPY

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Establishment of Electron Microscopy laboratory, providing it with necessary equipment was possible after winning the pilot project of competition announced by the Science Development Foundation under the President of the Republic of Azerbaijan. The main purpose of the project is to ensure the fulfillment of scientific and research works in the field of biology, medicine and other spheres, as well as to prepare young specialists. The Electron Microscope (JEM-1400) is equipped with a subcamera manufactured by JEOL which allows photographing and side-by-side digital cameras manufactured by OSIS Veletta. The laboratory performs scientific research works in the following directions:

Ultrastructure research of the structure of prokariot (bacteria, actinomycetes, blue-green algae), as well as eukaryotes (fungi, plant and animal cells) starting from viruses;

Detection of viruses and bacterial strains, identical and distinct morphological characteristics of various primary plant and animal species at a precision of 0.2 nm;

Investigating the possible role of ultrastructural changes in the genome carrier structures of plant and animal cells at various stages of the ontogenesis in the development of degenerative processes occurring in the cell and tissues;

Ultrastructural investigation of the molecular basis of the participation of cells (chloroplasts, mitochondria) in the activity and death of cells formed as a result of prokaryotes with eukaryotes symbiosis;

Determination of the ultrastructural study of bacteria that can contribute to the useful condition of soil and water basins contaminated with oil products in our Republic and determination of their activity levels;

Application of TEM in the differential diagnosis of malignant tumors, selection of treatment methods and prediction of treatment;

Investigation of ultrastructural changes in coronary, connective tissue and derivative organs of vital organs during experimental peritonitis and

their correctional pathways;

Ultrastructure characterization of changes occurring in histotopography and microstructure of cortex, vascular and nerve elements in different parts of central and peripheral nervous systems during acute endotoxemia;

Electron microscopic specification of the death forms of nerve cells in experimental edema of different origin;

Determination of the effects of nanoparticles obtained by national scientists and other authors on the morpho-functional condition of different organs and systems in living organisms;

Determination of mechanisms of synthesized animal and plant biological active substances on separate organs and systems and ultrastructural justification of healing doses.

EFFECT OF TOLUENE CHRONIC EXPOSURE ON MOTOR CORTEX STRUCTURE IN ADOLESCENT AND ADULT RATS

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The effect of toluene chronic exposure on the number of large, medium-size and small pyramidal cells in different layers of rat motor cortex was studied. Cortex was divided into two zones. In the lower Zone I, the number and area of soma of large pyramidal cells were evaluated; in the upper Zone II the same parameters of small and medium-size pyramidal neurons were measured. Adolescent and adult male Wistar rats were used. Toluene treatment was performed during 40 days, in the airtight chamber, saturated with toluene vapor, at the concentration 2000 ppm.The changes were found only in adolescent rats. Specifically, in cortical Zone I of these rats significant decrease of the number and area of large pyramidal cells were revealed. In adult animals no quantitative changes were detected. Therefore, age-dependent effect of toluene chronic exposure on the number and other quantitative characteristics of pyramidal neurons of motor cortex was described.According to literature data, the catabolism of toluene in the organism is associated with excessive production of free

radicals and the development of oxidative stress. Such changes result in neuronal cell death via both apoptosis and necrosis. The decrease of the number of cells observed in the present study, at least partly, might be related with these processes.

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PROCESSING OF CYTODIFFERENTIATION MANAGEMENT BIOMODEL OF TISSUE CULTURE BY USING PHYTOHORMONAL REGULATORY SYSTEM

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The Study of regulatory capacities of cytodifferentiation process of stem cells is important in terms of further development of a number of biomedical methods. At the same time, it's not sufficiently studied the issues of complete regeneration of stem cells to the organism's level, therefore it's important to find adequate models based on the use of eukaryotic organisms. In this regard, relatively successful is in vitro cultivation method of plant stem cells. With the help of this biomodel it's possible to realize the entire cycle of the genetic program of investigating organisms (totipotency). In our study was used tissue cultures of Datura stramonium L. and Daucus carota L. stem cells. Murashige-Skoog standard medium was added indole-3-acetic as a phytohormonal regulatory factor, it's synthetic analogue α-Naphthylacetic and 2,4-Dichlorophenoxyacetic (2,4-D). In case of the first two phytohormonal supplements, normal process of cytodifferentiation and rhizogenesis (D. stramonium) and somatic embryogenesis (D.carota) were observed during cultivation. By addition of 2,4-D in the medium, the process of structure generation was fully suppressed, however, after several cultivation, research tissue convey on medium containing natural phytohormones provoked restoration of cytodifferentiation process. Conducted studies have shown that even in case of cell lines derived from active proliferative activity, by the help of phytohormonal growth regulators compounds, makes possible to induce cytodifferentiation and still acquiring structural producing properties. Described biomodel might be used for purpose of conducting cytodifferentiation processes directly in non-organized proliferative tissue.

EFFECT OF LOUD WHITE NOISE ON THE PROCESS OF LEARNING AND EMOTIONAL SPHERE IN MALE AND FEMALE RATS

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Post-traumatic stress disorder, attributed to continuous high intensity white noise (HIWN) pollution is significant health problem. It provokes various pathologies that are more extensive in women comparing to men. The effect of HIWN is the subject of numerous investigations. In the present comparative study, we elucidate the effect of HIWN on the process of learning and emotional sphere in female and male adult rats. Wistar rats – P25-30 as adolescents, and P130 -135 as adults – were subjected to 100 dB during 10 days: 1 hour (h) per day. The process of learning was assessed immediately after exposure, in multi branch maze (10 day test; each day the rat had 10 trials, 5 minutes - each trial), by recording the number of errors (the entries in “blind” branches) and the time needed to pass the maze. To evaluate possible changes in emotional sphere, the cross-maze was used and different parameters, reflecting anxiety-like behavior were recorded. The results revealed that HIWN significantly affects the process of learning and emotional sphere in both, female and male rats. All alterations are more pronounced in female animals. The most changed was emotional sphere. Therefore, our data indicate that female adult rats are more vulnerable to white noise, than male rats.

THE RECOVERY PROCESS IN PATIENTS WITH STROKE WITH AND WITHOUT ARTIFICIAL FIBRILATION

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Atrial fibrillation (AF) is the most common disease among the well-known arrhythmias of the heart. According to the World Health Organization the morbidity of AF is 1-2% of the general population. Therefore, 1% of Georgia's population is diagnosed with AF. AF is characterized by high disability, premature mortality, increased risk of developing congestive heart failure and stroke. The aim of present comparative research was to study (i) patients with AF and ischemic stroke, and (ii) patients with stroke without AF. In both groups, we investigated the erythrocyte aggregation after an acute period and observed the recovery process. By the process of recovery, we meant learning the skills of reading and eliminating speech mistakes. The aggregation of erythrocytes was evaluated using a standard digital method. The results showed that in the patients of first group of patients the erythrocyte aggregation was higher than in patients of second group; however, in both groups the aggregation was increased compared with clinical norms. The recovery process in both groups was slow, but it was the slower - in the patients of first group. We suggest, that besides known mechanisms, such as hemodynamic, hemorheological, coagulation disorders, etc., this fact should be related with neuroplasticity. Neuroplasticity is observed at multiple scales, from microscopic changes in individual neurons to larger-scale changes such as cortical remapping in response to injury. Behavior, environmental stimuli, thought, and emotions may also cause changes through activity-dependent plasticity, which is significant for normal development, learning, memory, and recovery from brain damage.

RADIATION DOSE DEPENDENT EFFECT OF EXTRACELLULAR UBIQUITIN ON REGENERATING BONE MARROW

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Nowadays medicine is constantly faced up with the necessity to use radiotherapy during treatment of various oncological diseases, which can be a cause of healthy blood cells reduction. Our earlier works have shown that extracellular ubiquitin is able to regulate regeneration of hemopoiesis in mice. In this work we conducted comparative analysis of ubiquitin impact on bone marrow cells in a cytopenia model made by irradiation of mice. Two groups of mice with average weigh of 22±2gr were irradiated with doses of gamma radiation of 3 Gy and 5 Gy. In 72 hours after the irradiation, animals in each group were injected by 100 ug/ml of ubiquitin. Bone marrow samples have been taken every 24 hours after irradiation during 7 days. Azure-eosin stained smears were observed under the light microscope Levenhuk, USA. OriginPro, ImageJ and ANOVA were used for quantitative analysis. Evaluation of statistical data have shown that level of extracellular ubiquitin exposure on bone marrow total cell count in groups of high and low radiation dose dramatically differs from each other. It gives us possibility to conclude that the mechanism of extracellular ubiquitin effect may rely on damage level of bone marrow cells. The study of this problem is extremely interesting from the point of view of the application of extracellular ubiquitin for therapeutic purposes.

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POROSOME: THE UNIVERSAL SECRETORY NANOMACHINE IN CELLS

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Secretion is a fundamental cellular process in living organisms, from yeast to cells in humans. Since the 1950's, it was believed that secretory vesicles completely merge with the cell plasma membrane during secretion, resulting in the diffusion of intra-vesicular contents to the cell exterior. Observations of partially empty vesicles in cells following secretion however, suggested the presence of transient or so called 'kiss-and-run' mechanism that allows fractional discharge of intra-vesicular contents during secretion. This proposed mechanism is mediated by a nanoscale supramolecular cup-shaped lipoprotein structure at the cell plasma membrane called porosome. Porosomes range in size from 15 nm in neurons and astrocytes, to 180 nm in endocrine and exocrine cells. Neuronal porosomes are composed of nearly 40 proteins compared to 1,000 proteins that compose the 120 nm nuclear pore complex. Porosome structure, its chemical composition, and functional reconstitution into artificial lipid membrane and in live cells, and the molecular assembly of membrane-associated t-SNARE and v-SNARE proteins in a ring or rosette complex to establish the fusion pore at the porosome base, and the molecular mechanism of secretory vesicle volume increase required for intra-vesicular content expulsion with great precision, collectively provide a molecular understanding of cell secretion. Alterations in many of the porosome-associated proteins have been implicated in numerous diseases resulting from secretory defects. These results have overturned conventional belief that secretion occur only via the complete incorporation of the secretory vesicle membrane at the cell plasma membrane, resulting in a paradigm-shift in our understanding of the secretory process in cells.

POROSOME: THE SECRETORY MACHINERY AT THE NERVE TERMINAL

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Cup-shaped secretory portals at the cell plasma membrane called porosomes mediate secretion from cells. Membrane bound secretory vesicles transiently dock and fuse at the base of porosomes facing the cytosol, to expel pressurized intravesicular contents from the cell during secretion. The structure, isolation, composition, and functional reconstitution of the neuronal porosome complex have greatly progressed in the past decade, providing a molecular understanding of its function. Neuronal porosomes are 15 nm cup-shaped lipoprotein structures composed of nearly 40 proteins. Being a membrane-associated supramolecular complex, the porosome has precluded determination of its atomic structure. However, atomic force microscopy and small-angle X-ray solution scattering studies provide 3D structural details at sub-nanometer resolution, of the native neuronal porosome complex, providing insights on the molecular mechanism of its function. The participation of several porosome proteins previously implicated in neurotransmission and neurological disorders, further suggests crosstalk between these proteins and their coordinated involvement in porosome-mediated neurotransmitter release.

AFM BASED NANOMOTION DETECTION OF LIVING ORGANISM: MEDICAL AND ASTROBIOLOGICAL APPLICATIONS

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We recently observed that depositing living organisms onto an atomic force microscope (AFM) cantilever induces oscillations of the lever that stops as soon the organism dies1. The oscillations not only reflect the vitality of the deposited organism but also its metabolic state. We successfully applied the technique to bacteria, yeast, vegetal and mammalian cells. Any commercial AFM or homemade dedicated devices can be employed to highlight these oscillations. In our laboratory, we use this technique to assess the sensitivity of bacteria to antibiotics in a timeframe of minutes, instead of days or weeks, as it is usually required by the traditional sensitivity tests. After a brief description of the technique, we will discuss the potential applications of the method in the fields of clinical microbiology, oncology and space research.

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HIERARCHY OF SIGNS ATTRACTING VISUAL ATTENTION

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Upon elaboration of recognition and search strategy of the different characteristics (e.g. color, size, shape) of the objects and thereat alter their spatial location, it is clear that there must be definite hierarchical order of characteristics that is reflected in the recognition time for each particular parameter.

The aim of our research was to ascertain the importance of three characteristics of a visual object – size, color and localization in the visual field, in attention distribution process under central and peripheral conditions of vision.

At the first stage of the experiment, the subject was asked to simply fix glance on the fixable white spot projected permanently to the screen center and to press any button of the keyboard upon appearance of the stimuli, four Latin letters of different sizes and colors A, B, C, D in the visual field. At the second stage of the experiment, the subjects were required to read aloud the words presented in the white spot to be fixed as a running line and to react the emergence of stimulus by pressing the button.

Based on our data, data we suppose that an attention distribution in the visual field is due to the reading habit in accordance of which, while perceiving the scene, the eye starts to move from the upper-left corner to the right and then to the bottom. Therefore, irrespective of the stimulus parameters and intensity of data traffic, these stimuli are perceived fast which are located in the upper-left corner of the scene.

INFLUENCE OF VALPROIC ACID ON EEG IN CHILDREN WITH EPILEPSY

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OBJECTIVES. The work aimed to study the effect of Valproic Acid (VA) on the EEG in epileptic children. The analysis of the dynamics of EEG reveals possible early predictors of treatment's benefit/adverse effects.

METHODS. Forty-thee children aged 3-9, with different type of epilepsy were investigated. All the patients underwent three- fold recording of the EEGs: prior to Valproic Acid monotherapy and three and six months after the initiation of the treatment. Epileptiform elements and baseline EEG activities were analyzed. Following quantitative characteristics of interictal EEG were analyzed: absolute values of the power (AVP) spectra; EEG -Brain Topography.

RESULTS. Decreased AVP spectra due to reduce of low-frequency range, suppresses spontaneous epileptiform discharge and absence pattern.VA expressed of less influence spikes-polyspikes, sharp waves, generalized paroxysmal bursts provoked by functional tests. Brain Mapping reveals that presence with rhythmic monomorphic theta-waves of tempo-parietal localization is a predicting factor for seizures recurrence despite of the normalization of the patients' clinical condition. The presence of such pattern correlated with the reocurrence of seizures if VPA was withdrawn.

CONCLUSION. Brain mapping reveal the essential prognostic/predicting value of morphology the theta-waves and its distribution. Study of baseline EEG activity, spectral analysis and EEG mapping using qEEG approach during VA therapy allows correct determination of treatment strategy.

17th CENTURY GEORGIAN MANUSCRIPT – ATOMIC FORCE MICROSCOPIC STUDY

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The evaluation of the structural and chemical composition of historical manuscripts of Georgia is an important direction for the understanding Georgian history and culture. In the present atomic force microscopic study, we investigated different levels of iron-containing red ink, used for Georgian paper manuscripts in 17th century. The imaging of the ink was performed using Bioscope II (Veeco), by contact-mode, using the dnlp-29 cantilever and scanning forces in the piconewton range. The radius of the tip was 20-60 nm, and cantilever spring constant - ~ 0,175 to 0,7 N/m. Five red ink areas - 16 and 20 μm² each - were scanned. Morphological and mechanical parameters of ink surface - heights, depths, and roughness, as well as the volume measurements were recorded. Quantitative data were processed using ANOVA. The altered nano morphology of the ink was revealed. In particular, the irregular crystal nano cracks of various size on the ink surface were found. Such nano cracks divide solid amorphous ink into separated sections. Such heterogeneity of the ink surface should be at least one of the causes of partial detachment of manuscript from paper surface. The force distribution on the ink surface also was not homogeneous – due to specific irregularities. Special chemical analysis should reveal in more details, what causes the heterogeneity of ink surface, or why chemical composition of the ink is changed over the centuries.

MOLECULAR MECHANISMS OF NEURONAL GROWTH

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The neural stem cells are the background of neural growth specific molecular mechanisms. These cells are multipotent and are characterized by self-renew. The “stemness” condition as well as ability to differentiate are tightly controlled by molecular mechanisms. Epigenetic ones, including chromatin remodeling, DNA methylation, and noncoding RNAs (ncRNAs), have also regulatory roles in gene expression. It has been revealed, that epigenetic modulation and function have obvious and dynamic roles in neural growth and development. The epigenetic regulators are key players in neural-stem-cell self-renewal, fate specification, and final maturation of new neurons. Altered epigenetic regulation can result in a number of neurological and neurodevelopmental disorders. In our presentation the data of neural specific genes activity and epigenetic regulation of neural stem cells and neurogenesis are discussed.

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BRAIN MORPHOLOGY IN CASE OF THE CO-OCCURRENCE OF THE GOMEZ-LOPEZ-HERNANDEZ SYNDROME AND AUTISM

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The objective of this case study was description of the MRI-revealed morphological changes in the brain in patient diagnosed as having Gomez-Lopez-Hernandez syndrome (GLHs) and autism spectrum disorder (ASD). This is the first report on the GLHs in Georgian patient as well as the first incidence of the co-occurrence of GLHs and ASD. Patient, male, Georgian, 36 months, only child born to non-consanguineous parents. There were no similar cases in the family and among close relatives. MRI

study confirmed rhombencephalosynapsis and bilateral parieto-temporal alopecia, as a two obligatory symptoms of the GLHs. Among concomitant symptoms, the arched shape of the corpus callosum, probably due to the tower-like elongation of the skull in vertical axis is of special interest. Patient did not speak, disregarded guardians and clinician addressing him, did not make eye contact, was restless and occasionally displayed aggression and self-injurious behavior. These symptoms confirm the earlier diagnosis of Autism Spectrum Disorder (ASD). We suggest rhombencephalosynapsis and deformation of the corpus callosum to play role in the development of the ASD.

CHILDREN WITH AUTISM SPECTRUM DISORDER CAN FORM TIME-BASED EVENT EXPECTANCY

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OBJECTIVES. Studies show abnormal temporal cognition development in children with Autism Spectrum Disorder (ASD). However, it is currently unclear how Autism Spectrum Disorder effects on time-based event expectancies. The aim of the present study was to investigate the development of time-based event expectancies in children with Autism Spectrum Disorder.

METHODS. Twenty children with ASD and twenty-one typically developing children (TD) (6-13 years) completed a binary choice response task mimicking a computer game, in which foreperiod duration predicted the response target location with a probability of 0.8.

RESULTS. We found that children with ASD showed a characteristic pattern of forming a time-based expectancy significantly different from TD children. While TD children were not affected by the correlation between interval and event, children with ASD were significantly sensitive to the regularity. Namely, they were faster for expected combinations of interval

and event than unexpected ones, suggesting that they formed time-based event expectancy, suggesting that they formed time-based event expectancy.

CONCLUSIONS. In the present study, we found that children with Autism Spectrum Disorders are able to form time-based event expectancies, despite previous studies showing marked deficits in general timing ability.

ACETYL-COA CARBOXYLASE GENE OF GEORGIAN ENDEMIC WHEAT: NUCLEOTIDE SEQUENCE AND PHYLOGENETIC RELATIONSHIP

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2,144 bp length Acetyl-CoA Carboxylase (ACCase) gene exon from three Georgian endemic wheat's: T. monocccum var. hornemanii, T. timofeevi and T. macha were PCR-amplified and sequenced. This exon represents carboxyltransferase domain of ACCase, where alteration of one amino acid (isoleucine/Leucine) may change herbicide sensitivity in these plants. Diploid, tetraploid and hexaploid Georgian wheat species were used for a gene sequence comparison analysis, based on expectation, that sequence diversity among these species will reveal important information for the phylogenetic analysis and genome evolution. Comparative study among T. monocccum, T. timofeevi and T. macha revealed that within the Acc-1 gene 2,144 bp length exon, all three species express very high level (99%) of homology. Sequence comparison of T. monocccum and T. timofeevi revealed presence of 20 SNPs, where only 4 SNPs are non synonimous, which causes the amino acid substitution. 22 SNPs were found in T. monocccum in comparison of T. macha. 4 SNPs out of 22 were non synonymous and altered the amino acid sequence. More SNPs were observed during the sequence comparison of T. timofeevi and T. macha. 30 SNPs were detected and 6 out of them caused amino acid alteration. Evolutionary tree characterizing phylogenetic relationship of Zanduri wheat's and Triticum macha with the different wheat species are presented.

H-RAS NITROSYLATION ALTERS CELLULAR RESPONSE TO HYPOXIA IN DIFFERENTIATED/UNDIFFERENTIATED PC12 CELLS

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In the present study, we investigate the role of posttranslational modifications of H-Ras and possible implication of neuronal NO synthase (nNOS) in cellular response to hypoxia. We hypothesized that nNOS inhibition alters S-nitrosylation and palmitoylation of H-Ras terminal cysteine and induces H-Ras mislocalization, therefore, different response to hypoxia.

Hypoxic-ischemia stress causes severe brain injury, leading to disability and death. The oxygen-glucose deprivation markedly increased nitric oxide level, intercellular messenger in CNS, and nNOS activity. Small Ras-GTPases are activated following ischemic insults, and serve as intrinsic switches to regulate neuronal survival/regeneration. Their ability to integrate diverse intracellular signal transduction pathways makes them critical regulators and potential therapeutic targets for neuronal recovery after stroke. H-Ras possesses two cysteine residues (C181, C184) in the C-termini, which are palmitoylated once or twice. Palmitoylation is sufficient for promoting stable plasma membrane localization. We investigated the action of nNOS inhibitor, L-NAME, on the distribution of membrane-bound S-nitrosylated/palmitoylated H-Ras under hypoxic/normoxic conditions in undifferentiated/differentiated pheochromocytoma (PC12) cells.

TARGET PROTEINS WERE DETECTED USING WESTERN BLOTTING. RESULTS. L-NAME decreased the content of membrane-bound palmitoylated H-Ras and membrane-bound nytrosylated H-Ras in undifferentiated PC-12 cells under normoxic conditions. In differentiated PC-12 cells L-NAME changed only content of membrane-bound nitrosylated H-Ras. Hypoxia induced elevation of palmitoylated H-Ras content and abolished L-NAME induced effect. In contrast to normoxia, L-NAME increased HIF-1-alpha activity, possibly through elevation of cytoplasmic succinate content and decreased the cytotoxicity under hypoxic conditions in differentiated PC-12 cells.

CONCLUSION. L-NAME-induced H-Ras mislocalisation alters the response of differentiated PC-12 cells to hypoxia.

PRELIMINARY DATA ABOUT THE ROLE BRAIN NEUROPLASTICITY FOR TREATMENT OF SOME ONCOLOGICAL DISEASE

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Neuroplasticity is the ability of the brain to change. Changes may occur under the influence of the external environment and internal factors. Changes can be physical and functional. Neuroplasticity of the brain can change many aspects. The possibilities of brain neuroplasticity are not yet fully understood. The research team is working on issues of the postoperative period in patients with gastric cancer and presents this report. Naturally, our interest is the study of factors of inflammation, anemia and hemorheology after surgery. This is gold standard tests in postoperative period recommended by the European Society of Stomach Cancer. These factors indicate the clinical condition of the patient and the postoperative period. In our study, 6 patients were diagnosed with gastric cancer at the same phase. All patients underwent the same operation with splenectomy. All patients were prescribed standard treatment, monitoring of the above parameters and a daily course of psychotherapy. Of the group of patients, two were very pleased with the course, doing the daily task of a psychologist. They were aimed at a positive result. When monitoring all patients, it was these two patients who had the best parameters. Probably, in these two cases, remodeling occurred. Motivation and interest are the best helpers of neuroplasticity. If we can focus on what we want to acquire, we can change the functioning of the brain. Rebuilding the brain, we can achieve a qualitatively new level of its functioning. We intend to continue further research in this direction and associate our findings with brain neuroplasticity.

EFFECT OF PROPIONIC ACID ON SOCIAL BEHAVIOR, EMOTIONAL STATUS AND AMYGDALA'S UTRASTRUCTURE IN RATS

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Autism Spectrum Disorders (ASDs) are a cluster of neurodevelopmental disorders characterized by impaired socialization, reduced communication, limited, stereotyped interests and activities. Current prevalence of ASD is approximately 1 in 59 children. There is a strong genetic component of ASD's etiology. However, ASD can be exacerbated by several environmental factors. Propionic Acid (PPA) is one of them. Numerous data indicate that chronic administration of PPA in rodents produces alterations associated with human ASD.

In the present research, the effects of PPA on social and anxiety-like behavior and ultrastructure of amygdala's central nucleus in male, adolescent Wistar rats were evaluated. Experimental animals received single intraperitoneal injection of PPA, at dose 175 mg/kg. Control rats received the same dose of saline. Behavioral experiments and ultrastructural analysis were performed 2, 24 nd 48 hours (h) after treatment,

Social behavior was assessed using modified three-chamber test: novel rat versus novel object. Crossed T-maze was used to evaluate anxiety-related behavior. Under electron microscope, ultrastructural changes were evaluated.

The results show: (i) compared to control animals, PPA-treated rats show significantly less interest to social stimulus – novel rat. (ii) PPA treatment has no effect on anxiety-related behavior; (iii) PPA provokes a number of alterations in the ultrastructure of amygdala; they are more prominent in glia. Other ultrastructural changes were mostly reversible.

Therefore, our study indicates that even single injection of relatively low dose of PPA induces in adolescent rats, alterations in social behavior and amygdala's glial cells. Such changes are reminiscent with whose observed in ASDs.

LEARNING, ANXIETY-LIKE BEHAVIOR AND BRAIN ULTRASTRUCTURE IN ADOLESCENT AND ADULT MALE RATS

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In the present behavioral and electron-microscopic comparative research, the process of learning, emotional sphere and the ultrastructure of the hippocampus and central nucleus of amygdala in adolescent (P25-30) and adult (P135-140) Wistar rats were evaluated. The process of learning was measured in multi branch maze, by recording the number of errors (the entries in “blind” branches) and the time needed to pass the maze. The assessment of emotional sphere, in particular, anxiety like behavior was evaluated in the cross maze. Using conventional approaches of electron microscopy, the ultrastructure of neurons, glial cells and synapses of abovementioned regions of brain was described and quantitative evaluation of different forms of synapses and structural parameters of neuronal porosome complex were made. Quantitative data were evaluated using ANOVA. The results revealed some difference in the process of learning (tested in multi-branch maze) and anxiety-like behavior (tested in cross maze) between adolescent and adult rats. The ultrastructure of areas of interest in both aging groups was almost the same, however, in comparing with adolescent rats, in the amygdala and the hippocampus of adult animals presynaptic terminals with numerous synaptic vesicles and large, osmiophilic contact zone were often observed. The data reveal some specificity in the behavior and the ultrastructure of brain in rats at different physiological states.

SPEECH FEATURES OF CHILDREN WITH AUTISM SPECTRUM DISORDERS AND DOWN SYNDROME

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The goal of the study is to identify the speech features that are necessary and sufficient to assess the psychophysiological and neurological status of the informant. Participants in the study were 45 children with autism spectrum disorders (ASD), 20 children with Down syndrome (DS) biologically aged 5-16 years, and 300 typical development (TD) coevals. The acoustic, perceptual, and phonetic analysis were conducted. The speech of TD children is characterized by words, simple and complex phrases; the speech of ASD children is predominantly represented by simple words and simple phrases, syllables, vocalizations, speech-like constructions, repetitions of a part of an adult's speech, echolalia, and children with DS use simple words and simple phrases with fuzzy articulation. For all children with ASD voice and speech are characterized by high values of pitch, pitch range, abnormal spectrum, and well-marked high-frequency. We found significant differences of these acoustic features between ASD and TD children and children with DS in spontaneous speech. The speech of children with DS is characterized by a longer duration of words and stressed vowels in words, low values of pitch and third formant, a large number of unformed consonant phonemes vs. speech of TD and ASD children. We believe that the identified acoustic characteristics of the speech of children can be used in the diagnosis of the disease, and for ASD children to serve as biomarkers of autism.

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DEVELOPING TRANSLATIONAL ANIMAL AND HUMAN MODELS TO STUDY GENETIC, METABOLIC AND GUT MICROBIOME INTERACTIONS IN NEURO DEVELOPMENTAL DISORDERS

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Autism spectrum disorders (ASD) are an increasing problem in Western society. Although genetic factors play a major role in ASD, the alarming increase in this family of disorders imply environmental factors contribute to ASD risk. Recent research is examining ASD as a dynamic encephalopathic condition involving immune, digestive and metabolic dysfunction exacerbated by environmental triggers in genetically sensitive subpopulations. Clinical observations suggest that certain gut and dietary factors may transiently worsen symptoms in ASD. Furthermore, pre and post natal infectious processes, and antibiotic exposure, which collectively alter the host microbiome have been implicated as possible risk factors for ASD. There is a need to develop translational animal and in vitro models to ethically study broad effects of gut linked environmental factors in autism. Propionic acid (PPA) is a short chain fatty acid and an important intermediate of cellular metabolism. PPA is also a fermentation by-product of a subpopulation of opportunistic enteric bacteria (i.e clostridia, propionibacteria,desulfovibrio), a putative risk factor for ASD, and is also a common food preservative. PPA and other short chain fatty acids (i.e butyrate and acetate), affect diverse physiological processes such as cell signaling, neurotransmitter synthesis and release, mitochondrial function, lipid metabolism, immune function, and gene expression.

Pulsed intracerebroventricular infusions of PPA in adult rats through chronic indwelling brain canullae, induce predictable and enduring changes on brain neocortical, hippocampal and striatal electrical activity. PPA infusion immediately produces reversible repetitive dystonic behaviors, hyperactivity, turning, retropulsion, caudate spiking, the progressive development of limbic kindled seizures, object fixation, perseveration, and impairs social behavior, suggesting that this compound has central effects. Examination of brain tissue from PPA treated rats (brain sections, homogenate, ToF-SIMS imaging, gene arrays) reveals an innate neuroinflammatory response (reactive astrogliosis and activated

microglia, CREB activation), an increase in oxidative stress markers, alterations in phospholipids/acylcarnitines, reductions in cholesterol, mitochondrial dysfunction, and a reduction of glutathione, a broad spectrum xenobiotic detoxifier. Current studies in our laboratory are finding similar effects with dietary and systemic infusions of PPA at the perinatal and adolescent levels and with butyric acid, a related gut short chain fatty acid, and recently, epigenetic modulation of ASD associated genes. Further studies are being performed in vitro rodent PC12, human lymphoblast and microbiome cultures. These findings are consistent with those found in ASD patients, and are predictive of potential biomarkers in this disorder.

Collectively, these central effects of PPA and other enteric fatty acids suggest a testable link between diet, seizure, movement disorder, social impairment, neuroinflammation, increased oxidative stress, mitochondrial dysfunction, membrane fluidity, epigenetic modulation, environmental sensitivity, gut microbiome and gastrointestinal symptomotology found in ASD. We propose that some types of ASD may be partial forms of genetically inherited or acquired disorders of altered short chain fatty acid metabolism, resulting in increased exposure to these enteric metabolites at critical times during the life cycle. Multidisciplinary collaborations are underway to determine human populations at risk for increased exposure to elevated short chain fatty acid exposure at critical neurodevelopmental periods.

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REM SLEEP DEPRIVATION: METHODS AND EFFECTS

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OBJECTIVES. Since the discovery of rapid eye movement sleep (REMS), selective REMS-deprivation studies have been performed in animals and

humans to understand the mechanisms of regulation and functions of REMS. However, effects of REMS-deprivation are often controversial because of using of non-adequate or stressful techniques. This study was aimed to evaluate effect of REMS-deprivation on memory consolidation and sleep architecture.

METHODS. The experiments were carried out on the rats (n=24) and cats (n=8). REMS-deprivation was performed by (1) water-tank technique, (2) amitriptyline (AM) injection, (3) classical method of REMS-restriction and (4) REMS substitution with waking episodes. Effect of REMS-deprivation on active avoidance (AA) learning was investigated in rats and on the structure of sleep-wake cycle – in cats.

RESULTS. REMS reduction due to the AM administration or water-tank technique did not affect significantly AA acquisition or retention. The facilitation of the AA learning in the REMS-suppressed rats may be explained by the increase of exploratory behavior and decrease of fear reaction. During classical REMS-deprivation the homeostatic regulation of REMS is expressed by progressively more frequent attempts to enter REMS and by a compensatory rebound with increased quality of REMS after the deprivation ends. REMS substitution with waking episodes did not lead to the accumulation of REM sleep need or quantitative/qualitative changes in post-deprivation sleep-wake cycle.

CONCLUSIONS. An assessment of the findings allows us to doubt specific responsibility of REMS for learning or memory consolidation. This study clearly shows an adequate way to suppress REMS propensity through the insert of waking episodes.

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BEHAVIORAL CHANGES IN PSYCHOGENIC STRESS AND DEPRESSION MODEL OF RATS AT DIFFERENT HIERARCHY LEVEL

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According to the numerous experimental studies, chronic psychogenic stress is the initiating agent causing psycho-neural diseases including

depression. We used informational stress model for the purpose of modelling chronic psychogenic stress and depression. The aim of the research was to study behavior of dominant and submissive rats at different stages of stress and during depression state. The modeling of informational stress was performed by using modified original method of active avoidance reaction (Khananashvili M., Domianidze T., 1989). Experiments were performed on male Wistar rats. Initially we developed in rats active avoidance reaction towards conditional signal metronome and then towards tone. After development of two active avoidance reactions, we carried out testing of two active avoidance reactions during one experimental session (within 45 days stressing procedure). The tests of "open field", "elevated cross maze" and "forced swim" have been used for behavior study. The obtained results showed that after development of two active avoidance reactions towards metronome and tone sound signals, the dominant and submissive rats of experimental groups did not demonstrate depression-like behavioral changes, but the simultaneous testing of two active avoidance reactions during one experimental session proved to be insurmountable task to be overcome by dominant and submissive rats. The percentage of correct reactions to conditional signals did not exceed 30-50% in animals on various hierarchical level. The obtained results show that due to chronic stressing procedure both dominant and submissive rats of experimental groups revealed depression - like behavioral changes.

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THE EFFECT OF CHRONIC AND INTERMIITENT ALCOHOL USE ON THE CYTOARCHITECTURE OF THE HIPPOCAMPUS IN ADOLESCENT MALE RATS

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The negative significance of chronic alcohol use on the adolescent organism is well known. However, there is insufficient information regarding the effect of alcohol on adolescent brain structure. In the present study, the effect of chronic and intermittent alcohol use on the

cytoarchitecture of hippocampus of adolescent male Wistar rats (P40-45) was clarified. The animals were treated intraperitoneally, with 0.1 mL 99% alcohol (alcohol treated rats, n=15), or 0.1 mL normal saline (control group, n=5), during 20 days: two injections each day. Alcohol-treated animals were subdivided into three subgroups: five animals in each. In animals of first subgroup, the brains were investigated immediately after 20-day treatment; in animals of second group - after 20-day treatment + 20-day alcohol-free period; in animals of third subgroup - after 20-day treatment + 20-day alcohol-free period + 20-day additional treatment with 0.1 mL 99% alcohol (two injections each day). The rats were perfused with 2% of paraphormaldehyde and brain sections containing the hippocampus were stained with cresyl violet. Possible cell loss in different layers of hippocampal CA1 and CA3 areas was evaluated in comparing with saline-treated rats, in all experimental animals the hippocampal pyramidal cell loss was revealed. In all experimental animals, the alterations were more pronounced in the CA1 region. No significant difference between the hippocampi of rats chronically subjected to alcohol injections, and the hippocampi of rats that had two-week alcohol-free period was observed. However, in the case of intermittent treatment the hippocampal cell loss was more significant.

POSITIVE MOOD AND TIME-BASED EVENT EXPECTANCIES

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OBJECTIVES. The aim of this study was to examine whether positive mood effects on the formation of time-based event expectancies.

METHODS. Thirty younger adults with ages ranging between 18 and 31 years participated. After positive or neutral mood inductions, participants completed a binary choice response task, in which two target stimuli and two pre-target intervals (800 ms and 1600 ms) appeared overall equally often. However, one of the targets was paired with the short interval and

the other target with the long interval in 90% of the trials.

RESULTS. Our results showed that all participants responded more rapidly to expected combinations of interval and target than unexpected combinations, suggesting that both groups formed time-based event expectancy. However, participants from the positive and neutral groups showed deferent behavioral patterns while forming the time-based event expectancy. Specifically, the time-based expectancy was restricted to shorter one of two intervals for the positive group.

CONCLUSIONS. We found that positive mood modulates the formation time-based event expectancy making shorter intervals more optimal for temporal prediction.

NEUROTOXICITY OF MANGANESE IN NEONATAL AND ADULT RATS

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Manganese (Mn) is an essential trace element, but excess exposure leads to accumulation in biological tissues, including the brain. Chronically high Mn levels in the brain are neurotoxic and can result in a progressive, irreversible neurological disorder known as manganism. The effect of short-term per os intoxication by different doses (10, 20 mg/kg/day) manganese chloride (MnCl2.4H2O) on learning process of mature rats and 30-day-old offspring of dams, which 15 days prior pregnancy, during pregnancy and 30 days after delivery received manganese chloride were studied. The number of errors and the time, required for passing of maze were used for evaluation of learning ability. The process of learning in neonate whose parent was exposed to manganese was considerably hindered. They lagged behind the control pups by the level of maze test performance. Low dose of manganese did not significantly alter learning process of mature rats. Otherwise looked the process of learning of rats, which received intoxication by 20 mg/kg of manganese chloride. None of mature animals were able to become familiar with optimal trajectory for

maze passing. Manganese decreased the overall locomotor activity of the rat in the open-field arena as manifested by a significant increase in the latency to move from the central square and decreases in line crossing, frequency of defecation when compared to control values. Manganese in excess promotes unstable emotional behavior. Anxiety-like behavior of adult rats were observed in the elevated plus maze. It was shown that manganese intoxication of parents could increase anxiety and/or decrease exploratory/locomotor activity in their pups.

THE ROLE OF THE NITRIC OXIDE SYSTEM IN THE DEVELOPMENT OF OXIDATIVE STRESS IN CONDITIONS OF WHOLE BODY HYPERTHERMIA

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Hyperthermia is almost always used with other forms of cancer therapy, such as radiation therapy and chemotherapy. Hyperthermia may make some cancer cells more sensitive to radiation or harm other cancer cells that radiation cannot damage. It can also enhance the effects of certain anticancer drugs, which is mutually strengthening and makes healing more likely – the so-called synergistic effect of Hyperthermia.

It is also well known that Hyperthermia increases the generation of Nitric Oxide, Free Radicals and the development of Oxidative Stress. As we have shown earlier in our study, Whole Body Hyperthermia might be also used as one of the most effective triggering factor for launching of Hormetic Phenomenon, when in response to any stressors, the body develops a positive reaction (from a biological standpoint) - an adaptive stress-response.

This presentation describes the results of our research, conducted on white laboratory rats in conditions of moderate and high levels of Whole Body Hyperthermia, concerning of quantitative changes in the concentration of Reactive Oxygen Radicals, activity of Scavengers and Antioxidants, as well as the Index of Oxidative Stress in conditions of Nitric Oxide Synthases inhibition.

ANALYSIS OF THE EFFECTS OF ETHANOL CONSUPTION DURING PREGNANCY OF SOME PHYSIOLOGICAL INDICES OF THE OFFSPRING (EXPERIMENTAL STUDY ON RATS)

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In our experiments it has been established that during pregnancy the impact of ethanol high dose on rats' offspring induces a well pronounced increase of plasma viscosity, which is extremely important in blood circulation. The disruption of blood circulation causes a hypoxic condition (especially, in nervous tissues) and the disturbance of its functioning. This is the result of what has been seen in the behavioral experiments of female rats' offspring under the influence of ethanol high dose. We consider that it has a crucial importance, as we speak about the remote results of ethanol consumption, which are manifested not only in rats, taking ethanol, but also in its offspring.

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EFFECT OF ETHANOL ON THE ACTIVITY OF THE SYLVIAN DUCT EPENDIMAL CELLS' CILIARY APPARATUS IN VITRO

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BACKGROUND. Taking into account the importance of ciliated ependymal cells of the aqueduct in the circulation of cerebrospinal fluid and stabilization of intracranial pressure, as well as the lack of data on the effect of ethanol on the contractile activity of ciliary apparatus the short-term and direct effect of ethanol of various concentrations on the ciliary apparatus was studied by us.

METHODS. We studied the effect of various doses of ethanol (0.3 mol

- 20-22 μmol) on the contractile activity of the Sylvian aqueduct ciliary apparatus in frontal and sagittal sections (200-300 μ) of the central gray matter of white rat's brain. Sections were placed in glass chambers filled with nutrient medium.

RESULTS. The introduction of high doses of ethanol (0.3 mol - 0.07 mol) into the nutrient medium, the ciliary apparatus contractile activity stopped after 4 minutes. This effect was also maintained at lower concentrations (0.02mol-0.02mmol). With the introduction of 2.2 μmol the activity of the ciliary apparatus increased significantly and reached 60 minutes, and with a further decrease of the ethanol concentration (0.2 μmol - 20-22 μmol), the activity of the ciliary apparatus steadily increased and reached 130 minutes.

CONCLUSIONS. In vitro study of the effects of high and low concentrations of ethanol on the ciliary apparatus of Sylvian aqueduct ependymal cells of rat brain revealed that the duration of contractile activity depends on the concentration of ethanol and is expressed in the cessation of contractions at its high concentrations and the conservation of activity at ultra-low concentrations.

TRPA1 CHANNEL IS INVOLVED IN SLIGRL EVOKED THERMAL AND MECHANICAL HYPERALGESIA IN MICE

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Persistent itch (pruritus) accompanying dermatologic and systemic diseases can significantly impair the quality of life. It is well known that itch is broadly categorized as histaminergic (sensitive to antihistamine medications) or non-histaminergic. Sensory neurons expressing Mas-related G-protein-coupled receptors (Mrgprs) mediate histamine-independent itch. These receptors have been shown to bind select pruritogens in the periphery and mediate non-histaminergic itch. For example, mouse MrgprA3 responds to chloroquine (an anti-malarial drug), and are responsible for relaying chloroquine-induced scratching in mice.

Mouse MrgprC11respond to a different subset of pruritogens including bovine adrenal medulla peptide (BAM8–22) and the peptide Ser-Leu-Ile-Gly-Arg-Leu (SLIGRL). On the other hand, the possibility that itch mediators also influence pain is supported by recent findings that most non-histaminergic itch mediators require the transient receptor potential ankirin 1 (TRPA1) channel. We have recently found a significant increase of thermal and mechanical hyperalgesia induced by non-histaminergic pruritogens chloroquine and BAM8-22, injected into mice hindpaw, for the first 30-45 min. Pretreatment with TRPA1 channel antagonist HC-030031 did significantly reduce the magnitude of this hyperalgesia, as well as significantly shortened the time-course of hyperalgesia induced by chloroquine and BAM8-22. Here we report that MrgprC11 mediated itch by their agonist SLIGRL is accompanied by heat and mechanical hyperalgesia via the TRPA1 channel. We measured nociceptive thermal paw withdrawal latencies and mechanical thresholds bilaterally in mice at various time points following intraplantar injection of SLIGRL producing hyperalgesia. When pretreated with the TRPA1 antagonist HC-030031, we found a significant reduction of thermal and mechanical hyperalgesia. Further studies are needed to get more evidence for the potential role of TRPA1 channel inhibitors as modulators of preclinical and/or clinical itch and pain conditions.

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DYSLEXIA AND THE ROLE OF VISUAL PROCESSING

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OBJECTIVES. Dyslexia is the most common type of learning disabilities affecting 10-12% of population. Although neurological origin of dyslexia is evidenced, underlying mechanisms are not fully understood and are debated for a long time. Visual deficits are suspected to limit reading skills in

dyslexia. As magnocellular system provides main visual input to dorsal visual pathway deficit in that system is suspected in dyslexia. Using test batteries, we investigated visual processing in Georgian children with dyslexia.

METHODS. Children with dyslexia and their age (8-12 years old) and IQ match typically developing children participated in the study. Participants performed coherent motion, biological motion, visual search and visual N-back tasks.

RESULTS. We found no differences in performances of coherent motion task and visual search task between two groups of children. However, performances of biological motion task and visual N-back task was significantly different for two groups, children with dyslexia performing the tasks worse compare to typically developing children. Also reaction times of search task were different and longer for children with dyslexia. No correlation was found for any of groups between performances of different tasks.

CONCLUSIONS. We assume that magnocellular deficits in terms of coherent motion discrimination and visual attention is not specific for dyslexia and it can be related to more "object-selective" ventral rather than dorsal stream. We conclude that for reading deficit in dyslexia not only magnocellular pathway is responsible but also deficits in ventral pathways plays a role.

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ELUCIDATION THE CELL ATLAS UTILIZING DIFFERENTIAL EXPANSION MICROSCOPY & MACHINE LEARNING

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The physical expansion of biological samples in 3-D to obtain nanoscale (~70 nm) resolution using light microscopy employing hydration-

competent polymers, an approach termed expansion microscopy, has not been applied to assess the extent of expansion between different tissues and subcellular organelles. Ultrastructure of cellular organelles at the nanoscale using electron microscopy and the distribution of associated antigens can reflect cell health and is used in the detection and assessment of a wide range of pathologies. Using light microscopy, we performed organelle-specific fluorescent immunocytochemistry on formalin-fixed paraffin-embedded human and rabbit tissue slices, and formalin-fixed primary human muscle cell cultures, to determine the extent of expansion between different tissues and subcellular organelles. Optical evaluation of subcellular expansion of various organelles in the same and in different tissues demonstrates differential expansion, critical to the rapid and inexpensive optical evaluation, as opposed to electron microscopy. The differential expansion of cellular organelles indicates a growing need to better understand the interactions of the polymers with subcellular structures, the composition of different cellular organelles, and the differences of organelle composition between tissues. Differential Expansion Microscopy (DExM) has been developed to further our understanding of the structure and distribution of the various intracellular organelles and the spatial relationships critical to their function within cells. DExM demonstrates that different tissues and subcellular organelles vary in composition and exhibit differences in their capacity to swell with the hydration of the hydrogel. Machine learning is applied to better elucidate the structures, organizations, and compositions between the samples from DExM. A deep learning convolutional neural network can “learn” to recognize the markers associated with cellular changes that are present in the images that the human eye could not easily distinguish. Utilizing these techniques will provide a greater comprehension of the function and distribution of intracellular organelles, cell dynamics at the compositional, structural, and functional levels, and new revelations and understandings of the cell.

ATOMIC FORCE MICROSCOPIC STUDY OF RED BLOOD CELLS OF RAT SUBJECTED TO CHRONIC TOLUENE EXPOSURE

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Chronic exposure to toluene vapors provokes negative effects on various levels of organism. For understanding the mechanisms of toluene addiction, the elucidation of such effects is important. In the present study, we elucidate the nano scale level of red blood cells of adolescent male Wistar rats, subjected to chronic treatment with toluene. Such approach gives the possibility to reveal weather inhaled toluene binds to hemoglobin or other plasma proteins or just dissolves in plasma. In the special chamber, the rats were exposed to 4.000-ppm toluene vapor during 40 days. Four groups of animals were studied. (i) The first, control group consisted from untreated counterparts of experimental rats. The blood of animals (ii) from second group was investigated immediately after 40-day inhalation, (iii) from third group – after 40-day inhalation + 30-day of withdrawal, and (iv) from fourth group - after 40-day inhalation + 120-day of withdrawal. The blood was collected via jugular vein, centrifuged and nano scale morphology and nanomechanical properties of red cells were evaluated under atomic force microscope Bioscope II. For each case, ten cells and seven areas from each cell were scanned. The scanned areas varied from 16 to 35 μm2. The height, depth, roughness and force curves were recorded. Quantitative data were processed using ANOVA. Some difference between groups was revealed. The cells from rats of second experimental group were the most changed.

STRUCTURE OF DENDRITIC SPINES IN THE FOREBRAIN: AN ULTRASTRUCTURAL AND METABOLIC PERSPECTIVE

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Long-term modification in the efficacy of excitatory axospinous synapses is tightly coupled to changes in spine morphology. The reorganization of the actin cytoskeleton underlying this spine 'morphing' involves numerous proteins that provide the machinery needed for this adaptive cytoskeletal remodeling. I will address the chemical architecture of the spine, focusing on actin-binding proteins (ABPs). Accumulating evidence suggests that ABPs are organized into functionally-distinct nanodomains within the spine cytoplasm. This functional compartmentalization represents the structural basis for regulation of the spinoskeleton, and provides a novel perspective on mechanisms of synaptic plasticity.

In the second part of the talk, I will focus on the metabolic aspect of synaptic plasticity. Consumption of high-energy diets may compromise health and may also impair cognition; these impairments have been linked to tasks that require hippocampal function. Conversely, food restriction has been shown to improve certain aspects of hippocampal function, including spatial memory and memory persistence. The diet-dependent functional changes raise the possibility that the synaptic structure underlying hippocampal function is also affected. Using quantitative electron microscopy we found, that the organization of neuropil and the underlying synaptic efficacy of axospinous synapses are highly affected in the hippocampus in a diet dependent manner. Taken together, our ultrastructural data reveal previously unrecognized structural changes at hippocampal synapses as a function of diet, supporting a link between metabolic balance and synaptic plasticity.

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ROLE OF DENDRIC SPINES IN MENTAL DISEASES

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Psychiatric and mental disorders may arise from anomalies in neuronal connectivity downstream of pathologies in dendritic spines. However, the mechanisms that may link spine pathology to the abnormalities relevant to atypical behavior remain unknown. Using mouse models of schizophrenia (Arp3 KO) and autism (Cntnap2 KO) we report here ultrastructural mechanisms that reveal progressive spine loss and changes in synaptic landmarks in the medial prefrontal cortex (mPFC): we found a dramatic decrease in functional excitatory synaptic inputs in L2/3 mPFC of these KO mice accompanied by disrupted plasticity. Collectively these results reveal molecular and neural-circuit mechanisms, illustrating how diverse pathologies may converge to drive behaviors relevant to psychiatric disorders. In conclusion, the changes in synaptic architecture in these mouse models provide a structural substrate for the cognitive deficits previously reported.

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THE EFFECT OF MYELIN BASIC PROTEIN ISOMERS ON MACROPHAGE POLARIZATION

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OBJECTIVES. During a neuronal injury, a variety of immune cells infiltrates into the local microenvironment at the demyelination site. After the destruction of the intact myelin sheath, its major constituent myelin basic protein(MBP) dissociates from the plasma membrane and acts as a free ligand on the infiltrated immune cells. MBP exhibits charge microheterogeneity as a result of post-translational modifications, but the effect of various isomers of MBP on the activity of macrophages is not known.

BACKGROUND. Previously we have shown that MBP charge isomers can change cytokine profile of macrophages. The main goal of our experiments was to investigate the effect of MBP isomers on the macrophage polarization.

METHODS. RAW 264.7 macrophages were polarized with and without MBP isomers. Inducible nitric oxide synthase (iNOS) (M1 marker) and arginase-1 expressions (M2 marker) were determined by ELISA. To assess the expression of receptor for advanced glycation end-products (RAGE) and high mobility group box1 (HMGB1) protein were assayed by western blot analysis.

RESULTS. Our results have shown that minimally modified C1 component of MBP increases the expression of arginase-1 in cells, decreases the expression of iNOS, does not change the secretion of HMGB1 protein, but significantly elevates surface expression of RAGE. On the other hand, highly modified deiminated isomer C8-MBP increases the secretion of HMGB1 protein but does not change the expression of arginase-1 or the content of RAGE.

CONCLUSION.These data indicate that deiminated- C8-MBP tends to polarize macrophages into M1 phenotypes, whereas C1 enhances the activity of M2 phenotype markers.

FIRING HOMEOSTASIS IN NEURONAL CIRCUITS: FROM BASIC PRINCIPLES TO MALFUNCTIONS

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Maintaining average activity level within a set-point range constitutes a fundamental property of central neural circuits. Accumulated evidence suggests that mean firing rate (MFR), reflecting an average level of spontaneous spiking activity over extended timescales, represents a physiological variable regulated by homeostatic systems in central neural circuits. However, some central questions have remained open. What are the mechanisms that establish the specific values of MFR set-points? Are MFR set-points fixed (predetermined) or adjustable in central neural circuits? If they are adjustable, do separate mechanisms control negative feedback responses and MFR set-point value? And finally, whether re-adjustment of dysregulated firing set-points may provide a new conceptual way to treat brain disorders associated with aberrant network activity? I will present our new approach, integrating genome-scale metabolic modeling and experimental study of neuronal homeostasis, to predict homeostatic regulators in specific neural circuits. Next, I will show our new results on the role of mitochondrial signaling in the regulation of activity set-points in hippocampal circuits ex vivo and in vivo. Finally, I will provide the evidence for a new potential strategy to suppress seizures by lowering firing set-points.

RESTING STATE FMRI AND VOXEL-BASED MORPHOMETRY IN PATIENTS WITH ANOREXIA NERVOSA

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INTRODUCTION. The significant increase in the number of adolescents with anorexia nervosa (AN) requires a deeper understanding of structural & functional disorders in these patients.

MATERIALS AND METHODS. MRI Toshiba 1.5 T with MPRAGE, using VBM (Freesurfer) and fMRIrs was applied to 30 females (13-20 years old): 17-AN and 13- controls. All the patients were comparable in terms of their age.

RESULTS. VBM. in AN group: the cerebellum was reduced on 20%, left (l) amygdala–18%, right (r) amygdala–17%, r thalamus – 11% and r hippocampus– 13%; pallidum – 10%, III ventricle – 14%; l entorhinal cortex – 14%, r EC –28%, r parahippocampal gyrus–20%, l frontal pole (FP)–12%, r FP–16%. L MidFG –11%, right–13%, r fusiform gyrus–14%. fMRIrs. in AN group: an increased activation in precuneus and cuneal, decreased in SMG in SMN, in DMN - higher activation of the r MPFC; in VisN - increased activation in the l precuneus and reduced in RPFL. In the SN- increased activation in MFG, pre-, postcentral gyrus, additional motor cortex of the LH. In the DN- increased activity in the precentral gyrus. In the EN- the paracingular gyrus of the LH and the LPFL is increased. In LN- increased activity of the pCG, r SFG, SMG in RH ($p \leq 0,05$).

SUMMARY. Significant reductions in the volume of structures indicate pathological changes in AN patients brain and the connectivity of the neural networks. It will contribute to the selection of structural and functional markers in anorexia nervosa.

MICRO-RNAs, THEIR TARGET PROTEINS, PREDISPOSITIONS AND MEMORY OF FILIAL IMPRINTING IN DOMESTIC CHICKS

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Visual imprinting is a learning process whereby young animals come to recognize a visual stimulus by being exposed to it (training) and subsequently prefer it to other objects. Much evidence has implicated a restricted forebrain region, the intermediate medial mesopallium (IMM), in memory for visual imprinting in the domestic chick. Learning-related, time-dependent molecular changes occur in the IMM after imprinting, indicating molecular regulation during memory formation. We have inquired whether certain micro-RNAs (miRNAs) are involved in such regulation. Twenty-four hours after training, miRNA spectra in the left IMM were compared between chicks termed good learners, characterised by high preference score (a measure of memory strength), and chicks with low preference scores (poor learners). Using criteria of effect size and expression level, we chose gga-miR-130b-3p for further study and found down-regulation correlated with learning strength. No effects were detected in the posterior pole of the nidopallium (PPN), a brain region not involved in imprinting. We further studied gga-miR-130b-3p two targets, cytoplasmic polyadenylation element binding proteins 1 (CPEB1) and 3 (CPEB3), in two subcellular fractions (P2 membrane-mitochondrial and cytoplasmic) of IMM and PPN. Only in the left IMM was a learning-related change observed: a positive correlation between amount of membrane CPEB3 and preference score, with protein amount increasing only when learning occurred. Analysis of residual variances from the regression with preference score and analysis of variances of trained and untrained chicks revealed that for the gga-miR-130b-3p the correlations were attributable not to training but to a predisposition, i.e. capacity to learn, independent of training, whereas the increase in membrane CPEB3 with preference score was a results of training and specific to learning.

DRUGS AND NEUROPLASTICITY IN DEPRESSION AND PARKINSON'S DISEASE

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With the aging population growing and the incidence of neurodegenerative diseases on the rise, the researches in the field are yet more urgently challenged to slow and/or reverse the devastating consequences of such progression. The challenge is further enhanced by psychiatric co-morbid conditions, particularly the feeling of despair in this population. Fortunately, as our understanding of the neurobiological substrates of maladies affecting the central nervous system increases, more therapeutic options are also presented. In this presentation, while providing evidence of shared denominators between Parkinson's disease and depression, novel therapeutic targets and drugs are presented. The emphasis will be on neuroplasticity underscored by roles of neurotrophic and inflammatory factors.

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IMPACT OF CHEMICAL CHAPERONES ON THE STABILITY AND REFOLDING OF GLOBULAR PROTEINS

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Recent theoretical and experimental studies have shown that protein environment plays a key role in the stability and functional activity of globular proteins, diversely affecting proteins' free energy landscape. The aim of our study was to determine an impact of the nonspecific additive, dimethyl sulfoxide (DMSO), on the thermal unfolding of a model protein α-chymotrypsin (α-CT) over a wide range of the additive concentrations.

DMSO is a small organic molecule widely used in research and medicine. It appeared to cause both, stabilization and destabilization, or even eventual denaturation of globular proteins.

We applied the method of differential scanning calorimetry (DSC) to investigate thermodynamic pattern of α-CT melting in buffered DMSO solutions. Thermodynamic parameters were measured in the presence of 0 to 70% (v/v) DMSO in acidic (pH 2.6) and alkaline (pH 8.1) environments. Both series of experiments revealed enthalpic stabilization of α-CT within the DMSO concentration range of 0 to 20-25 %, followed by the gradual destabilization. However, in contrast to alkaline series, at pH 2.6, specifically, a monotonic decrease of the melting temperature and remarkable protein folding reversibility were observed. Moreover, for the 20% DMSO solution calorimetric melting peaks were almost restored and remain stable even after multiple repetitive temperature scanning.

The stabilizing and chaperone effects in the presence of moderate DMSO concentrations can be explained by positive preferential solvation of water, which has a smooth maximum at 20-30% DMSO. The additive molecules strengthen interfacial water networks of native-like states remotely enhancing the protein stability and refolding ability.

RODENT PROPIONIC ACID MODEL OF AUTISM: ULTRASTRUCTURE OF LIMBIC AND NEOCROTICAL REGIONS OF RAT BRAIN

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Numerous data indicate that chronic injection of propionic acid (PPA) in rodents of different age affects cognitive flexibility, social skills, and produces various other alterations, compatible to whose, observed in individuals with autism. Therefore, it was proposed, that some types of autism might be partially related with alterations in PPA metabolism (MacFabe 2013). In the present research, we investigate how PPA

treatment is reflected on the ultrastructure of hippocampal CA1 and CA3 areas, central amygdala and prefrontal cortex of adolescent male rats. In addition, the effect of treatment on social behavior was described. The animals were treated intraperitoneally, with single, relatively low dose of PPA (175 mg/kg). The studies were performed 24 hours after treatment. Social behavior was assessed in three-chamber apparatus, modified to linear one (Lee et al. 2016): stranger rat (social stimulus) versus inanimate object (non-social stimulus). Social propensity was evaluated by: (i) numbers of visits to social stimulus and unsocial stimulus, and (ii) time spent with conspecific or with new object. ANOVA revealed that even single injection of relatively low dose of PPA produces the decreased interest in social stimulus (one of the main characteristics of ASD), while interest for inanimate stimulus remains the same. Ultrastructural modifications were seen in the hippocampus and amygdala. The most prominent alterations (mostly reversible) were in the CA1 area. Glial cells were most modified: the changes in pericapillary glia, astrocyte proliferation and microglia activation were detected. Other alterations included the changes of numbers of synaptic vesicles, presynaptic terminals and mitochondria.

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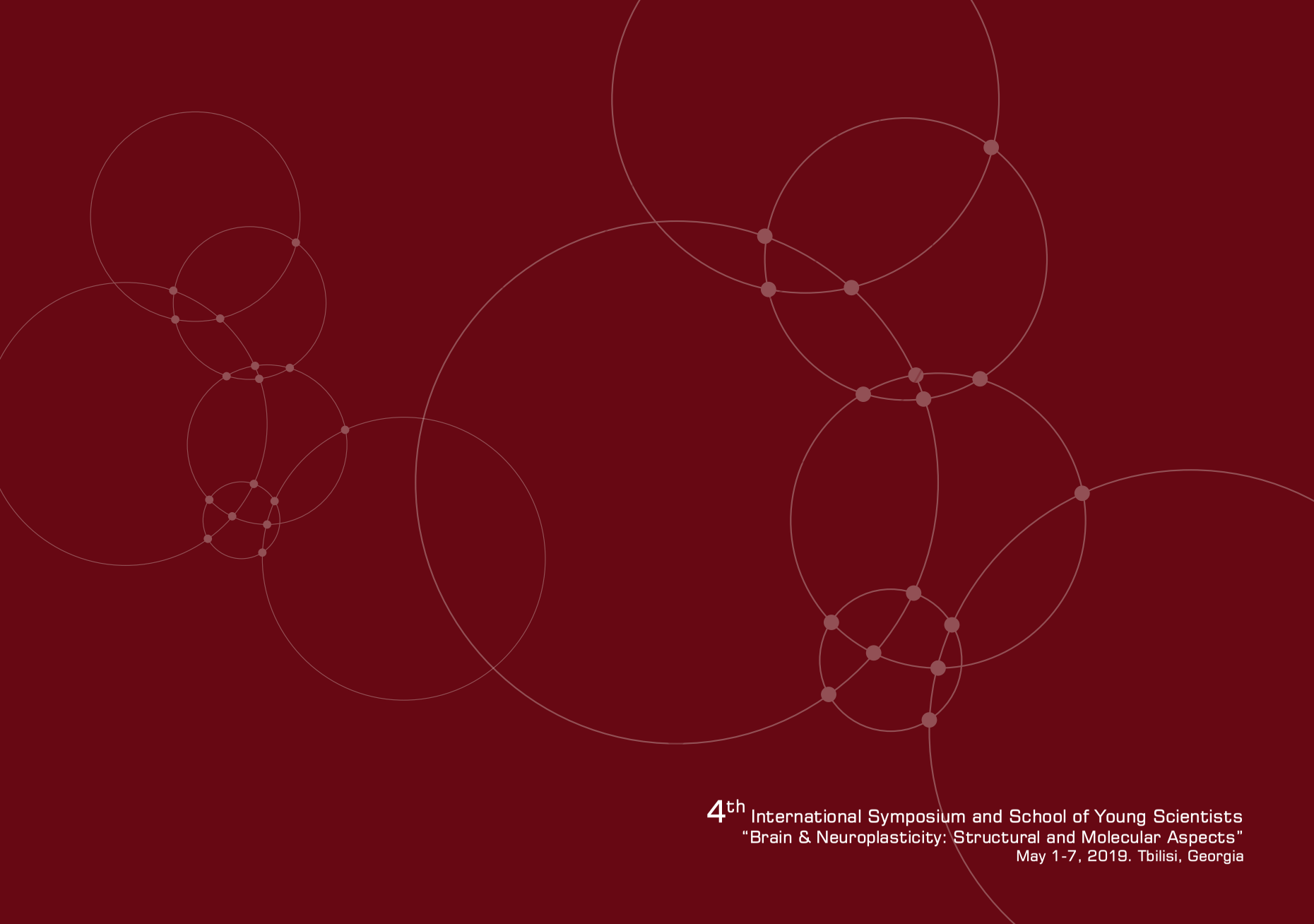

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