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ABSTRACT BOOK

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BRAIN & NEUROPLASTICITY: STRUCTURAL & MOLECULAR ASPECTS

ABSTRACTS

ილიას სახელმწიფო უნივერსიტეტი
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MORAL DISENGAGEMENT AND AGGRESSIVE BEHAVIOR, IMPACT OF BRAIN INJURY ON THEIR REVEAL

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Keywords: Moral disengagement, aggression, brain injury

The hypothesis about the connection between theory of moral disengagement and aggression appears still in the process of forming this theory. Moral disengagement can be a release mechanism that allows a person to engage in aggressive behavior without remorse. As a result of studies, it has been revealed that adolescents with behavioral disorders actively resort to various mechanisms of moral disengagement and their use contributes to the commission of delinquent behavior, while limiting the use of mechanisms reduces the externalization of deviant behavior. This study is an attempt to study this phenomenon among Georgian youth through the instrument obtained based on the adaptation of Celia Moore's moral disengagement test and Bassey-Perry's aggression test. The study of participants revealed gender differences in the detection of various forms of aggression, in particular, the expression of anger with young men is more often manifested in a physical form, while young women "get angry" more often. Based on the cluster analysis, it was revealed that individuals with a high rate of anger and hostile tendencies had a high manifestation of moral disengagement, the research did not confirm the same in the case of physical aggression. Accordingly, it can be said that Georgian youths who actively use the mechanisms of moral disengagement have high rates of aggression. According to the research, this is related to the type of aggression of anger and hostility and is not related to physical aggression. Among the participants, there was a group of individuals who had brain injury during their lifetime. Head injuries may compromise expected changes in moral disengagement via neuropsychological deficits in brain regions that are implicated in moral decision-making. A continued investigation of this link would inform both criminological theory and intervention programming.

A MULTIVARIATE ANALYSIS OF SOME POTENTIAL MARKERS OF SCHIZOPHRENIA

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Keywords: Schizophrenia, EEG, cognitive deficit, multivariate statistical methods, classification

Introduction: Although previous research identified several potential behavioral and electroencephalographic (EEG) markers of schizophrenia, substantial individual differences exist in the patient population in terms of these markers, as well as clinical symptoms.
Objectives: Our goal was to explore the relationship between a set of behavioral and electrophysiological variables, and to identify the features in both modalities that best discriminate between patients and controls.
Material and Methods: 47 patients with schizophrenia and 42 matched controls participated

in our research, under which we examined certain aspects of basic visual processing and face perception, as well as visual and acoustic Mismatch Negativity, and processes related to higher-level cognitive functions such as emotional face recognition and working memory. Resting state EEG functional connectivity strength and Minimum Spanning Tree measures were also analyzed. For statistical analysis, we applied multivariate methods that can effectively deal with high-dimensional data (regularized canonical correlation, group regularized canonical correlation, and stepwise logistic regression).
Results: Based on the results of the stepwise logistic regression analysis, we have chosen 5 out of 76 variables. 10-fold cross-validation resulted in a classification accuracy of 82.5% (95% CI = 77% - 88%).
Summary: Our preliminary results show that disturbed visual processing (specifically related to magnocellular pathway deficit), as well as weaker resting-state functional connectivity in the alpha and delta frequency ranges, and some variables related to distractibility can be the most important features in the classification.
Support/grant information: Supported by the ÚNKP-22-3-II New National Excellence Program of the Ministry for Culture and Innovation from the source of the National Research, Development and Innovation Fund; Hungarian Research Found - OTKA PD 115837; Bolyai Research Fellowship Program of the Hungarian Academy of Sciences; Higher Education Institutional Excellence Programme of the Ministry of Human Capacities in Hungary, within the framework of the Neurology thematic programme of Semmelweis University.

ALTERATIONS IN SPATIAL MEMORY ACROSS LIFESPAN IN A RAT MODEL OF AUTISM

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Keywords: Rat model of autism, valproic acid, aging, spatial memory

Autism (autism spectrum disorders - ASD) is a lifelong disability affecting the functioning of the brain. Despite progress in understanding of autism, relatively little attention has been paid to date to the process of aging. The largest bulk of research on ASD focuses on children and adolescents, with very few studies focusing specifically on adults, older adults, or on longitudinal data. The present study was designed to evaluate age-related alterations of spatial memory in the valproic acid (VPA) rat model of autism. To induce autism-like animal model, the pregnant rats were intraperitoneally injected 500 mg/kg NaVPA at the gestation day 12.5. Experiments were carried out on three age groups of male offspring: prepubertal adolescence (1 month), adult (6 months) and old (22 months) rats at the start of experimentation. The learning process and long-term spatial memory was assessed in the Morris water maze (MWM). The results of MWM experiments showed that all rats exhibited decreased latency in finding the hidden platform across the training trials. Both control and VPA-treated rats met the learning criteria by the end of the training period. During the probe test, which was performed 24 h after task acquisition, the control and VPA-treated adolescent and adult rats as well as VPA treated aged rats showed normal spatial learning and memory abilities in the MWM task, however rats within the control aged group exhibited a retention deficit 24 h after training. In conclusion, we found that spatial memory function in VPA induced rat model of autism is relatively age-resistant and it is our hope that further research will enhance our understanding of aging in an abnormal central nervous system.
This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG): Grant # - FR-22-10650.

ELECTRIC MAGNETIC STIMULATION FACILITATES COGNITIVE FUNCTION IN STRESSED RATS OF BOTH SEX

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Keywords: Electric magnetic stimulation, stress, cognition

Introduction. Electric magnetic stimulation (EMS) is a noninvasive treatment method which is used in many neurodegenerative diseases. The aim of study was to investigate the correlates of cognitive function in chronic immobilization stress model of rats both sexes on the background of EMS.
Methods. Experiments were conducting on intact and gonadectomized rats both gender (n=32, 4–6 months old, 190- 220 g). Gonadectomy was performed under ether anesthesia, using standard procedure. Parameters of EMS was detected in experiments (10000 -15000 Hz, 1,5 m/Tesla, during 20 min, 10 days). Chronic immobilization stress (CIS) performed 2 hours, during 10 days. The process of learning in rats was studied using elevated multi-branch maze. The rats were tested for learning ability 7, 14 and 30 days after the learning test. Data reliability was assessed using one- and two-way layout of factorial analysis (ANOVA).
Results. After immobilization, the learning process in the maze test was prolonged in rats of both sexes, compared to intact rats, stressed rats found it difficult to remember the correct trajectory ($P \leq 0.01$). The number of made mistakes was higher than in unstressed rats. The immobilized rats could not complete the task even on the 5th day of training. They sat in a corner of the maze and were able to cross the maze only after the intervention of the experimenter. In gonadectomized rats, compared to intact rats, learning time was improved only by the exposure to EMS ($P \leq 0.01$). EMS might affect the imbalances of neurotransmitter systems and hyperactivity of HPA axis, which are essentially responsible for the expression of depressive-like behavior and fear responses.
Conclusion. EMS has an anxiolytic effect in immobilized rats. This treatment improves learning and retention of information in stressed rats both sexes.

ELECTRIC MAGNETIC STIMULATION EFFECTS ON EMOTIONAL MOTIVATED BEHAVIOR AFTER CHRONIC CORTICOSTERONE INJECTION

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Keywords: Behavior tests, corticosterone, electric magnetic field

Background: Stress consistently exhibit hyperactivity of the hypothalamus-pituitary-adrenal (HPA) axis and enhanced release of glucocorticoids. Prolonged injection of corticosterone (CORT) might develop condition like stress condition. The electric-magnetic stimulation (EMS) is a noninvasive treatment method which is used as a complementary to the drugs, for treating different neurodegenerative diseases arise from stress. So, the goal of this investigation was to study the effects of EMS on the activity of the HPA axis, which can change behavior activity.
Methods: The experiments were conducted on albino male rats, weighing 150- 200 g (n=14). Proceeding from the goals set, the experimental group (corticosterone-treated-5mg/ per animal for 20 days) and the control subjects received no CORT. Each group was divided into subgroups. Some rats from the subgroup were given EMS. EMS parameters: 10000 -15000 Hz frequency, 1,5 m/Tesla, for 15 min, during 10 consecutive days. The Forced Swimming (FST) and the Open Field (OFT) tests were choosing for monitoring of behavior indicators. The obtained results were processed using statistical program ANOVA.
Results: A single injection produced prolonged elevations in circulating titers of CORT equivalent to those seen during stress. On the background of CORT injection, the time of immobilization was increased, the active swimming time, the time of the struggling and the time spent under the water were decreased. EMS reduced immobility time in the FST and increased struggling behavior, swimming in the FST, and the time spent under the water in the CORT-treated rat. CORT caused changes in motivational-emotional behavior in OFT: all parameters of research-motor activity were reduced compared to normal (untreated) rats. The EMS after CORT injection recovered research-motivated activity.
Conclusion: Against the background of high doses of corticosterone, EMS reduces the alarm response and increases research activity by restoring the activity of the HPA system.

FILIAL IMPRINTING IN DOMESTIC CHICKS; CYTOPLASMIC POLYADENYLATION ELEMENT BINDING PROTEIN 3, PREDISPOSITION AND LEARNING

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Keywords: Cytoplasmic polyadenylation element binding protein 3, IMM, mesopallium, learning, predisposition, prion-like, recognition memory

Visual imprinting is a learning process, whereby young animals come to prefer a visual stimulus after exposure to it (training). Available evidence indicates that the intermediate medial mesopallium (IMM) in the domestic chick forebrain is a site of memory formation during visual imprinting. We have found previously that cytoplasmic polyadenylation element binding protein 3 in the P2 plasma membrane mitochondrial fraction (CPEB3-P2) is upregulated in a learning dependent way in the left IMM 24 h after training. CPEB3 has two forms, soluble and aggregated. Soluble CPEB3 represses translation; the aggregated form (CPEB3-AF) is amyloid like and can promote translation. Our previous study did not show which of these two forms is increased after imprinting. We have now resolved this matter by measuring, 24 h after training, CPEB3-P2 and CPEB3-AF in the IMM and a control brain region, the posterior pole of nidopallium (PPN). The methods include imprinting training with a visual stimulus, behavioral measurement of preference, preparation of aggregated CPEB3, western immunoblotting, quantitation of proteins, statistical linear modeling. Only in the left IMM were the level of CPEB3-AF and learning strength correlated, increased CPEB3-AF level reflecting a predisposition to learn readily. CPEB3-P2 level also increased with learning strength in the left IMM, but as a result of learning. No correlations were detected in the right IMM or PPN. We propose two separate systems, both modulating synaptic strength through control of local translation. They are represented by CPEB3AF (associated with a predisposition to learn) and soluble CPEB3 (associated with learning itself).

SOME ASPECTS OF THE REGULATION OF NA-K-ATPASE BY NORADRENALINE

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Keywords: Na-K-ATPase, modulatory effect of noradrenaline, brain and kidney

A comparative kinetic analysis was performed on Na,K-ATPase from rat brain synaptic and kidney plasma membrane fractions, with a focus on understanding the different sensitivity of these fractions to the neurotransmitter noradrenaline. The results showed that noradrenaline inhibits rat brain synaptic membrane Na,K-ATPase and shifts the enzyme system from MgATP to Mg 2+ dependent cycle, while kidney plasma membrane fraction Na,K-ATPase is not sensitive to noradrenaline. Further investigation into the mechanism underlying this difference revealed that the enzyme velocity dependence upon the concentration of Mg 2+ showed different kinetic features for synaptic and kidney plasma membrane Na,K-ATPase. Addition of ethylene glycol tetra acetic acid to the reaction medium also affected the geometric form of the 1/V=f(Mg 2+) function differently. Further analysis revealed that this different modulatory effect of noradrenaline can be explained by different kinetic features of Na,K-ATPase alpha subunits. Specifically, alpha2/3 possess an Mg 2+ dependent cycle, while it is not manifested for alpha 1 subunit. Overall, this study provides insight into the different sensitivity of Na,K-ATPase from rat brain synaptic and kidney plasma membrane fractions to noradrenaline and the underlying mechanisms responsible for this difference.

THE NEUROPLASTICITY OF SOCIAL INTERACTION: HOW DO OTHERS CHANGE OUR FUNCTIONAL SELF-PROCESSES?

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Keywords: Social interaction, functional brain processes, neuroplasticity

Social interaction requires rapid, real-time adaptation to dynamically shifting information. It is inherently a process of change. Every time we interact with the same person, we get to know their perspective and identity a little better, and we may also adopt some of their beliefs or traits. Repeated interactions with the same person embeds them in our minds and changes us in small ways. With enough repeated interactions with the same person, temporary neuroflexible adaptations underlying these social exchanges may transform into persistent neuroplastic changes. However, the neuroplasticity of social interaction has never previously been studied. This talk will present theoretical aspects underlying the effects of social interaction on functional brain processes and two experiments examining temporary neuroflexible adaptations and persistent neuroplastic changes after repeated social interactions. Implications for clinical groups with social deficits will be discussed.

LONGITUDINAL SLEEP EEG DATA IN TYPICALLY DEVELOPING AND MEDICATION-FREE ADOLESCENTS WITH ADHD

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Keywords: Longitudinal sleep, adolescents, attention deficit hyperactivity disorder

Adolescence is a transition period from childhood to adult life characterized by a fundamental neurobiological reorganization for both the brain and the body. Sleep is one aspect of behavior that changes greatly across adolescence. Developmental research provides the evidence that sleep EEG represents a valuable tool to investigate the maturation of brain electrophysiology.
Attention deficit hyperactivity disorder (ADHD) is one of the most commonly diagnosed neurodevelopmental disorder occurring in about 5-10 % of children. The growing evidence from neuroimaging studies indicate that ADHD is a problem of delayed rather than deviance in cortical maturation. Brain electrophysiological evidence for a maturational delay is mixed. The adolescent NREM sleep EEG maturation provides an opportunity to investigate whether longitudinal changes in adolescent brain electrophysiology corroborate a maturational lag associated with ADHD. Data concerning longitudinal changes in (1) sleep EEG across adolescence and (2) within-night slow-wave EEG dynamics in typically developing and drug-naïve ADHD children, will be discussed.

This work was supported by the Shota Rustaveli National Science Foundation of Georgia, grant FR17_94.

ANTIOXIDANT EFFECTS OF SOME HERBAL PREPARATIONS

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Keywords: Hyperthermia, herbal preparation, free radicals, antioxidants

According to modern scientific concepts, oxidative stress is a prerequisite for the development of more than a hundred diseases (neurodegenerative disorders, oncological diseases, the development of the ischemic cascade, Parkinson's and Alzheimer's diseases). In the present study, we decided to conduct an experimental analysis (tests on rats) and compare the antioxidant activity of different modifications of Folium (Folium immuno, Folium pX, Folium relax). Experiments were performed on rats under conditions of oxidative stress induced by whole body hyperthermia. As in the trials it was revealed that the amount of reactive oxygen metabolites (d-ROMs) was reduced by only one Folium preparation (Folium relax), this preparation also caused a sharp increase in blood antioxidants (PAT). The same drug causes both the risk of disturbing the balance of oxidative stress and a decrease in the index of oxidative stress. Based on all of the above, we can conclude that although all three types of Folium exhibit antioxidant properties, Folium relax is the most effective and expressive.

BIOLOGICALLY POSITIVE CHARACTERISTICS OF TRANSITION STATE BETWEEN NORM AND PATHOLOGY CAUSED BY PSYCHOGENIC STRESS IN RAT

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Keywords: Psychogenic stress, self-regulation, depression, rat

Introduction. The aim of research was to study biologically positive self-regulatory, compensatory behavioral manifestations in dominant and submissive rats at different stages of chronic psychogenic stress -between norm and pathology condition.
Material and Methods. Experiments were performed on male Wistar rats. The dominant and submissive rats of experimental groups were subject to stressing procedure (within 45 days). Stressing was performed in a special device, the so-called "stress box". The model is a modified version of active avoidance reaction method. Initially, we developed in the group of rats an active avoidance reaction towards the metronome and tone sound signals. After development of two active avoidance reaction, we carried out testing of two active avoidance reactions during one experimental session. Animals' behavior was studied in a "stress-box", also using "forced-swim" and "open- field" tests.
Results. At the initial stage of psychogenic stress in the course of experiment in the "stress- box" one could observe an increase in animals' motor activity, intersignal movements, rearing and

grooming activity, being more clear-cut in dominant rats. At prolonged stressing the increased motor activity gradually decreases, rearing and intersignal movements disappear altogether. Dominant rats react to a conditioned signal (CS), in spite of this percentage of correct responses to a signal does not exceed 30-50 %. In contrast to dominants, submissive animals no longer react to CS and remain in a central compartment and spring into side sections only in response to painful irritation.
Summary. The chronic stressing procedure carried out on rats using an psychogenic stress model leads to the development of depression both in dominant and submissive rats, but animals' behavior before development of depression is biologically positive, directed toward elevation of organism's stability in response to a stressogenic influence and it is viewed by us as a manifestation of self-regulation, defensive mechanism.

INVESTIGATION OF ANTIEPILEPTIC POTENCY OF QUERCETIN-LOADED MAGNETIC NANOPARTICLES IN ANIMAL MODELS OF EPILEPSY

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Keywords: Epilepsy, quercetin, nanoparticles, magnetic field

Introduction: Epilepsy is one of the most frequent neurological disorder, characterized by repetitive seizures and various mental health problems. Currently 30% of patients suffer from treatment-resistant epilepsy. It is known that the basic cause of the disease is the disbalance in excitatory and inhibitory processes of brains neuronal circuits. One of the major candidates for new antiepileptic drug development are flavonoids - plant derived antioxidants. Objectives: In our project we have focused on Quercetin - the antioxidant with anti-inflammatory properties, but with low bioavailability. We studied the influence of quercetin-loaded magnetic nanoparticles (Q-MNP) on the hippocampal electrophysiological activity and behavioral disturbances in the laboratory rats with kainic acid status epilepticus (KA-SE).
Material and Methods: KA-SE-model of rats were used to define anticonvulsant potency of Q-MNPs. In ketamine-anesthetized animals Q-MNPs were injected in the tail vena under the unilateral external static magnetic field (ESMF) directed on the temporal lobe. Behavioral experiments were performed in the open field and T-maze tests. Prussian blue stain was applied to determine the Fe content in the brain. Statistical analyses was conducted by program PRIZM.
Results: Behavioral experiments demonstrated that ESMF/MNPs alone do not change the behavior of animals, while 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. Electrophysiological recordings revealed that KA-SE alters the effectiveness of quercetin. Injection of Q-MNP with the presence of ESMF significantly changed the amplitude and frequency of neuronal discharges in the hippocampus. The effect of Q-MNP was inhibitory.
Summary: The data analysis showed that ESMF improves quality of delivery of Q-MNPs to the brain. Inhibitory effects of Q-MNP on neuronal activity of hippocampus explains its positive effect on behavioral disturbances caused by status epilepticus.
Supported by Shota Rustaveli National Science Foundation of Georgia, Grant FR17_629.

THE PLATELET POROSOME AND EXOCYTOTIC MACHINERY IN GRANULE SECRETION

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Keywords: Platelet, porosome, exocytosis

Although a circulating blood cell, the platelet has several surprising similarities to the neuronal synapse. During the course of their development, platelets are formed from the tips of proplatelets that emanate from the megakary, ocyte cell body in a manner that mimics the relationship of the synapse to the neuronal cell body. Like the synapse, the forming platelet is connected to the body of the megakaryocyte via a thin filamentous structure rich in microtubules. The platelet receives its allotment of organelles – granules, mitochondria, lysosomes - from a central nucleated body during megakaryopoiesis. These cell components are delivered to developing platelets via kinesin motors that travel on microtubule tracks. Once mature, the platelet must, like the neuron, release its granules with exquisite temporal and spatial precision to avoid pathological consequences. The platelet is replete with granules that are primed for rapid release upon cell activation. To achieve efficient release of its granules, the platelet possesses an unusual secretory structure termed the open canalicular system (OCS). We and others have defined the SNARE proteins required for platelet granule release and demonstrated the importance of cytoskeletal proteins in the platelet release reaction. Our studies have also demonstrated the role of dynamin-related protein 1 (Drp1) in platelet granule fusion. These multiple components are reminiscent of the neuronal porosome of the synapse. This talk will compare the mechanisms of platelet formation from proplatelets to synaptic formation from axons. We will also compare granule release in the platelet with neurotransmitter release from the neuronal synapse. Finally, we will explore the novel hypothesis that the OCS is the platelet porosome and compare the structure of the OCS to that of other porosomes including the neuronal porosome complex.

SPEECH AND EMOTIONAL DEVELOPMENT OF ORPHANS WITH INTELLECTUAL DISABILITIES

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Keywords: Orphans, intellectual disabilities, mixed specific developmental disorders, emotional speech

The study is a part of complex research aimed at development of the approach to the diagnostics of emotional sphere in children with atypical development and developmental disorders. The goal of the study is to reveal the peculiarities of speech development and emotional state manifestation in speech, facial expression and behavior of orphans with intellectual disabili-

ties (ID) and mixed specific developmental disorders (DD). Audio recording of speech and video recording of behavior of 5-13 years old orphans (n=55) with ID, DD and typical development (TD) were made during children's testing by Child's Emotional Development Method (Lyakso et al., 2022). Perceptual (groups of listeners), spectrographic, and linguistic analysis of children's emotional speech were conducted. Facial expression of children was assessed by "FaceReader" program. Expert analysis (6 experts with professional experience working with children) was used for description of the elements of children's behavior. Perceptual analysis revealed low speech intelligibility in preschool orphans with ID, but high accuracy in comfort and discomfort states recognition via children's speech. Acoustic features of children's emotional speech were described, high values of pitch and vowels duration in the speech of children with ID and DD and lower vowel articulation indexes in the speech of children with ID were revealed. The analysis of the texts of dialogues between adult and children showed that orphans with ID use less replies containing complex sentences than TD children. Children with ID answered less to adult's questions vs TD children. The number of responses of children with ID and DD increases if adults talk emotionally. Orphans with ID less often than orphans with DD and TD manifest neutral state in facial expression. The data obtained can be used in diagnostics of violations in speech and emotional spheres of children.

The study was supported by the Russian Science Foundation (Project 22-45-02007).

EPILEPTOGENESIS INHIBITION BY MYO-INOSITOL: BEHAVIORAL, ELECTROPHYSIOLOGICAL AND MOLECULAR STUDY

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Keywords: Epileptogenesis, myo-inositol, antiepileptogenic substance

Epilepsy is one of the wide spread neurological diseases that currently cannot be cured pharmacologically. A complex process of molecular, cellular and network changes in the central nervous system, referred as epileptogenesis, transforms a normal brain into an epileptic one. Currently, there is no medically approved therapy that prevents or significantly modifies the process of epileptogenesis. From this point of view, it is important that myo-inositol (MI) has been recently identified as a potentially promising antiepileptogenic drug in behavioral and biochemical experiments. To evaluate the entire range of antiepileptogenic potential of MI, we investigated the effects of MI at molecular, cellular and systemic levels in kainic acid (KA) epilepsy model rats in a multidisciplinary study. We have showed that long-term treatment with low, threshold concentration MI (30 mg/kg) in statistically significant manner: (i) decreases the number and duration of behavioral spontaneous recurrent seizures (SRS) (ii) decreases the frequency and duration of and electrographic SRS in the hippocampus; (iii) has an ameliorating effect on spatial learning and memory deficit associated with epileptogenesis, and (iv) attenuates cell loss in the hippocampus (v) the MI treatment also altered the expression some of the proteins associated with epileptogenesis. Furthermore, in a preliminary study we also tested higher concentrations (60 mg/kg and 120 mg/kg) of MI. Behavioral and electrophysiological experiments suggest that the 60 mg/kg MI concentration is of optimal potency. MI effects are still present even 4 weeks after MI treatment ceased. Our results indicate that MI is effective antiepileptogenic substance within the framework of the used epilepsy model.

ULTRASTRUCTURAL CHARACTERISTICS OF MICROGLIAL CELLS OF THE CEREBRAL CORTEX IN EXPERIMENTAL ENDOTOXEMIA

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Keywords: Microglia, cerebral cortex, endotoxemia, ultrastructure

Introduction. Microglia originates from red bone marrow, keeps its number stable, has an irreplaceable role in providing plasticity, which is important according to existing conditions, in the regulation of the activity of nerve circuits in the central cerebral cortex. The aim of the present study is the morphological study of the changes in microglia-neuronal connections in the model of severe endotoxemia.

Material and methods. Acute experimental endotoxemia model was created by intravenous injection of E. coli endotoxin (LPS-Serotype 0111: B 4 group) dissolved in 0.5 ml of physiological solution at 1 mg/kg and injected into the tail vein of white rats (n=10). In the control group into the vein injecting only 0.5% physiological solution. After 2 hours, pieces were taken from the temporal cortex, and after fixation and postfixation, Araldite-Epon blocks were prepared. Semithin sections (1-2 mkm) were obtained with the aid of Leica EM UC7 ultramicrotome for further investigation by light microscope Primo Star (Zeiss) Stained ultrathin sections (50-60 nm) were examined under the Transmission Electron Microscope JEM-1400 at 80 kV.

Results. Microglial cells of light and dark forms are less abundant in the control group, singly, mainly located between the astrocytic feet around the synaptic connections of neurons. The most distinctive ultrastructural feature of microglial cells from neurons and other glial cells is their heterochromatin dominance associated with the nuclear envelope. Both in control and during endotoxemia, the areas between the bodies and protrusions of microglial cells and the corresponding structures of neurons can be detected only under 80,000 magnifications of the electron microscope. In the temporal cortex of white rats, under the influence of endotoxin (LPS), severely degenerated dark neurons are detected in neurons with and without close contact with microglia cells.

Summary. The detection of close contacts with microglial cells at the level of neuronal bodies, protrusions, and synaptic connections during both control and severe endotoxemia allows for the implementation of ligand receptor and paracrine effects between the discussed cell structures. Degenerative changes in neurons that are not in direct contact with microglial cells are related to the fact that they themselves express TLR4, which can interact with LPS.

THE EFFECT OF TOLUENE INTOXICATION ON THE OLFACTORY BULB NEURONS IN RATS OF DIFFERENT AGE GROUPS

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Keywords: Toluene, olfactory bulbs, rats of different age-groups

In the last years, implementation of the volatile solvents in order to get a narcotic high, used via inhalation (sniffing), increased significantly, especially in the youth. Substances containing these agents induce hallucinations and euphoric state. In the present study the influences of toluene intoxication on quantity of the mitral and granular cells in olfactory bulbs was analyzed in young and adult rats. An inhalation route of intoxication was used in our experiments - animal inhaled toluene until attaining a sidewise laying position. This procedure was performed in the closed glass container, in which air was beforehand saturated with the toluene vapors. Experiments was carried out on two age groups (n=20 animals): one - and two months' age rats. Inhalation period was 40 days. Each age group consisted of ten animals and was divided into the two subgroups: I - control animals (n=5), II - experimental animals (n=5). Assessment of the neurons' quantity in different structures was made according to the fractional approach method proposed by M. West. The results obtained showed that number of mitral neurons in the olfactory bulb of the Subgroup II of the rats, sniffing since the age of one and two months, significantly decreased by 45% (p<0,05) and by 30% (p<0,01), respectively. Meanwhile, the granular cells remained unaltered in experimental animals of both age groups. Decrease of the projection mitral neurons, in its turn, results in disruption of the projections to olfactory cortex and hampers proper functioning of the olfactory analyzer.

COMPARATIVE ANALYSIS OF THE MITOCHONDRIAL PROTEOME IN A MOUSE MODEL OF RETT SYNDROME

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Keywords: Neurodevelopment, mitochondria, oxidative stress

Rett syndrome (RTT) is a neural development disorder caused by spontaneous mutation of *MECP2* gene in chromosome X, which codes methylated CpG binding, gene expression regulator protein. The majority of patients are young girls. Due to the neuron's abnormal small size, the brain´s general volume is reduced and synaptic structures are weakened. RTT patient's postnatal development appears normal during the first 6 to 16. After that, phenotype signs start to gradually emerge, such as mental problems, lack of communication and more severe organ specific symptoms. During RTT general mitochondrial mass is increased, ultra-structure is damaged and organelle functions are hindered. Cells suffer from higher concentrations of free radicals, oxidative stress, lack of ATP, and increased susceptibility to hypoxia. Main goals of this research was broad-range comparative proteomic analyses and untargeted metabolomic studies of crude mitochondrial fraction obtained from the brain tissues of wild type and *Mecp2* gene knockout male mice. Additionally mitochondrial proteome experiments involved an *ad hoc* approach for mitochondrial dynamics regulatory proteins. Collected data shows that mitochondrial proteome of RTT mice clearly differs from wild type and can be cause or result of various molecular and metabolic abnormalities. Findings show an upregulation of cytochrome b-c1 complex subunit 1 and prohibitin-1, as well as a downregulation of gamma-enolase and cAMP-dependent protein kinase catalytic subunit alpha in RTT cortex and hippocampus. Also, mitochondrial dynamics regulation proteins were decreased in RTT mice, specifically mitofusin 1 and DRP-1. Untargeted metabolomic data revealed 101 significantly altered metabolites. These differences cover more than 31 metabolic pathways, including pivotal aspects of cellular metabolism, such as pyruvate metabolism, glycolysis, citrate cycle and oxidative phosphorylation. All these results shed further light onto the mitochondrial and the metabolic alterations that appear as part of the pathogenesis of RTT in MeCP2 deficient brain tissue.

FIBRINOGEN AND FIBRINOLITIC ACTIVITY AS BLOOD FLUIDITY FACTORS IN PATIENTS WITH ATRIAL FIBRILLATION

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Keywords: blood flow, fluidity structure, fibrinogen

Introduction. Atrial fibrillation is a multidisciplinary disease, which is very often the background of neurological disorders. The percentage of strokes on the background of atrial fibrillation is growing every year, therefore, this study, from our point of view, makes it difficult to be at a 5th Biennial International Symposium and School for Young Neuroscientists "Brain and Neuroplasticity. Structural and Molecular Aspects" where we researchers can bring our research into discussion and receive comments from brain experts. Atrial fibrillation is one of the most common and studied cardiac arrhythmias, occurring 10 times more often than all other variants of paroxysmal supraventricular tachycardia. Atrial fibrillation is a deep biomedical scientific and applied medical, and social problem that requires the involvement of all parts and approaches of clinical and laboratory research. Identification of factors predisposing to its development and risk factors for its complications is one of the most pressing problems in cardiology.
Objectives. Our interest was the study of fibrinogen and fibrinolitic activity, as one of the factors determining rheology, coagulation and, as a result, blood fluidity.
Material and Methods. The study included 60 patients (39 men and 21 women); mean age 33.9±9.8 years (from 15 to 49 years); with disease age of 7.3±5.2 years. Turn-off parameters 2

weeks or less patients took medication. Concomitant other diseases of the cardiological profile, malformations of the cardiovascular system.
All patients underwent clinical and biochemical studies, the state of the cardiovascular system was studied: ECG, echocardioscopy, ECG monitoring, electrophysiological examination of the heart, chest X-ray, bicycle ergometry or stress echocardioscopy (the so-called routine studies). But within the framework of this abstract, we will present data on fibrinogen and fibrinolytic activity of blood, which, together with the rheological properties of blood, determines the fluidity of blood.
The control group consisted of 20 practically healthy people aged with an average age of 33±15.4 years. Statistical processing of the material included the determination of Student's criterion (t), differences were considered significant at $p<0.05$.
Results. Fibrinogen was 2.55±0.55g/l in group with patients and 2.85±1.26g/l in control group (P=0.09). Fibrinolytic activity was 8.41±6.97 min in group with patients and control group was same (P=0.94). I The change of Erythrocyte aggregation index in the group of patients with control was statistically significant (P=0.05)
n the group of patients, significant deviations of fibrinogen parameters were found and significantly fibrinolytic activity did not change in the group of patients compared to the norm.
Conclusion. As can be seen from our earlier work, erythrocyte aggregation affects fluidity and forms its profile, but the aim of this work was to establish the effect of fibrinogen on fluidity. It turned out that the fibrinogenic component behaves in two ways. Therefore, based on our data, we cannot unambiguously conclude that fibrinogen forms a fluidity profile. We believe that this research should be continued and expanded with the involvement of neuroscience specialists and clinical neurologists. This study will lay the foundation for the following approaches, where we will investigate the factors that form blood fluidity in patients with strokes caused by atrial fibrillation.

CHRONIC LOUD NOISE AFFECTS ANXIETY-LIKE BEHAVIOR AND ULTRASTRUCTURE OF AMYGDALA IN ADULT MALE RATS

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Keywords: Chronic noise, emotional behavior, amygdala, ultrastructure, adult male rat

Noise pollution is a severe public health problem. Constant exposure to even moderate noise levels between 55-65 dB can lead to various pathologies. In this research, we elucidate the ultrastructural changes in rat limbic region, basolateral amygdala, considered as non-classical auditory pathway. In addition, anxiety-like behavior was assessed. Adult male rats were exposed to 100 dB noise, one hour daily, for 10 consecutive days. The evaluations were performed on day 11. Exposure to noise induced anxiety-like behavior as evidenced by time spent in the closed arm of elevated-plus maze. In parallel, ultrastructural changes in basolateral amygdala were noted. Specifically, noise resulted in neuronal apoptosis, chromatolysis, cytoplasmic organelle destruction, and glial activation. Mild alterations were observed in amygdala axo-dendritic synapses. Last changes indicate to moderate changes in neurotransmission. These results provide further evidence of detrimental consequences following exposure to loud noise even in

non-classical auditory pathway.
The research is financially supported by Shota Rustaveli National Scientific Foundation: Project #DP2016_17

ADDICTION MEMORY: FUNCTIONAL CONNECTIVITY AND NEUROPLASTICITY IN THE BRAIN REWARD CIRCUITRY

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Keywords: Addiction memory, deep brain stimulation, synaptic modification

Addiction is caused, in part, by powerful and long-lasting memories of the drug experience. Relapse caused by exposure to cues associated with the drug experience is a major clinical problem that contributes to the persistence of addiction. Accumulated evidence suggests that drugs of abuse can hijack synaptic plasticity mechanisms in key brain circuits, most importantly in the mesolimbic dopamine system, which is central to reward processing in the brain. Reversing or preventing these drug-induced synaptic modifications may prove beneficial in the treatment of one of society's most intractable health problems. Two new promising treatment strategies include using neuromodulatory approaches such as deep brain stimulation (DBS) and targeting the orexin system through developing effective pharmacological agents. It is believed that DBS has the potential to correct pathological synaptic functions and inhibit the development of addictive responses, since the disease is related to behavioral alterations caused by drug-evoked synaptic plasticity of glutamatergic transmission in the brain reward system. Moreover, a great body of evidence has recently revealed the therapeutic effects of orexin receptors antagonists especially orexin type 1 receptor blockers in suppression of a wide range of reward-related behaviors via interfering the drug-induced synaptic plasticity processes. Nevertheless, more investigation in this area is required to propose DBS and orexin receptor antagonists as effective therapeutic alternatives for treating substance use disorders.

USING THE RADIATION EXPOSURE MODEL FOR EVALUATION OF THE GENETIC SPECTRUM DURING AGING OF ORGANISMS

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Keywords: Irradiation, aging, genes, bioinformatics, RNA-sequence

Ionizing radiation is a completely unique factor capable of dose-dependent regulation of the aging processes. Thus, the "radiation aging" effect can be used in numerous research to study mechanisms of gerontological processes. Aging is the main risk factor for socially significant

chronic disorders and it is essential to discover accurate model to artificially cause aging process. In this investigation we studied aging associated biological processes to find a way to accelerate the normal aging process by ionizing radiation. We examined the processes involved in the aging effect, by means of analyzing RNA sequences acquired from Publicly available database to find differently expressed genes of old mice, young mice and mice after radiation exposure and further comparison of obtained set of genes with genes commonly recognized as age associated. For implementation of the RNA sequence study and data analysis bioinformatic techniques were applied. Investigation was accomplished on Galaxy web platform and in Python. The assessment of differently expressed genes under the influence of radiation in young and old mice made it feasible to indicate most vulnerable to radiation set of genes in terms of radiation-induced aging. Taking into the account the possibility to dose the acceleration of aging process by varying radiation exposure, the identification of specific genes can considerably narrow the genetic spectrum which is most essential for the aging of organisms. This methodological approach can lead us closer to unification of integrative mechanisms of aging, and the development of methods for biomedical monitoring of this process.

THE POROSOME SECRETORY NANOMACHINE: DISCOVERY TO THERAPY

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Keywords: Secretion, porosome, discovery to therapy

Secretion is a highly regulated fundamental cellular process in living organisms, from yeast to cells in humans. Cellular cargoes such as neurotransmitters in neurons, insulin in beta cells of the endocrine pancreas, or digestive enzymes in the exocrine pancreas are all packaged and stored in membrane-bound secretory vesicles that dock and fuse at the cell plasma membrane to release their contents during secretion. Cup-shaped plasma membrane-embedded lipoprotein structure called porosomes were first discovered in 1996 in live pancreatic acinar cells using atomic force microscopy (AFM) and subsequently confirmed in all cells examined including neurons using AFM, electron microscopy (EM), and solution X-ray. The porosome exhibits dynamics and its chemical composition demonstrates the utilization of energy in the form of both ATP and guanosine triphosphate (GTP), the participation of molecular motors, ion channels, and soluble N-ethylmaleimide-sensitive factor activating protein receptor (SNARE) membrane fusion proteins, among others. Porosomes are composed of nearly 30 proteins. Porosomes range in size from 15 nm in neurons and astrocytes to 100–180 nm in endocrine and exocrine cells. Porosome has been functionally reconstituted into artificial lipid membrane and in live cells. During secretion, secretory vesicles dock at the base of the porosome complex via v-SNARE proteins at the secretory vesicle membrane and t-SNARE proteins at the porosome base. In the presence of calcium, the v-SNARE and t-SNARE proteins in the opposing bilayers interact in a circular array to establish conducting channels or fusion pores. An increase in volume of the docked secretory vesicle via the rapid entry of ions and aquaporin-mediated rapid entry of water molecules results in increased intra-vesicular pressure, enabling the fractional release of vesicular contents from the cell with great precision. Defects in one or more proteins within the porosome complex, have measurable, often highly potent effects on the regulation of secretion, establishing links between secretory defects and disease. Secretory disease states such as diabetes, cystic fibrosis, cancers and neurological disorders, can now be better managed and novel drugs and therapies developed.

MOLECULAR MECHANISMS OF POROSOME-MEDIATED SECRETION

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Keywords: Secretion, porosome, molecular mechanisms

Cup-shaped plasma membrane-embedded lipoprotein structure called porosomes were first discovered in 1996 in live pancreatic acinar cells using atomic force microscopy (AFM) and subsequently confirmed in all cells examined including neurons using AFM, electron microscopy (EM), and solution X-ray. The porosome exhibits dynamics and its chemical composition demonstrates the utilization of energy in the form of both ATP and guanosine triphosphate (GTP), the participation of molecular motors, ion channels, and soluble N-ethylmaleimide-sensitive factor activating protein receptor (SNARE) membrane fusion proteins, among others. Porosomes are composed of nearly 30 proteins. Porosomes range in size from 15 nm in neurons and astrocytes to 100–180 nm in endocrine and exocrine cells. Porosome has been functionally reconstituted into artificial lipid membrane and in live cells. During secretion, secretory vesicles dock at the base of the porosome complex via v-SNARE proteins at the secretory vesicle membrane and t-SNARE proteins at the porosome base. In the presence of calcium, the v-SNARE and t-SNARE proteins in the opposing bilayers interact in a circular array to establish conducting channels or fusion pores. An increase in volume of the docked secretory vesicle via the rapid entry of ions and aquaporin-mediated rapid entry of water molecules results in increased intra-vesicular pressure, enabling the fractional release of vesicular contents from the cell with great precision.

THE ALLEVIATING EFFECT OF HERNIARIN ON IONIZING RADIATION-INDUCED CHANGES IN LIMBIC SYSTEM

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Keywords: Herniarin, ionizing radiation, cognitive impairments, hippocampus

Background: Radiation-induced brain injury is often revealed after fractionated radiation therapy or whole-brain irradiation. Radiation-induced cognitive impairments are related to the hippocampus, a key subcortical structure in the mammalian brain, involved in three primary

functions: the formation of new memories, spatial learning, and emotions. Acute high-dose radiation induces bystander impairment of the CNS, leading to decreased hippocampal neurogenesis and the development of neuroinflammation, which results in memory deficits and cognitive disorders. Furthermore, CNS responses to radiation are determined by different factors: formation of reactive oxygen species causing DNA and cell membrane damage, and disruption of electrochemical connections between neurons. Therefore, synthetic compounds or drugs, such as Herniarin, that can directly scavenge free radicals can be promising radioprotectors for reducing behavioral deficiencies. Herniarin is simple coumarin. Coumarins are found mainly in vegetables and fruits and play an important role as a dietary antioxidant in the human body. Moreover, coumarins can be used for the treatment of cancers such as leukemia, and renal cancer and also have the ability to decline side effects caused by radiotherapy.
Objective: To understand ionizing radiation-induced behavioral impairments and evaluate morphological changes in the hippocampus and entorhinal objective of our study was white mice Mus musculus. Methods: Mice whole-body irradiation with 137Cs was performed at a dose rate of 1,1Gy/min for a total dose of 5 Gy with a "Gamma-capsule-2". Irradiated mice were treated with Herniarin (20 mg/kg) for five days before irradiation and the same dose was administrated after one hour of irradiation. Spatial learning and formation of memory were estimated in the elevated-type multi-way maze. Locomotor activity and anxiety-like behavior were estimated in an open field maze. Two parameters of an elevated-type multi-way maze were evaluated to monitor the process of spatial learning and memory formation: the mean number of errors and time for crossing the maze. The number of neurons was determined in the CA1 and CA3 regions of the hippocampus, dentate gyrus and entorhinal cortex.
Results: During early post-irradiation period the number of neurons in the control and irradiated groups was the same, in late post-radiation period - on the 90th and 180th day, the number of granular neurons in the dentate gyrus decreases to 38%, and in the entorhinal cortex and CA1 and CA3 fields of the hippocampus to 33%. In irradiated (5 Gy) and Herniarin-treated mice, the number of neurons in the corresponding period was equal to the data of the control group. Monitoring of the spatial learning process in the elevated maze did not reveal significant difference between irradiated and Herniarin-treated animals. During late post-irradiation period number of errors and mean time for crossing the maze significantly decreases in 5 Gy irradiated mice, though Herniarin-treated group improves the results.
Conclusion: The results of the present study indicate that ionizing radiation (5Gy) causes behavioral and morphological impairments. Changes are preserved during different post-irradiation periods. The use of Herniarin as a potential antioxidant significantly reduces ionizing radiation-induced neurophysiological disorders.

NANOMOTION BASED DIAGNOSTIC

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Keywords: Atomic force microscopy, nanomotion, diagnostic

Several years ago our team demonstrated that the presence of living organisms onto an atomic force microscope (AFM) cantilever induces nanometric scale oscillations of the lever [1]. The oscillations are detected relatively easily by using traditional AFMs, dedicated homemade devices or simple optical microscopes. This technique can be applied to rapidly detect pathogens antibiotic susceptibility [2,3], cancer cells sensitivity to antimitotic drugs or to explore mitochondrial metabolism in a label free manner [4, 5]. During the presentation, the working principle of the technique will be developed and its potential applications in the field of microbiology, mitochondrial diseases and cancerology will be discussed.

1. Longo, Rapid detection of bacterial resistance to antibiotics using AFM cantilevers as nanomechanical sensors. /G., Alonso-Sarduy, L., Rio, L Marques., Bizzini, A., Trampuz, A., Notz, J., Dietler, G. and Kasas, S.// Nature nanotechnology 2013, Vol.8, n°7, P. 522-6.
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INSTRUMENTATION TO DETECT CELLULAR NANOMOTION

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Keywords: Atomic force microscopy, nanomotion, different technologies

About 10 years ago, our team demonstrated that the presence of living organisms onto an atomic force microscope (AFM) cantilever induces nanometric scale oscillations of the lever [1]. These oscillations, referred to as nanomotion, are nowadays used to conduct rapid antibiotic, antifungal and anticancer sensitivity tests. Cellular nanomotion oscillations amplitude is in the order of the nanometer. Its detection 10 years ago was only accessible to atomic force microscopes. However, in the recent years numerous alternative techniques were developed to detect nanomotion. During the presentation, different technological solutions will be described and their respective advantages and drawbacks will be discussed.
1.Longo, Rapid detection of bacterial resistance to antibiotics using AFM cantilevers as nanomechanical sensors. /G., Alonso-Sarduy, L., Rio, L Marques., Bizzini, A., Trampuz, A., Notz, J., Dietler, G. and Kasas, S.// Nature nanotechnology 2013, Vol.8, n°7, P. 522-6

EFFECTS OF MYO-INOSITOL TREATMENT ON EPILEPTOGENESIS INDUCED INFLAMMASOME PROTEIN COMPLEX EXPRESSION IN RAT BRAIN

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Keywords: Epilepsy, epileptogenesis, myo-inositol, kainic acid; inflammasome protein complex

Epilepsy is a severe neurological disease characterized by spontaneous recurrent seizures (SRS). Approximately 1% of the human population in the world suffer from epilepsy. Multifaceted pathophysiological process referred as epileptogenesis transforms normal brain into epileptic brain. Epileptogenesis is a dynamic and multifactorial process of molecular, cellular and functional reorganization in the brain, characterized with inflammation in the central nervous system (CNS). Currently available antiepilepsy drugs (AEDs) offer only symptomatic relief by suppressing SRS, but they are not able to prevent or cure epilepsy. There are no widely recognized drugs that could effectively prevent the process of epileptogenesis or modify the disorder in humans or experimental animals. At present, myo-inositol (MI) has been identified as a promising antiepileptogenic drug that suppresses biochemical, cellular, electrophysiological and behavioral manifestations of epileptogenesis in kainic acid epilepsy model rats. However, to date, the effects of MI on the epileptogenesis associated inflammation in the CNS, which is a significant therapeutic target, have not been investigated. To address this question, the expression of NLRP3 inflammasome protein complex that participate in inflammatory response in neurons has been characterized in the hippocampus and neocortex during epileptogenesis induced with kainic acid in rats. Quantitative analyses of multiprotein oligomers were carried out with Western Immunobloting technique. SRS were scored according to a modified Racine scoring system. The study has showed that the inflammasome protein complex expression increases in the hippocampus during epileptogenesis (n=5) as compared with control (n=5) (P<0.05). Importantly, the expression of the main components of the protein complex was suppressed in the hippocampus after repeated treatment with MI (30 mg/kg) (P<0.05) (n=5). The study suggests that the MI treatment inhibits inflammation and, thus, contributes to the suppression of epileptogenesis progression.

RODENT PROPIONIC ACID MODEL OF AUTISM: EMOTIONAL AND ULTRASTRUCTURAL CHANGES IN RAT AMYGDALA

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Keywords: Propionic acid model of autism, emotional sphere, amygdala, ultrastructure

Propionic acid (PA), short chain fatty acid, produced as gut microbiome metabolite, is important for health. However, excessive levels of PA provoke various pathologies, including autism. In rodent brain PA provokes molecular and immune modifications that are reminiscent of alterations observed in people with autism (MacFabe). However, little is known about PA-induced brain structural changes. Here we evaluate social behavior, spatial memory as well as the cytoarchitecture and ultrastructure/presynaptic architecture of amygdala central nucleus in adolescent male Wistar rats subjected to single intraperitoneal injection with 175 mg/kg dose of PA. It is well-known that amygdala is not only important in emotional information processing, but also represents the part of the so-called autistic and social brain. Behavior and amygdala ultrastructure were assessed 2, 7 and 21 days after treatment. We show that even such, relatively low dose of PA produces fast (2 days after treatment) and relatively long-lasting (7 and 21 days after treatment) decrease of social motivation, modifications in spatial memory, significant decrease of amygdala neurons and the increase of glial cells. Mostly moderate ultrastructural pathologies were relatively numerous on 7th day after treatment; however, some defects were irreversible. Morphometric analysis revealed modifications of some synaptic parameters. The most significant were alterations in mitochondria. The data are consistent with the proposal that PA may provide the mechanism, where the microbiome dynamically modulates the emotional sphere, including synapse architecture.

The research is supported by FR-21-4759, Shota Rustaveli National Science Foundation, Georgia.

XVII CENTURY GEORGIAN BLACK INK MANUSCRIPT SURFACE STUDY WITH ATOMIC FORCE MICROSCOPY, SCANNING ELECTRON MICROSCOPY AND ENERGY-DISPERSIVE SPECTROPHOTOMETRY

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Keywords: Georgian manuscript of 17th century, atomic force microscopy, energy-dispersive spectrophotometry

Surface measurements of XVII century Georgian manuscripts on paper were made using Atomic Force Microscopy (AFM) and Energy-dispersive X-ray spectroscopy (EDS). From AFM data, the surface quantities (skewness, kurtosis, and average roughness) for red ink and its microcrystals were calculated on different areas of red ink manuscript. From EDS data, chemical element content on the surface of XVII century Georgian red ink manuscript samples were estimated. AFM data were collected from 9.5 μm2, 30 μm2, and 100 μm2 manuscript surface scan areas. EDS data were recorded out of 5 μm2, 50 μm2, 100 μm2, 500 μm2, 1 mm2, and 2.5 mm2 scan areas of manuscript. The angles of 5 microcrystals corresponding to ink surface plane were evaluated. All of them were approximately 80 °. Analysis of both data indicate that on the surface of red ink the α-HgS trigonal microcrystals were formed. In particular, in HgS molecule, mercury content is 86% and sulfur is 14%, which is very close to our EDS data. These results approve that XVII century Georgian red ink manuscript contains HgS molecules rather mercury and sulfur atoms separately. The results indicate that the crystals presented on the surface of XVII century red ink manuscript have α-HgS nature.

STRUCTURAL ALTERATIONS OF BRAIN STRUCTURES DURING PHYSIOLOGICAL AGING

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Keywords: Brain aging, brain volume, amygdala, hippocampi

Background: The differentiation between physiological aging and initial or subclinical forms of dementia is a rather demanding task. The main goal of this study was to determine which brain structures are the most prominently prone to aging.
Methods: The study group was composed of 40 healthy patients who were, based on age, divided in two groups, younger with average age 26,75 +/-2,47 SD and older group which averaged 68,5 +/-5,26 SD years. All patients were scanned with an MR scanner and volumes of their brain structures were calculated by voxel based morphometry.
Results: In the group of older patients compared with younger group, there was statistically significant decrease of total cerebral volume ($p<0.001$), total gray matter volume ($p<0.0001$), total white matter volume ($p<0.024$), average thalamic volume ($p<0.0001$), average putamen volume ($p<0.0001$) and average caudate volume ($p<0.004$), while the average volumes of lateral venticles presented statistically significant increase ($p<0.002$). There was no significant decrease of hippocampal ($p=0.438$) and amygdala ($p=0.373$) volumes between two groups.
Conclusion: Hippocampi and amygdala seem to be the most resistant to volume loss in healthy brain aging compared to other brain structures.

BEHAVIORAL CONSEQUENCES OF SOCIAL STRESS ON GROUPS OF RATS

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Keywords: Social stress, depression, fluoxetine, rats

Introduction. The tendencies of social interactions in today's word, such as conflicts and violence, mass migration, social and economic factors jointly trigger different mental disorders, including increasing cases of depression. The social environment is commonly considered to be an important source of stressors. Based on the available studies, socially dependent animals of submissive behavior type appear to be rather sensitive to stress and are likely to develop depressive behaviors. Consequently, the aim of our research was to study the effect of social stress on behavior of group of rats.
Methods. Experiments were performed on Wistar male rats. In experimental groups (A, B) dominants were subjected to a stressing procedure. For the purpose of stressing, a psychogenic stress model was employed which is a modified method of active avoidance reaction. Stressing procedure was performed with testing of two active avoidance reactions in one experimental session within 7 days. In submissive rats of experimental groups B, under stressing of dominants, fluoxetine at a dose of 15 mg/kg was administered. In order to study depression-like behavior of rats the "forced swim" and "elevated cross maze" tests have been used.
Results. The obtained results are as follows: stressing of dominants submissive rats manifested depression-like behavioral changes (groups A). In particular, in "elevated cross maze" test, the time spent on open arms decreased, while in the "forced swim" test, the duration of immobility increased. The submissive rats of experimental groups B, under administration of fluoxetine did not demonstrate depression- like changes.
Summary. Thus, according to the obtained results stressing of a dominant from a small group of rats resulted in depression-like behavioral changes in submissive rats. Therefore, we suppose that the influence from the part of a dominant seems to be a stress factor of a social character.

STUDY OF SOME PHYSICAL-CHEMICAL PROPERTIES OF GIANT PROTEIN SMITIN AMYLOID FORM BY MEANS OF DIFFERENT METHODS IN VITRO

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Keywords: Giant protein smitin amyloid form, smooth muscle, in vitro methods

Amyloids are insoluble fibrous protein aggregates sharing specific structural features: high content of β-sheet structure ability to bind to Congo red (CR) and thioflavin T, are resistant to solvents and proteases. Amyloids accumulate in a different organs and tissues in the form of insoluble fibers and cause the development of pathological processes. Due to their high firmness they are capable mechanically destroy cell membrane, cause impairment of its viability and eventually its death.
We studied some physical- chemical properties of the amyloid form of giant protein smitin, isolated from chicken smooth muscle (stomach) in vitro. The protein was transferred to the amyloid form using a solution of 0,15 M glycine /KOH, pH 7,0-7,5, I = 0,1. We determined the amyloid nature of smitin using the specific dye Congo red, which binds to amyloid protein and paints it red or pink. We have studied the process of amyloid formation depending on time (20 min, 4h, 24 h); in 20 minutes the formation of amyloid fibrils begins.
We studied smitin circular dichroism spectra before and after the formation of amyloid fibrils. Smitin, under particular conditions, in a diluted solution very quickly creates aggregates of different order and length - According to our data, the secondary structure calculated from the CD spectrum of smitin after chromatography was: α-helix 2,59%, β- sheet 22,24%, random structure 75,17 %. The secondary structure after the formation of aggregates was as follows: α-helix 3,2, β- sheet 30,5%. According to the obtained results, the transition of native smitin to the amyloid form occurs rapidly and the further increase of the incubation time does not cause any change in the secondary structure. The thermal denaturation of amyloid smitin was studied by calorimetric method. The analysis of melting curves indicates that second domain of smitin native molecule and that causes the increasing of denaturation temperature by 10^0 C.

HEMODYNAMIC PARAMETERS IN ISCHEMIC HEART DISEASE ASSOCIATED WITH ARTERIAL HYPERTENSION AND WITHOUT IT. RESEARCH PERSPECTIVES ON STROKE

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Keywords: Ischemia, stroke, pressure

Introduction. At the heart of coronary heart disease is a mismatch between the heart's need for oxygen and the delivery of oxygen to the heart muscle. Most often, the cause of this discrepancy is the narrowing of the lumen of the vessels of the heart by atherosclerotic plaques, which can cause angina attacks. One of the central factors provoking ischemic heart disease is an independent disease - arterial hypertension. The main danger of each of these diseases is provoking a violation not only of organ circulation, but also of macrocirculation and microcirculation of the entire circulation. Violation of microcirculation is always associated with impaired blood circulation in the brain. The problem of study of coronary heart disease and arterial hypertension are multifactorial and deserves special attention from representatives of all areas of biomedicine. Therefore, we present this report to the 5th Biennial International Symposium and School for Young Neuroscientists "Brain and Neuroplasticity. Structural and Molecular Aspects".

Objective. The specific aim of our work was to examine patients with coronary heart disease with moderate arterial hypertension, with coronary heart disease (without arterial hypertension) and patients with arterial hypertension (without coronary heart disease). Materials and methods. The main group of examined patients was coronary heart disease with moderate arterial hypertension aged 50 to 72 years, who underwent coronary angiography. Angina in history less than 1 year was observed in 28% of patients, from 1 to 5 years - in 50%, from 5 to 10 years - in 12% and more than 10 years - in 10% of patients. At the same time, the age of arterial hypertension in 50% of the examined patients ranged from 1 year to 5 years, from 5 to 10 years in 26% and more than 10 years in 24%. The mean systolic blood pressure at the time of the examination was 151±9 mm Hg. Art., diastolic - 88±7 mm Hg. Art. Patients with coronary heart disease (without arterial hypertension) and patients with arterial hypertension (without coronary heart disease) served as controls for the main group. Patients of the main group were divided into 3 subgroups depending on the degree of damage to the coronary arteries. The 1st subgroup included patients who did not have stenosis. Patients in the second subgroup had moderate changes in the coronary arteries (stenosis≤70% in no more than two arteries), the third subgroup consisted of patients with coronary artery disease with hypertension and lesions of two or more coronary arteries with stenosis (more than 70%) in at least one from the coronary artery.

Results. Our data showed an increase in the end-diastolic volume of the left ventricle in patients with isolated forms of coronary heart disease and arterial hypertension, as well as in the group of patients with coronary heart disease against the background of arterial hypertension and coronary artery stenosis. At the same time, there is an increase in end-diastolic pressure,

a decrease in stroke volume and ejection fraction as coronary artery disease progresses in patients with coronary heart disease with arterial hypertension.

Conclusion. Our data are particularly interesting in terms of predicting the course of the disease. Naturally, the more so-called. "Degrees of freedom in diseases", the more difficult it is to standardize treatment and personalize patients. This kind of research is especially important, since they will be able to form a unified systematic approach to determine the likelihood of developing brain strokes. That is why we decided to present this abstract for discussion before our colleagues, neurologists and neuroscience.

EFFECT OF WHITE NOISE ON ADULT RATS' COGNITIVE FUNCTIONS, EMOTIONAL FIELD AND LOCOMOTOR ACTIVITY

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Keywords: White noise, rat, behavior, auditory pathways, electron microscopy

Introduction. A noise pollution is considered to be a severe public health issue since a continuous exposure at even a moderate noise levels can lead to various pathologies, including some neurological states. According to the World Health Organization, about 20 % of Europeans from urban places are negatively affected by a high intensity white noise (HIWN) exceeding 65 dB, which represents the safety threshold.

Objectives. Our goal was to assess the ultrastructural alterations in selective auditory pathways of the rat brain following high intensity white noise exposure. In addition, we intended to assess learning, anxiety-like behavior, short-term memory and locomotor activity.

Material and Methods. We actually had two series of experiments. In first one adult male rats were exposed to 100 dB noise, one hour daily, for 10 consecutive days. The evaluations were performed on day 11. In the second series male female and male rats were exposed to 100 dB noise, one hour daily, for 30 consecutive days. For behavioral experiments multi-branch maze, elevated plus maze, Morris Water Maze and circular open field arena were used. The conventional electron microscopy was also used.

Results The results did not show any major significant difference between males and females in either behavioral tests. Summary Experiments revealed that a white noise generally has a minor influence on rat's behavior, but brain's areas were significantly altered.

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SPEECH FEATURES AND EMOTIONAL SPHERE CHARACTERISTICS OF CHILDREN WITH ATYPICAL DEVELOPMENT

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Keywords: Children with atypical development, speech features, emotions recognition, emotions manifestation

Developmental disorders and atypical development are characterized by the peculiarities of the organization of different levels of the speech and emotional sphere. The range of manifestations of emotional state may be limited due to the disease, atypical, reduced, inverted, not age appropriate. Children with autism spectrum disorders (ASD) have a wide range and a vivid pattern of manifestations of impairments. The goal of the study is to identify acoustic features of speech that could be biomarkers of diseases and specificity of the emotional sphere of children, depending on age and psychoneurological state. The participants of the study were typically development children, children with ASD, Down syndrome (DS), intellectual disabilities aged 5-16 years. The complex approach including spectrographic, linguistic, perceptual analysis and automatic recognition of speech was used. The Child's Emotional Development Method (CEDM) for assessing the emotional development of children by determining the ability to express their own emotions, the adequacy of emotions and recognition of the emotional states of others was developed. The approach includes information about the development of the child obtaining from parents; interview methods, psychological tests, play situations. The assessment uses a score on the Likert scale. Perceptual and automatic recognition of the emotional state of children with TD, ASD and DS by facial expressions and voce was carried out. The set of acoustic features of speech specific for children with three different types of diagnosis were revealed. The fact of the stability of the revealed acoustic features in a wide age range is noteworthy. Differences in scores for tasks on emotions manifestation and perception by children with different psychoneurological status were revealed. The creation of applications to support, education and socialization of children with atypical development is discussed.

The study was supported by the Russian Science Foundation (Project 22-45-02007).

THE ULTRASTRUCTURE OF RAT AMYGDALA IN YOUNG, ADULT AND AGED RATS. ELECTRON MICROSCOPIC STUDY

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Keywords: Aging, amygdala, ultrastructure, rat

Anxiety is commonly observed in aging population. The understanding of neurobiological basis of such changes should be of great importance for potential intervention. Amygdala is a limbic region which plays significant role in emotions. Earlier we show that aged rats were more anxious than the other groups as evidenced by their scores in the elevated plus maze. In the present study, using transmission electron microscopy, we elucidate the ultrastructure/presynaptic architecture of the central nucleus of amygdala in rats of various age groups: adolescent, adult, and aged animals. In addition to qualitative analysis, we performed morphometric study of different parameters of axo-dendritic synapses. The results revealed that the aged rats had a lower presynaptic area as well as number of such synapses, but surprisingly a higher number of presynaptic mitochondria. Since presynaptic mitochondria provide the energy for neurotransmission, it may be concluded that compensatory mechanisms are still operational during aging, and hence, may be a target for therapeutic intervention at this stage of life span.

The research is financially supported by Shota Rustaveli National Scientific Foundation: Project #DP2016_17

MICROBIAL MODULATORS OF METALS, MATERNITY, METABOLISM, MITOCHONDRIA, MEMORY, MOOD, AND MIND: THE ROLE OF NUTRITION AND THE MICROBIOME IN BRAIN HEALTH AND DISEASE

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Keywords: Autism spectrum disorder (ASD), gut microbiome, short chain fatty acids (SCFA)

Clinical observations suggest that gut and dietary factors, transiently worsen, and in some cases appear to improve, symptoms in many neurological conditions but the reason for this is unclear. Recent evidence suggests many conditions including autism (ASD), anxiety, mood disorder, obsessive compulsive disorder, dementia, long haul Covid and post-traumatic stress disorder may be systemic disorders of increasing incidence manifesting altered immunity, metabolism and gene expression, and altered components of the gut microbiome. Pre or perinatal infection, antibiotics, hospitalization, diet or recent human migration are emerging as a major risk factor for many neurodevelopmental and neuropsychiatric conditions. It has proposed that short chain fatty acids (SCFA) represent a group of compounds produced by the host microbiome from dietary carbohydrate fermentation, which can induce widespread effects on host gut, brain, immunity and behavior that are time and dose sensitive. Collectively SCFA provide a mechanism where the microbiome may "sculpt" brain development, cognition and behavior throughout the lifecycle. Imbalances in SCFA metabolism may link the diverse symptoms and findings in ASDs, but also many CNS conditions.

This research offers further support that gut microbiome metabolites, such as dietary or enteric bacterially produced SCFA are: 1) underappreciated modulators of brain development, function and behavior that are time, tissue and dose specific , 2) may be plausible environmental agents that can trigger and possibly prevent many neurological condition, 3) offer potential novel preventative and therapeutic therapies throughout the lifecycle, and 4) deserve further exploration in basic science, agriculture, nutrition, public health policy and clinical medicine.

Nutrition, not only at the personal level but also in public health and education, has tremendous evidence based and cost-effective potential to prevent and treat many metabolic, immune and CNS disorders in advanced and developing societies, particularly in "disadvantaged" groups. Further interdisciplinary studies in the mechanistic understanding of the role of nutrition, environment, microbiome, metabolism and immune host interaction have great potential in promotion of mental health and a functioning society.

THE KILEE PATCHELL-EVANS AUTISM RESEARCH GROUP – USING MULTIDISCIPLINARY TECHNIQUES TO EXAMINE NUTRITIONAL, IMMUNE, METABOLIC, EPIGENETIC AND MICROBIOME INTERACTIONS IN BRAIN HEALTH AND DISEASE

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Keywords: Neuroplastic changes, gut microbiome, short chain fatty acids (SCFA), autism spectrum disorder (ASD)

There is emerging evidence that alteration of diet (reduction of "refined" carbohydrates, and promoting increases in inulin containing fibres, traditionally fermented foods, butyrate, omega 3's, carnitine) may potentially improve neurocognition and immunity through microbiome mediated pathways. This may occur via alteration of microbial populations, their metabolites (increased butyrate/reduced propionate) and neuroplastic changes (synaptic, gut/blood brain barrier, microglial/ immune, energy production, lipid alteration and gene expression).

Dr. MacFabe and his collaborative team have found, through basic and translational research and clinical studies, that dysregulation of enteric SCFA, present in diet and produced by the gut microbiome, particularly by opportunistic gut bacteria following carbohydrate ingestion, may be key triggers in ASD.

Propionic acid, a SCFA fermentation product associated with ASD associated gastrointestinal bacteria and also, a common food preservative, when administration in rodents, elicits behavioral (hyperactive, antisocial, object fixation, perseverative) electrographic (seizure, tics), neuroinflammatory, metabolic (lipid, mitochondrial, redox, glutathione, acylcarnitine) and epigenetic changes closely resembling those found in ASDs and related conditions. Similar studies have been found with lymphoblasts and neuronal stem cells from neurotypical and ASD cell lines and isolated mitochondria. Thus, these SCFA directly or indirectly contribute to acquired mitochondrial, immune, synaptic and epigenetic dysfunction, and are predictive novel biomarkers in a large cohort of ASD patients. Of note, diet (refined carbohydrate/low inulin), and common medications (antibiotics, omeprazole, acetaminophen) may impair mitochondrial/ redox function by mutually enforcing means, by altering gut flora, inhibiting carnitine transport or glutathione metabolism, and inducing immune, neuroplastic and epigenetic changes, providing a mechanism for many neurodevelopmental and neuropsychiatric conditions, and metabolic disorders (metabolic syndrome).

Closer investigation of older "archaic modern" agricultural practices stressing local, unprocessed and fermented foods, such as that found in the Georgian Republic and its role in health and disease is strongly warranted.

PROPOSED RELATIONSHIP BETWEEN BLOOD RHEOLOGY AND NEOPLASTICISM

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Keywords: Ischemic stroke, blood rheology, neuroplasticity

Ischemic stroke is a serious medical and social problem. Residual effects of varying degrees after a stroke are observed in more than 75% of patients. There are three levels of recovery of motor functions after a stroke. True recovery is a complete resumption of motor function. It is possible in the absence of neuronal death, the pathological focus consists of inactivated cells; compensation - functional restructuring and involvement of new, previously unused structures; readaptation or adaptation to an existing defect. Understanding the role of neuroplasticity is critical to optimizing functional recovery and reducing disability in stroke survivors. According to the World Health Organization, neuroplasticity is the ability of cells of the nervous system to regenerate anatomically and change functionally. At the same time, the processes of neuroplasticity are associated not only with the neurons themselves. Qualitative and quantitative changes in neuronal connections and glial elements, the development of new sensorimotor pathways are also important. One of the new drugs used at all three levels of recovery is (8beta)-10-Methoxy-1,6-dimethylergoline-8-methanol 5-bromo-3-pyridinecarboxylate (C24H36BrN3O3). However, our study was aimed at studying the rheological parameters in vitro. Trade name not mentioned to avoid conflict interests between scientific, medical and pharmaceutical society. It turned out that the test substance (C24H36BrN3O3) has a positive effect on all rheological parameters. Our research has led us to believe that the rheological regulation of circulation is involved in the process of neuroplasticity. Although, to confirm our assumption, it is necessary to continue multidisciplinary research together with neurophysiologists, neurologists, researchers of the brain and neuroplasticism.

SOCIAL STRESS CAUSES DEPRESSIVE-LIKE BEHAVIOR IN SUBMISSIVE RATS

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Keywords: Social stress, depressive behavior, rats

Introduction. The social stress represents the main provoking factor of mental disorders, including depression. Therefore during the last decade there is a renewed interest in the use of

the social stress in animal models of stress pathology. The aim of our research was to study in small groups of rats the impact of social stress induced by dominant's stressing on the behavior of submissive rats.
Methods. Experiments were performed on Wistar male rats. In experimental groups dominants were subjected to stressing procedure. The selection of animals was made via dominant and submissive according to the recorded behavioural parameters in conflict situations under high nutritional and first motivations. For the purpose of stressing dominants the immobilization stress model was used (during 7-days). In order to study anxiety and depression-like behavior of rats we used "forced swim" and "elevated cross maze" tests. We determined the concentrations of serotonine in the hypothalamus and corticosterone in the plasma of the rats.
Results. The obtained results demonstrated that after stressing of dominants submissive rats manifested depressive-like behavioral changes. In particular, in "elevated cross maze" test, the time spent on open arms decreased, while in "forced swim" test increased duration of immobility. Therefore we suppose that the influence from the part of a dominant seems to be a stress factor of a social character. Against the background of behavioral changes serotonine concentration increased in the hypothalamus both in dominants and submissives, suggesting that serotonine is implicated in the stress reaction mechanism.
Summary. The obtained results show that the stressing of dominants (during 7- days) in groups of rats induces depressive-like behavior in submissive ones. The obtained results emphasize the importance of social stress factors in the development of stress related diseases.

AGING AFFECTS THE ULTRASTRUCTURE OF RAT HIPPOCAMPUS

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Keywords: Aging, hippocampus, ultrastructure, morphometry, rat

Aging affects many systems of the organism including central nervous system. Among such alterations are cognitive changes. Although the basis of such changes is not well known, ultrastructural alterations in corresponding brain areas are likely contributing factors. Earlier, using Morris water test and multi-branch test, we described the process of learning and spatial memory in adolescent, adult and aged male Wistar rats. We have shown significant impairments in few indices of cognitive functions in both tests in aged rats compared to the other two age groups. Both cognitive processes depend from the function of the hippocampus. In the present research, we performed ultrastructural analysis of the CA1 region of the hippocampus in male Wistar rats of the same aged groups. We described some ultrastructural alterations in neurons, glial cells and synapses in aged animals. In addition, electron-microscopic morphometric analysis was shown that a total number of presynaptic vesicles as well as vesicles in the resting pool were significantly lower, whereas postsynaptic mitochondrial area was significantly higher in aged rats compared to the other age groups. No significant differences in presynaptic terminal area was detected between the three age groups. These results indicate that selective ultrastructural changes in specific hippocampal region may accompany cognitive decline in aging rats.

EFFECTS OF RESVERATROL AND QUERCETIN ON MORPHO-FUNCTIONAL DISORDERS CAUSED BY EXCESS OF MANGANESE

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Keywords: Manganese, quercetin, resveratrol, brain, behavior

Trace amounts of manganese (Mn) are essential for good health, but overexposure to this element has been associated with neurotoxicity. Natural compounds oxidative stress plays a central role in Mn-induced neurotoxicity and therefore the potential neuroprotective effect of several antioxidants has been investigated. Wistar rats were assigned to groups: rats in control groups (male, female) were given regular water, while rats in other groups drank water with final manganese concentration of 20 mg/ml (male, female), with manganese, manganese and resveratrol (20 mg/kg) and manganese with quercetin (25 mg/kg) for three months. To study exploratory and anxiety behavior rats were tested in open field, home cage and elevated plus maze. To estimate learning and memory status a multibranched maze was used. Intoxication with manganese compounds has a significant impact on the aggressive behavior and emotional state of animals. Decreased locomotor activity is observed in female rats. Rats intoxicated with manganese ions lag behind control animals in learning and memory ability. Disorders in the learning process are more pronounced in male individuals. Accumulation of manganese ions from areas of the brain is particularly pronounced in the hippocampus and cerebral cortex. Changes in the number of neurons from the hippocampal region were observed in the CA3 field and the dentate gyrus. Resveratrol as an antioxidant has a positive effect on shifts caused by intoxication of manganese compounds, but the effect is quite small. More effective was quercetin exposure on behavioral disorders, especially it was revealed in female rats. It also was revealed in the number of neurons. In some regions of brain this effect was statistically significant. We can assume that administration of quercetin (25 mg/kg) to Mn-exposed rats showed improvement of histopathological alteration in comparison to Mn-treated rats.

MORPHOLOGICAL CHANGES OF LIMBIC SYSTEM IN ADULT RATS INDUCED BY PRENATAL ALCOHOL INTOXICATION

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Keywords: Prenatal alcohol intoxication, fetal alcohol syndrome

Alcoholism is one of the actual problems in modern neuroscience and medicine. It is especially important to study the morpho-functional changes in brain disorders of the offspring as a result of prenatal intoxication with ethanol. Drinking alcohol by women during pregnancy causes fetal alcohol syndrome (FAS) in their offspring. Alcohol intoxication during pregnancy

inhibits the growth of the fetus, damages the brain structures, causes damage to neurons and finally their death, respectively degeneration of afferent and efferent connections, which leads to functional disorders and cognitive deficit. The aim of our study was to study how morphological changes caused by prenatal alcohol intoxication are preserved in the structures of the limbic system of adult rats. Experiments were conducted on 2 groups of 6-month-old offspring of white barren rats: intact and experimental (female rats received 15% ethanol solution instead of water during puberty). Quantitative changes of pyramidal neurons in the cortex of the limbic system (entorhinal cortex, cingulate gyrus) and hippocampus, multipolar neurons in the medial and lateral nuclei of the transparent septum, and granule cells and glial cells in the dentate fascia of the hippocampus were determined. The experimental material was processed by the method of variance statistics (ANOVA). According to the obtained data, it is clear that the number of neurons in the examined cortical and subcortical structures in the 6-month-old offspring suffering from FAS syndrome is reduced compared to the control group. In the medial and lateral nuclei of the septum pellucida, in the CA1 and CA3 fields of the hippocampus, and in the dentate fascia, this reduction is statistically significant, and in the entorhinal cortex and cingulate gyrus, this reduction appears to be a trend. As for the study of the quantitative changes of glial cells, a similar picture was revealed. Thus, in 6-month-old offspring suffering from FAS syndrome, the decrease in the number of nerve and glial cells caused by prenatal ethanol intoxication is preserved in 1-month-old animals with the same syndrome.

HYPOTHALAMIC-PITUITARY-HORMONAL AXES: NEW INSIGHTS ON THE REGULATION OF NEUROCOGNITIVE FUNCTION

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Keywords: Hypothalamic-pituitary adrenal axis, Cushing's syndrome, structural changes in the hippocampus

This talk will review the hypothalamic-pituitary adrenal axis and disorders associated with glucocorticoid excess. The effects of Cushing's syndrome on the brain and neurocognitive function will be explored, highlighting data on memory, circadian rhythm and structural changes in the hippocampus associated with hypercortisolism.

ROLE OF ANTIOXIDANT SYSTEMS, Na/K- ATP AND HORMETIC EFFECTS OF RADON ON THE BEHAVIOR OF EPILEPTIC RATS

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Keywords: Epilepsy, KM rat strain, behavior

The KM rat strain differs from the Wistar rat strain in the nature of the locomotor activity, a higher level of exploratory activity, and increased emotionality. For rats of the KM rat strain, instability of behavioral reactions is characteristic, which manifests itself in all areas of their activity in the "open field" test. As for memory in epileptic rats, the behavior based on negative stimuli is not impaired in their psycho-neurological memory. Conditioned-reflex behavior developed on a positive stimulus, which we studied in a trestle-type maze, the obtained results showed that 10 epileptic rats complete the exit of this maze in 1 minute, already after 7 days without error. We have studied three sections of social environment awareness. It was determined that the time ($p<0.001$) and the number of contacts ($p<0.001$) were statistically significantly reduced among KM male rats. Decrease in indicators of social interaction: Group KM reliably spent less time in the compartment with animals ($p<0.01$) and spent more time near its cell. As a result of movement in the cross-maze, it was determined that KM rats spent more time in the closed arm, had more interrupted and rotated (tail-to-front) grooming than in the open arm, and also had a higher number of stand-ups than in the open arm, which is an indicator of its high anxiety.

COLLECTION OF HUMAN BRAIN DEVELOPMENT AT THE INSTITUTE OF HUMAN MORPHOLOGY

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Keywords: Human brain atlas, human prenatal development, fetal brain, forebrain, neurogenesis

The human fetal brain maturation has received particular attention with the development of neuroimaging techniques (MRI, CT) and their routine use in clinical practice. Due to the much lower resolution of these methods, the obtained results should be compared with histological maps of the brain. However, recent histomorphological data on the human brain development are quite fragmentary. The Collection of the prenatal human development is assembled at the Laboratory of Nervous System Development of Research Institute of Human Morphology, Moscow. The Collection was founded more than 40 years ago. Up-to-date it consists of more than 200 human embryos and fetuses which staged from the second postconceptional week (2 pcw) to birth. The Collection is presented as wet material, also as histological and immunohistochemical microscopic preparations, including serial sections of the developing brain. In 2021, the online project "The Collection of human brain development of the Research Institute of Human Morphology" has been selected for a grant of the FENS History Committee. (https://brainmicroscopy.com/en/collection/homo/brain-development/).
The recent project has been granted by RSF, which allows our team to start making the first digital multimodal atlas of human brain development in Russian and English on the basis of the Collection. This Atlas will contain both macro- and micro-preparations, annotated atlases and the results of immunohistochemical studies with the main markers of human neuro- and gliogenesis of human brain. To date, the project website (https://brainmorphology.science/) provides general information, a description of the main methods, a brief description and virtual sections of the embryonic and fetal brain at 10-16 gestational weeks. The development of

such an Internet resource has been requested by both basic and applied science researchers and physicians involved in obstetrics and neonatology.
The study is supported by the Russian Science Foundation (RSF) grant #22-15-00172.

FABP-7 DEVELOPMENTAL IMMUNOMORPHOLOGY OF TELENCEPHALON IN THE PRENATAL HUMAN ONTOGENESIS

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Keywords: Human fetuses, brain development, gliogenesis, astroglia, glial markers

A brain-fatty acid-binding protein (FABP-7) – is hypothesized to participate in radial glia establishment, neuroblast migration, and in astrocyte proliferation, associated with CNS injury. It is expressed by the astroglia subpopulations in adult human brain. This study is a part of the Human Brain Development Atlas project: autopsy brain samples from fetuses aged from eight pcw to birth had been studied with a wide panel of markers, including astroglia (GFAP and ALDH1L1) ones and anti-FABP-7. Developmental FABP-7-immunoreactivity profiles have been described for the human fetal telencephalon structures. FABP-7-immunorecrive neuroblasts firstly appear at the beginning of the pre-fetal period (8pcw-12gw) in the restricted zone of dorsolateral lateral ganglionic eminence (LGE) (but not medial (MGE)) and adjunct field of the subventricular (svz) and intermediate (iz) zones of neocortex, olfactory bulb and septal ventricular zones. At the 13-14gw separate FABP-7-neuroblsts are described within caudate nucleus, putamen, diagonal band, substantia innominata, and paleocortical plate; FABP-7-immunoreactive fibers, not neuroblasts, are described in iz, lateral migratory curve, insular cortex, internal capsule. At the 15,5gw FABP-7-neuroblasts are abundant within whole striatum, including amygdala. Such FABP-7-immunoreactivity pattern continued up to the end of early fetal period (20-21gw). Only at the middle fetal period FABP-7-neuroblasts are demonstrated in the cortical plate of neocortex, insular and entorhinal cortices. The FABP-7-neuroblast localization shift from the ventricular zone to the periventricular and deep area is described during the early fetal period for the LGE; and later for MGE – at the end of early fetal and beginning of the middle fetal periods. Developmental FABP-7-immunomorphology of telencephalon has revealed different spatiotemporal translational profiles by the FABP-7- and specific pan-astrocyte GFAP-/ALDH1L1-antigens. FABP-7/GFAP and FABP-7/ ALDH1L1 double and FABP-7/ GFAP/ALDH1L1 triple immunolabeling results have also question FABP-7-cells exclusively belonging to the astrocyte population in the developing human telencephalon.
This study is supported by the Russian Science Foundation grant-22-25-00370.

STRUCTURAL FEATURES OF THE ZUCKERKANDL ORGANS AND INTERACTION WITH ADRENAL GLANDS IN HUMAN ONTOGENESIS

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Keywords: Organs of Zuckerkandl, adrenal medulla, chromaffin cells, human ontogenesis, neuroendocrine interaction

Organs of Zuckerkandl (OZ) are a group of paraganglia located in the aortic region and a part of sympathoadrenal system. OZ are thought to be provisional organs expressing endocrine function in intrauterine period, which undergo reduction up to 3 years of live. In some animals OZ are a source of chromaffin cells for adrenal medulla (AM) development. Embryogenesis of AM and the role of OZ in this process in human remains under investigated, as the majority of researchers use animal models. The aim of our study is to clear up the structural and immunohistochemical features of OZ in comparison with adrenal medulla. The study was performed on OZs and AMs from 3 human embryos (including two twins), 1 prefetus and 7 fetuses using immunoperoxidase labeling with antibodies to bIII-tubulin, tyrosine hydroxylase (TH) and S100. OZ in human embryos and fetuses are relatively gross group of paraganglia located in the aortic zone in close contact with sympathetic ganglia. OZ consist of nests of chromaffin cells with prominent cytoplasmic reaction to TH and bIII-tubulin surrounded by S100-positive cells. At the same stages AM was represented by small nests and groups of cells with scarce cytoplasm, which had positive cytoplasmic reaction to TH and bIII-tubulin. The number of chromaffin cells in the part of adrenal anlage adjacent to OZ was much more than in its distant part. OZ are large organs at investigated stages of human ontogenesis. OZ are located in direct contact with adrenal anlage and may be a source of cells for developing adrenal medulla. The immunohistochemical characteristics with the use of antibodies to bIII-tubulin and TH were similar in OZ and adrenal medulla.
The study was done with a support of the state assignment (Theme No. 122030200535-1).

CASE-CONTROL ANALYSIS OF SINGLE-CELL RNA-SEQ STUDIES

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Keywords: Computational biology, brain disorders, scRNA-seq, epilepsy, statistics

Single-cell RNA-seq (scRNA-seq) assays are being increasingly utilized to investigate specific hypotheses in both basic biology and clinically-applied studies. The design of most such studies can be often reduced to a comparison between two or more groups of samples, such as

disease cases and healthy controls, or treatment and placebo. Comparative analysis between groups of scRNA-seq samples brings additional statistical considerations, and currently there is a lack of tools to address this common scenario. Based on our experience with comparative designs, here we present a computational suite (Cacoa – case-control analysis) to carry out statistical tests, exploration, and visualization of scRNA-seq sample cohorts. Using multiple example datasets, we demonstrate how application of these techniques can provide additional insights, and avoid issues stemming from inter-individual variability, limited sample size, and high dimensionality of the data.

THE EFFECTS OF CHRONIC WHITE NOISE: THE ULTRASTRUCTURE OF THE RAT HIPPOCAMPUS

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Keywords: High intensity chronic white noise, hippocampus, transmission electron microscopy, rat

Objectives/Introduction: Noise pollution is a significant problem for public health. High intensity white noise (HIWN) affects many systems of the organism, including central nervous system. Specifically, HIWN provokes various neurological and/or neuropsychiatric symptoms, including sleep disorders, altered cognition, and emotions.
Methods: In the present study, using transmission electron microscopy (TEM), we assessed the ultrastructural alterations in the hippocampus CA1 area of the rat following HIWN. Rats were exposed to 100 dB of noise for one hour daily for 30 consecutive days. The evaluation was performed on Day 31. Besides qualitative description, quantitative analysis of some parameters of axo-dendritic and axo-spine synapses was performed. One-way ANOVA and two-sample t-test of quantitative data were used.
Results: Mainly moderate alterations were found, but in some cases, irreversible modifications, such as neuronal apoptosis, chromatolysis and significant destructions of several cytoplasm organelles were described. In addition, in some places, significant glial activation was present. Some quantitative changes were also present. The most significant were alterations in presynaptic mitochondria and the number of synaptic vesicles. Specifically, the decrease of the total number of vesicles was detected. Such results suggest that due to continuous transmission, the majority of vesicles are unable to replenish their cargo via transporters.
Conclusion: The results provide evidence that detrimental effects of loud noise are reflected on the hippocampus ultrastructural level.
This research was supported by Shota Rustaveli National Science Foundation of Georgia under award number FR-21-1501 and Ivane Beritashvili Center of Experimental Biomedicine.

AgRP NEURONS ARE NECESSARY FOR EXPLORATORY BEHAVIOR DURING CALORIE RESTRICTION AND THEIR ROLE IN AGING

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Keywords: Reduced food intake, NPY/AgRP neurons, aging

The hypothalamic melanocortin cells are pivotal to metabolic adaptation. Calorie restriction can prolong healthy life span in mammals. The underlying mechanisms involved in this process are ill-defined. We show here that reduced food intake promotes the activity of NPY/AgRP neurons in the brain, and that disrupting the normal function of AgRP cells lead to impaired behavioral but not metabolic responses to calorie restriction (CR). These findings highlight the pivotal role of the NPY/AgRP neurons during CR in regulation of complex behaviors. In addition, the quality of the function of AgRP neurons determines the effect of caloric restriction on lifespan. Therefore, we also examined the intracellular parameters of AgRP and POMC cells at different ages using quantitative electron microscopy. Our data show that most parameters of AgRP cells are stable, however, the intracellular structure of POMC cells is highly susceptible to changes. We confirmed that AgRP neurons are smaller, compared to POMC cells. Interestingly, the density of lysosomes is stable in AgRP cells, however, in POMC cells they decrease until mid-age and then increase in the last phase of aging. Importantly, the density of residual bodies in POMC cells increased steadily, while this increase was less obvious in AgRP cells. Comparing these parameters in animals that were maintained on either a standard diet (SD) or a high-calorie diet (HFD) we found that in POMC cells, but not in AgRP cells of HFD animals, the number of residual bodies was significantly increased, similar to aging. HFD has been shown to promote the development of age-related chronic diseases in mice. Taken together, AgRP neurons are more resistant to aging and HFD may promote ageing of POMC cells.

AgRP NEURONS SHAPE THE PERIADOLESCENT BRAIN AND RELATED BEHAVIORS

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Keywords: Hypothalamic AgRP neurons, medial prefrontal cortex, higher-order brain functions, development, mice

Hypothalamic agouti-related peptide and neuropeptide Y-expressing (AgRP/NPY) neurons have a critical role in in driving food intake, but also modulate complex, non-feeding behaviors of newborn, adolescent, and adult mice, suggesting their broad modulatory impact on brain functions. Here we show that constitutive impairment of AgRP neurons or their peripubertal

chemogenetic inhibition resulted in both a numerical and functional reduction of neurons in the medial prefrontal cortex (mPFC) of mice. These changes were accompanied by alteration of oscillatory network activity in mPFC, impaired sensorimotor gating, and altered ambulatory behavior that could be reversed by the administration of clozapine, a non-selective dopamine receptor antagonist. The observed AgRP effects are transduced to mPFC in part via dopaminergic neurons in the ventral tegmental area and may also be conveyed by medial thalamic neurons. Our results unmasked a previously unsuspected role for hypothalamic AgRP neurons in control of neuronal pathways that regulate higher-order brain functions during development and in adulthood.

HONEY AND BLACK SEED SYNERGESTICALLY PROMOTE REGENERATION OF OLYGODEDNROCYTES IN CUPRIZONE INTOXICATED QUAIL BRAIN

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Keywords: Multiple sclerosis, cuprizone, black seeds, honey, oligodendrocytes, cerebellum

Multiple sclerosis (MS) is a complex disorder, characterized by demyelination and loss of axonal parts of neurons in the central nervous system involving multiple genetic and environmental factors. Although, the demyelinated lesions develop throughout the brain, but more frequently are extensive in white matter. Currently, three different approaches are being utilized to treat MS, where synthetic drugs are the most frequently used but they do not cure the disease. Secondly, the stem cell therapy but this too has limited success in treating MS in humans. The thirds technique involving administering hormones has been found to be most effective method but this too have some significant side effects. Alternatively, natural products can potentially serve as an affordable and effective substitute for the treatment of MS with minimum or no side effects. Black seeds (Nigella sativa) and honey possessing potent neuroprotective, antioxidant, and anti-inflammatory properties with no reported side effects can be a prospective candidate for an alternate remedial treatment of MS in animal model as well as in humans. In this study we established a new animal model (quail), to assess the synergistic efficacy of honey and black seed against demyelination within brain. A total of 35 male quails were used, among 10 were non treated and 25 were treated with 200 mg/kg/day cuprizone (CPZ) demyelination for six months to induce demyelination. After that they were divided into seven groups of five animals each where 3 CPZ treated groups received either honey, black seed oil or mixture of both for 6 weeks after demyelination. Behavioral tests were performed at the end of treatment. Afterwards, oligodendrocyte population was estimated in cerebellar white matter after histology. It was found that all three treatments efficiently induce remyelination. Interestingly, the mixture of honey and black seed was significantly more efficient than honey and black seed alone. Our data support the need of clinical trials for administration of N. sativa and honey in MS patients.

CORTEX OF PROTEIN-FREE NUTRITIONAL STRESS

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Keywords: Neuroglial cells, orbital cortex, rats, stress, transmission electron microscopy

Introduction. Orbital cortex structures play the role of an integrative center and are subjected to destructive changes as well as adaptive reactions in various experimental conditions.
Objectives. In the present study compared to control groups the changes occurring in the nerve and glial cells located in the orbital cortex of the brain of resistant to stress white rats fed with protein-free food were studied by TEM.
Materials and Methods. In the experimental group, 90-120 db sound wave were used as a stress stimulus for 2 minutes. Pieces were taken from the orbital cortex on the 30th day of the experiment. Samples were prepared in Araldite-Epon blocks. Semithin sections were prepared using a Leica EM UC7 ultramicrotome, stained and viewed under a Primo Star microscope. Ultrathin sections of 50-70 nm thickness obtained from the same blocks were first stained with 2% uranyl-acetate and then with 0.4% pure lead citrate. Electrongrams were recorded by examining the sections in a JEM-1400 TEM under a voltage of 80-120 kV.
Results. While the average diameter of glial cells in the control group did not exceed 6 μm, the average diameter of all microglial cells found in the experimental group corresponding to the hypertrophic group was 7.26±0.43 μm. Microglial cells of this type are located around most neurons. Despite the fact that there is usually a space of 20 nm between glial cells and neurons, in some areas of the latter, the density of plasmolemms surrounding microglia and neurons is so high that the 3-layer structure characteristic of membranes is not observed even with a 100,000 magnification in electron microscope. At the same time, structures specific to communication (nexus) relations are not found among the structures shown. Also, in the experimental group, dark neurons that undergoing degenerative changes are detected.
Summary. The location of activated glial cells not near degeneratively altered dark neurons, but around neurons with accumulations of altered riboprotein complexes in the nucleus and cytoplasm may indicate the protective function of microglial cells.

THE EFFECT OF FLAVONOID NOBILETIN ON THE ACTIVITY OF REGULATORY PROTEIN KINASES UNDER HYPOXIA-HYPOGLICEMIA CONDITIONS

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Keywords: Nobiletin, hypoxia, PC 12 cell line, cell signaling pathway

It is known that ischemia-reperfusion disorders are correlated with the increase of free radicals

and the activation of intracellular signaling pathways. It is known that ischemia-reperfusion disorders are associated with changes in intracellular signaling pathways. The aim of the experiment was to study the preventive effect of the flavonoid nobiletin on intracellular signaling pathways. In particular, what signaling pathways are activated by the treatment of cells with nobiletin. To induce chemical preconditioning, we used nobiletene in PC12 cell culture. Disruption of Akt and Erk-mediated signal transduction significantly contributes in the pathogenesis of various neurodegenerative diseases. AKT pathway regulates cell growth, proliferation, survival, mobility and invasion. ERK is kinase regulates proliferation, differentiation, and survival of the neural cell. We determined AKT and ERK, two representatives of the main signaling system, by incubating PC12 cells with two concentrations of nobiletin under conditions of normoxia, hypoxia and oxygen-glucose deprivation. Hypoxia does not alter cytoplasmic ERK levels in PC12 cells compared to normoxia. Cytoplasmic ERK levels in PC12 cells are increased under hypoxia-glucose deprivation. Both applied concentrations of nobiletin increased cytoplasmic phosphorylated AKT signaling pathway levels under both hypoxia and oxygen-glucose deprivation conditions. When comparing the ratio of cytoplasmic ERK and phosphorylated ERK, it was found that phosphorylated ERK decreases in hypoxic conditions, while glucose-free and hypoxic environments cause an increase in phosphorylated ERK in relation to both hypoxic and normoxic conditions.

ULTRASTRUCTURAL EFFECT OF KAINIC ACID ON HIPPOCAMPAL NEURON. ELECTRON MICROSCOPIC STUDY

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Keywords: Kainic acid-produced rat model of epilepsy, hippocampus, ultrastructure, morphometry

Temporal lobe epilepsy (TLE) is the most common form of partial epilepsy in adults. Several experimental models have been developed to mimic TLE, in order to identify potential mechanisms of epileptogenesis, seizure genesis, or comorbidities. The rodent kainic acid (KA) model is one of the most commonly used. In the present research, we elucidate the ultrastructure of the CA1 area of the hippocampus in adult male Wistar rats at different stages after KA i.p. treatment. In order to achieve epilepsy-like activities, the modified protocol of Hellier was used (an initial dose of KA was followed by repetitive injections until status epilepticus was induced). The hippocampal area was evaluated 24 h, 7 days and 21 days after treatment. Besides qualitative analysis of area, the quantitative analysis of some parameters of axo-spine and axo-dendritic synapses was performed. The special accent was made on the number of synaptic vesicles from different vesicle pools. In parallel with electron-microscopic study, the behavior of animals was examined. The results show that the appearance of status epilepticus is accompanied with significant damages in the ultrastructure of the hippocampus and alterations in total number of vesicles and vesicles located in close vicinity from synapse active zone (readily releasable pool). On seventh day and 21-day after status epilepticus, the ultrastructural alterations were lesser, however significant changes in the hippocampal presynaptic architecture were still observed. These data indicate to progressive alterations in neuronal networks of the rat hippocampus as a result of KA-treatment.

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CITRULINATION – THE IMPORTANT POST TRANSLATIONAL MODIFICATION OF THE MYELIN BASIC PROTEIN

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Keywords: Myelin basic protein, macrophage polarization, astrocytes

Introduction: Myelin basic protein (MBP) is one of the principal constituents of the mammalian myelin sheath and plays a structural role in maintaining myelin stability. Alteration of MBP cationicity may represent a regulatory mechanism for normal myelin assembly or a degradative mechanism in demyelinating disorders. MBP shows extensive posttranslational modifications, among these modifications, deimination is the most significant that involves the conversion of MBP arginine into citrulline by the enzyme peptidylarginine deiminase. Deiminated MBP is structurally less ordered and more susceptible to proteolytic attack.
Objectives: The main objective of our research is to investigate the effects of citrullinated and the most cationic isomers of MBP on the functional activity of different cells. Material and Methods: MBP was isolated and purified from bovine brain white matter. RAW 264.7 macrophages were cultured in DMEM supplemented with heat-inactivated fetal bovine serum. For evaluation of macrophage polarization following treatment of the cells with MBP charge isomers, inducible nitric oxide synthase (iNOS-M1 phenotype marker) and arginase-1 expressions (M2 phenotype marker) were determined in cell lysates by ELISA.
Results: We have found that citrullination of MBP leads to the abnormal formation of myelin membranes. Deiminated C8 isomer tends to polarize RAW macrophages into M1 phenotypes, whereas nonmodified C1 form enhances the activity of M2 phenotype markers. Also, citrullinated isomer of MBP, elicits an inflammatory response in astrocytes.
Summary: Citrullinated myelin basic protein may be important for induction, maintenance and resolution of brain inflammatory processes.

FORMATION OF SOME PHYSIOLOGICAL PARAMETERS DURING EXPOSURE OF LABORATORY MICE TO IONIZING RADIATION

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Keywords: Radiation, cognitive functions, motor functions, behavioral tests

The potential adverse effects of radiation exposure on the human body have long been a concern. Acute gamma radiation exposure can cause brain damage, including the death of nerve cells and changes in brain chemistry, which can negatively affect cognitive and motor functions. Experimental research on the effects of ionizing radiation on living organisms is gaining significance as new radiation-based devices and technologies are introduced in the therapeutic and diagnostic fields of medicine every year. In this study, we investigated the impact of acute gamma radiation exposure on cognitive and motor functions in lab mice. We used two main behavioral tests, including the standard rodent open field test to evaluate motor functions and the Morris water maze to study cognitive functions. The mice were irradiated on a gamma device (source: 137Cs; dose rate: 1.1 Gy/min), with doses ranging up to 4 Gy. We carried out a comparative analysis of the results of the tests on groups differentiated by age and designated learning scheme. To study the learning process, observations were made both in the pre-radiation and post-radiation stages. We found that the negative dynamics of the general physiological state and the decline of related cognitive functions had the most significant impact on the efficacy of learning. The results obtained from both pre-radiation and post-radiation schemes indicate a direct dependence of cognitive functions on the severity of general radiation syndromes.

HOMEOSTATIC REGULATION AND DYSREGULATION OF ACTIVITY SET-POINTS IN CENTRAL NEURAL CIRCUITS

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Keywords: Homeostatic regulation, neural circuits, dysregulation of activity set points

Maintaining average activity level within a set-point range constitutes a fundamental property of central neural circuits. Accumulated evidence suggests that firing rate distributions and their means represent physiological variables regulated by homeostatic systems during sleep-wake cycle in central neural circuits. While intracellular Ca2+ has long been hypothesized as a feedback control signal, the source of Ca2+ and the molecular machinery enabling network-wide homeostatic responses remain largely unknown. I will present our experimental framework on identification of homeostatic regulators in neural circuits. Next, I will show our new results on the molecular machinery underlying regulation of activity set-points and feedback responses. Finally, I will provide an evidence of state-dependent dysregulation of activity set-points at the presymptomatic disease stage in familial Alzheimer's models.

MOLECULAR MECHANISMS OF RECOGNITION MEMORY OF VISUAL IMPRINTING IN CHICKS – SINGLE NUCLEI RNA-SEQ STUDIES

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Keywords: Imprinting, mesopalium, single-nuclei RNA sequencing

Visual filial imprinting in the domestic chick is a learning process whereby young animals come to prefer a visual stimulus after exposure to it (training). It is a type of learning having favorable characteristics for memory research. For visual imprinting memory strength may be measured in terms of behavioral preference, namely approach to the training stimulus relative to approach to a stimulus not previously seen and correlated with molecular changes. The available evidence indicates that the intermediate medial mesopallium (IMM) in the domestic chick forebrain is a site of memory formation during visual imprinting. IMM is composed of multiple cell types that play different roles in imprinting learning and memory, however this topic is less explored. Identification of learning and memory related molecular changes in individual cell types will be of great importance. In our experiments IMM tissues from the left hemisphere were obtained 24h after imprinting from trained (strong memory) and control (naïve) chicks. More than 53000 nuclei from IMM were subjected to a single-nuclei RNA sequencing (snRNA-SEQ) analysis by 10X genomic methodology to elucidate contribution of specific cell types in memory formation. At least 35 different cell groups were identified by gene expression analysis, which included numerous subtypes of glutamatergic and gamma-aminobutiric acid (GABA) neurons. Differentially expressed genes include number of a coding as well as long-non coding RNAs. These differentially expressed transcripts were allocated to specific cell groups. One of the significantly upregulated genes in Glutamatergic and GABA –ergic cells, but not in astrocytes or oligodendrocytes was identified as a LUC7-like protein. This protein is a component of U1 small nuclear ribonucleoprotein (U1 snRNP) complex and bind distinct factors regulating unique alternative splicing events. We have further shown the level of LUC7-like protein correlates with memory strength only in the left IMM and not in the right IMM or other control brain regions. The correlation studies for long-nom coding RNAs are in progress.

3D ORGANIZATION OF TRANSCRIPTIONAL COMPETENT rDNA CHROMATIN: A MULTIFOLD LOOP MODEL AS REVEALED BY ELECTRON TOMOGRAPHY OF UBTF

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Keywords: Nucleolus, rDNA chromatin, fibrillar centers, RNAP I, UBTF, 3D ultrastructure

Although apparent achievements the question how active r-genes are spatially packed within nucleolar territory remains largely unsolved. In this respect upstream binding transcription factor (UBTF), posed as a key co-regulator of the RNA Polymerase I (RNAP I), has become recognized as reliable marker to trace rDNA genes. Here we used these data to improve our previous model of 3D organization of rDNA gene within fibrillar centers (FCs). As an architectural transcription factor, UBTF plays a role in the maintenance of "open" r-DNA, in its bending, looping and folding. Meanwhile, no data exist on UBTF ultrastructural localization, its 3D organization or its reorganization during of rRNA transcription inhibition induced during mitosis or by drugs. UBTF exists as two splicing variants UBTF1 and UBTF2 which cannot be discerned with antibodies raised against UBTF. We investigated the ultrastructural localization of UBTF in cells synthesizing GFP-tagged UBTF1 or UBTF2 isoforms by using anti-GFP antibodies and pre-embedding nanogold strategy. This strategy was chosen to obtain a strong signal to noise ratio allowing to perform precise electron tomography. We used medium voltage scanning-transmission electron tomography to reveal changes in spatial distribution of UBTF isoforms within nucleolar components during rRNA Synthesis Inhibition. In control cells, these two isoforms are mainly localized within FCs but showed a different repartition. Electron tomography demonstrated that UBTF isoforms are disposed as fibrils which are folded in loop-like structures. Thus, UBTF1 and UBTF2 show a similar distribution along extended 3D loop-like structures. Finally, when rRNA synthesis is inhibited during Actinomycin D treatment or mitosis, their localization is identical and they remain organized as extended 3D loop-like structures. Altogether these data suggest the key role of UBTF in the loop-like packaging of active and inactive rDNA genes within FCs.

NEUROINFLAMMATION AND NEUROPLASTICITY IN NEURODEGENERATIVE/NEUROPSYCHIATRIC DISEASES: ROLE OF THE GUT-BRAIN AXIS

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With the number of aged people growing and the incidence of neurodegenerative diseases rising, there is an urgent need to slow and/or prevent the devastating consequences of such progressive diseases. This need is further underscored 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 become tangible. Recent advances in elucidation of the interplay between the gut microbiome and the brain, commonly referred to as gut-brain axis, has opened new opportunities in this regard. Here, while examining the role of neuroinflammation and neuroplasticity in Parkinson's disease and depression, novel therapeutic targets and the role of gut microbiota will be presented.

BASIC CONCEPTS IN PHARMACOLOGICAL EXPERIMENTS

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Keywords: Important points in an experimental design, specific questions, their compliance

Here, following a brief description of different pharmacological disciplines and some basic pharmacological concepts (e.g., pharmacodynamics, pharmacokinetics, receptors, drug interactions, etc.), important points in an experimental design to answer specific questions are touched upon. For example, if the goal is to investigate potential usefulness of a drug in depression, selection of a suitable animal model, evaluations of critical end points, interpretation of the data and conclusions, including future directions are discussed. It is expected that the attendees will become cognizant of the important points that need to be considered in any experimental design.

INFLUENCE OF THE TRIAL NUMBERS IN ACTIVE AVOIDANCE TASK ON MEMORY FORMATION IN RATS

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Keywords: Active avoidance, Kamin effect, incomplete learning, number of trials, memory

Avoidance is a response to danger without which animals cannot survive. The active avoidance (AA) experimental procedure is a tool through which avoidance behavior can be studied, in particular motivated instrumental behavior. This procedure is also used to study the formation of implicit memory in animals. To this end, the paradigm of incompletely learned AA is often used. Leon Kamin made an experimental series, where rats were trained to make AA task with incomplete learning. In his study rats were given avoidance task with 25 learning trials in each session. The data obtained by Kamin resulted in a U-shaped retention curve (Kamin, 1957,1963). The purpose of this study was to study the influence of increased learning trials (32) on the Kamin effect formation in rats. Experiments were carried out on 71 inbred albino adult laboratory rats, both male and female. For experimental group learning task was 32 trials of AA procedure, with CS-US interval of 5s, time interval between trials with 1 min and the retention interval between learning and relearning sessions was 0hr; 0,5hr; 1hr; 1,5hr; 2hr; 3,5hr; 4hr; 5hr and 6hr. We measured the mean number of avoidances for each AA session to assess the learning level of the given task. Obtained data indicates that the Kamin effect curve has two minimums and that the intensity of active avoidance learning has no influence on the dynamics curve shape. The Decreasing phase of Kamin effect curves duration has shortened by mere increase of active avoidance trials.

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HYPERALGESIA AND ALLODYNIA IN ACUTE ITCH: TRPA1 AND TRPV1 CHANNELS

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Introduction. Itch (pruritus) is an unpleasant sensation associated with the desire to scratch that occurs primarily in the skin. Like pain, acute itch provides a warning signal for the organism to scratch away insects or plant spicules from the skin surface. Chronic itch is a common sensory experience that is prevalent in patients with inflammatory skin diseases, as well as in those with systemic and neuropathic conditions. The pathological consequences of itching affect the quality of life just as much as pain. Chronic pruritus conditions such as atopic dermatitis, allergic contact dermatitis, or psoriasis pose a significant socioeconomic burden. Hyperalgesia and allodynia are prominent symptoms in patients with neuropathic and inflammatory pain and itch. The respective corresponding phenomena of alloknesis and hyperknesis are also present in the context of pruritus.
Discussion. Itch is considered to be encoded by two major neuronal pathways: histaminergic and nonhistaminergic. In the majority of cases, the crosstalk among keratinocytes, the immune system, and nonhistaminergic sensory nerves is responsible for the pathophysiology of chronic itch. In this report, we review the latest evidence on thermal hyperalgesia and mechanical allodynia induced by histamine and non-histaminergic pruritogens, with a respective involvement of transient receptor potential (TRP) channels TRPV1 and TRPA1, respectively, in itch sensation. The present and previous findings indicate that histamine and the non-histaminergic pruritogens chloroquine, BAM8-22, and SLIGRL induced thermal hyperalgesia and mechanical allodynia which appear to coexist with itch. Histamine acts via TRPV1 but not TRPA1, while the non-histaminergic pruritogens act via TRPA1, underscoring the importance of these ion channels in mediating enhanced pain that accompanies acute itch elicited by these ligands.
Conclusion. One implication of these data is that antagonists of these TRP channels may be useful in the clinical management of increased pain and allodynia, which may be symptomatic in patients with chronic pruritus.

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TRANSDIAGNOSTIC EEG MICROSTATE ANALYSIS IN SCHIZOPHRENIA AND AUTISM SPECTRUM DISORDER

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While schizophrenia (SCH) and autism spectrum disorder (ASD) are clinically differentiable disorders with heterogeneous symptom manifestation, both can be understood as disconnection syndromes of the brain. EEG microstates are global patterns of scalp potential topographies offering a novel method to investigate the integrity of brain networks at the subsecond-level. We aim to investigate how EEG microstate parameters are altered in SCH and ASD, respectively, and whether these alterations can be linked to the severity of clinical symptoms. We have recruited SCH patients (N = 23), ASD patients (N = 27), and controls (N = 16). Participants performed two minutes of resting state with eyes closed and two minutes of resting state with eyes open. Symptom severity was measured by the Positive and Negative Symptom Scale (PANSS) and the Autism Diagnostic Observation Schedule (ADOS). While in previous research SCH has been most consistently linked to alterations in microstates C and D, we found that SCH patients differed from healthy controls in the properties of microstate A. ASD has been previously linked to alterations in various properties of microstates A, B, C and D. In our study, microstates A and B differed between healthy controls and ASD patients. There was a significant relationship between the properties of microstates A and B and clinical symptoms. As microstates A and B have been associated with the auditory and visual resting state networks, our results suggest that these brain networks may be altered in ASD and SCH.

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HYPOTHALAMIC CIRCUITS CONTROLLING ENERGY METABOLISM

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Obesity has become a major public health problem worldwide. The fundamental cause of obesity is the energy imbalance between calorie intake and expenditure. However, genetics, individual, social and environmental factors also play role in the etiology of this complex metabolic disorder. The hypothalamic arcuate nucleus (ARC) Agouti-Related Peptide (AgRP) and Proopiomelanocortin (POMC) neurons play important roles in hunger and satiety feelings, respectively. Our recent findings have shown the importance of Tyrosine hydroxylase (TH) neurons in the hypothalamic feeding pathways. These three circuits process and maintain energy balance. Signaling between the brain and peripheral factors is usually impaired in obesity and metabolic syndrome. Recent discovery of opto/chemogenetic techniques have allowed neuroscientists to better elucidate the hypothalamic circuits controlling energy metabolism by selective excitation or inhibition of specific neuron groups. Use of viral vectors and transgenic mice technology are very useful tools in examining AgRP, POMC and TH projections and circuitry in the brain. In this presentation, utilization of electrophysiology (including patch-clamp technique), opto/chemogenetic and fluorescent microscopy methods in neuroendocrine research will be reviewed.

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