MULTIFACETED NEUROSCIENCE: CELEBRATING 140 YEARS OF IVANE BERITASHVILI

Abstract Book

June 12-14, 2025
Tbilisi, Georgia

The conference is held within the framework of Science Week, supported by the Ministry of Education, Science and Youth of Georgia

ISBN 978-9941-8-7923-4 DOI- 10.48616/openscience-618

LEPL Ivane Beritashvili Center of Experimental Biomedicine

MULTIFACETED NEUROSCIENCE: CELEBRATING 140 YEARS OF IVANE BERITASHVILI

ABSTRACT BOOK

The conference was held within the framework of Science Week, supported by the Ministry of Education, Science and Youth of Georgia

12-14 JUNE 2025
TBILISI, GEORGIA

ORGANIZING COMMITTEE

Prof. Revaz Solomonia, PhD, ScD – Chair
Prof. Gvantsa Chkadua, PhD, ScD
Prof. Sophio Uchaneishvili, PhD
Prof. Mzia Zhvania, PhD, ScD
Prof. Tamar Bikashvili, PhD
Dr. Nino Pochkidze

THE ROLE OF MUTATIONS IN THE HOMEOSTATIC IRON REGULATORY GENE IN NEURODEGENERATIVE DISEASE

James R. Connor

Pennsylvania State University, PA, USA

The homestatic iron regulatory gene (HFE) limits iron uptake into cells by interacting with the transferrin receptor. There are two primary mutations in the HFE gene that disrupt this interaction. One, C282Y is associated with hemochromatosis. The other mutation, H63D, is one of the most common mutations in Caucasians (1 in 7 or up to 15%) and its impact on health has been poorly understood. We began a series of studies to determine how the H63D mutation could impact health. We demonstrated that the mutation is beneficial in Motor Neuron Disease as it slows disease progression. The incidence of the H63D mutation in this population nearly doubles because those people with MND with the H63D mutation live longer and are over-represented. Similarly in environmentally induced Parkinson's Disease there is slower progression and less expression of biomarkers associated with the disease. Stroke patients with the H63D mutation have better outcome as do some Alzheimer's patients. We have attempted to study the mechanisms underlying the impact of this mutation on disease by creating a mouse model. In these mice we have recapitulated the human findings for stroke and Parkinson's disease and have begun a study on Alzheimer's disease. Furthermore, we have shown improved outcomes in the mouse model of traumatic brain injury. To probe the mechanism by which the HFE mutation positively impacts disease progression, we began with the hypothesis that there was activation of the anti-oxidant system because of the potential that the presence of H63D HFE would allow more iron into the brain but not enough to cause damage. Indeed, we found there was an activation of Nrf2, a key player in the anti-oxidant pathway that included activation of proteins that are protective of mitochondria. Moreover, GPX4 is also elevated which limits the possibility of ferroptosis. To explain our findings we have invoked hormesis which is a biological phenomenon where exposure to a low dose of a stressor or toxin, in this case iron, can have a beneficial effect, while it is well-known that higher doses of the same stressor will cause damaging oxidative stress that will lead to cell death and neurodegeneration. The finding of the high prevalence of H63D in neurological disease and its ability to slow disease progression is an exciting opportunity to develop therapeutic targets but it also important to be taken into consideration during clinical trials that should be stratified for this genotype.

OBESITY AND THE CARDIOVASCULAR DISEASE

Fausto Pinto

University of Lisbon, Lisbon, Portugal

Obesity is a significant public health issue hindering global health, social development, and economic progress. It is defined by the existence of excess body fat (adiposity) and is a risk factor for many non-communicable diseases, including cardiovascular disease (CVD), diabetes and several cancers. When excess body fat impairs the health of the individual, obesity can manifest both as a disease in itself and as a risk factor for other diseases, similar to diabetes. It is thus critical to any global and national progress on non-communicable diseases (NCDs) in particular CVD.

It is estimated that over 1 billion people - 159 million children and adolescents and 878 million adults - are living with obesity worldwide. In 2022, the prevalence of obesity was 14.0% and 18.5% in men and women, and 9.3% and 6.9% in boys and girls. If current trends continue, obesity prevalence among adults is projected to rise to 17% of men and 22% of women by 2030, with almost 2 in 3 adults over the age of 25 years having overweight or obesity by 2050.

In 2021, 3.7 million deaths and 128.5 million disease-adjusted life years (DALYs) were lost due to a high body mass index (BMI). For CVDs alone - the leading cause of death globally - high BMI was associated with 1.9 million deaths. This is equivalent to 10% of cardiovascular deaths worldwide.

The links between obesity and CVD are well established with multiple obesity-related mechanisms underpinning the development of CVD, contributing to increased morbidity and mortality. The pathophysiological mechanisms linking obesity to CVD include:

- Adipose Tissue Dysfunction: Excess adipose tissue secretes pro-inflammatory adipokines, leading to systemic inflammation and endothelial dysfunction.
- Insulin Resistance: Obesity-induced insulin resistance promotes hyperglycemia and dyslipidemia, accelerating atherosclerotic processes.
- Hypertension: Increased adiposity elevates blood pressure through sympathetic nervous system activation and renin-angiotensin-aldosterone system dysregulation.
- Dyslipidemia: Obesity alters lipid metabolism, resulting in elevated triglycerides and low-density lipoprotein (LDL) cholesterol, which contribute to plaque formation in arteries.
- Prothrombotic State: Enhanced coagulation and impaired fibrinolysis in obesity increase the risk of thrombus formation, leading to adverse cardiovascular events.
- Other mechanisms: Increased adipose tissue increases circulatory volume, increased adrenergic tone, and sleep-disordered breathing, factors that play a key role in the origin of several CVDs.

Obesity significantly elevates the risk of various cardiovascular diseases (CVDs) through multiple pathophysiological mechanisms:

- Coronary Heart Disease (CHD): Excess adiposity leads to dyslipidemia, characterized by elevated low-density lipoprotein (LDL) cholesterol and triglycerides, and reduced high-density lipoprotein (HDL) cholesterol. These lipid abnormalities promote atherosclerosis, increasing the risk of myocardial infarction.
- Hypertension: Increased adipose tissue activates the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system, and increases circulatory volume, resulting in elevated blood pressure.

- Heart Failure: Obesity contributes to left ventricular hypertrophy and diastolic dysfunction due to increased cardiac workload and hemodynamic changes, predisposing individuals to heart failure with preserved ejection fraction. Obesity can also cause dilated cardiomyopathy through several disease mechanisms.
- Atrial Fibrillation: The pro-inflammatory state associated with obesity, along with structural and electrical remodeling of the atria, in addition to a higher prevalence of hypertension and obstructive sleep apnea, heightens the risk of atrial fibrillation.
- Venous Thromboembolism (VTE): A prothrombotic state induced by obesity, characterized by increased fibrinogen and plasminogen activator inhibitor-1 levels, elevates the risk of deep vein thrombosis and pulmonary embolism.
- Other CVD Conditions That Could Be Caused By Obesity: Ventricular arrhythmias, sudden cardiac death, hypertensive cardiomyopathy can be caused by obesity.

TRP CHANNELS IN PAIN AND ITCH SENSATIONS

Ears Carstens

University of California, Davis, CA, USA

Transient receptor potential (TRP) ion channels participate in many sensory systems including pain and itch. David Julius and Ardem Patapoutian received the 2021 Nobel Prize for pioneering studies of TRP channels in pain and touch. Pain and itch exact annual socioeconomic costs in the hundreds of billions of dollars. Improved understanding of the underlying neural mechanisms will aid the development of better therapies for chronic pain and itch. In rodents, pain is assessed by the duration of hindpaw licking or flinching, or the time to withdraw the hindpaw from a painful thermal or mechanical stimulus. Hyperalgesia (increased pain) and allodynia (touch-evoked pain) are manifested by shortened withdrawal latency. Itch, an “unpleasant sensation associated with the desire to scratch”, is assessed by counting hindpaw scratches directed to an itchy site. Alloknesis (touch-evoked itch) is scratching elicited by a weak mechanical stimulus. The “cheek” model distinguishes between pain (singular forelimb wipes) and itch (hindlimb scratches of the stimulated cheek). Pain and itch share partly overlapping neural pathways. Most first- and second-order neurons that respond to itchy stimuli also respond to algogens like capsaicin. We hypothesize that itch is signaled by activation of pruritogen-responsive neurons, while pain is signaled by a larger population of algogen-sensitive but pruritogen-insensitive neurons. TRPV1 is directly activated by heat >42ºC and capsaicin. In knockout mice lacking TRPV1, capsaicin-evoked pain is abolished and thermal pain is significantly reduced. TRPA1 is associated with chemical pain. Pain from mustard oil is abolished in mice lacking TRPA1. Pruritogens act at G-protein-coupled receptors (GPCRs) which then activate TRP channels, depolarizing the pruriceptor to open sodium channels initiating action potentials. Histamine-evoked scratching is reduced in mice lacking TRPV1. Non-histaminergic itch mediators (chloroquine, BAM8-22) act at Mas-related GPCRs to activate TRPA1. Scratching elicited by chloroqine is abolished in mice lacking TRPA1. Serotonin-evoked scratching is abolished in mice lacking TRPV4. TRPM8 mediates cooling. Histamine-evoked itch is reduced by cooling and topical menthol in a manner requiring TRPM8. Focal application of

histamine to human skin elicits itch and surrounding areas of flare, alloknesis and hyperalgesia; that is, itch and pain co-exist. In mice, several itch mediators elicit thermal hyperalgesia and mechanical allodynia. Histamine-evoked hyperalgesia/allodynia were prevented by pretreatment with a TRPV1 but not TRPA1 antagonist. In contrast, hyperalgesia/allodynia elicited by non-histaminergic itch mediators were prevented by an antagonist of TRPA1. Ongoing trials are investigating the efficacy of TRPV1 and TRPA1 antagonists in treating pain, hyperalgesia and itch.

NOVEL DEVELOPMENTS AND APPLICATIONS OF NANOMOTION DETECTION IN BIOLOGY AND MEDICINE

Sandor Kasas[1,2]

[1]Laboratory of Biological Electron Microscopy (LBEM), Ecole Polytechnique Fédérale de Lausanne (EPFL), Université de Lausanne, Lausanne, Switzerland; [2]Center Universitaire Romand de Médecine Légale (UFAM), Université de Lausanne, Lausanne, Switzerland

Nanomotion detection is a relatively novel technique for assessing the metabolism of living organisms in real time and in a label-free manner [1]. The method relies on detecting nanometric oscillations that occur in living organisms and that desapears as soon the organism dies [2]. The earliest devices for detecting nanomotion were based on atomic force microscopy. More recently, we demonstrated that nanomotion can also be detected using a conventional optical microscope equipped with a basic camera or even a simple smartphone [3]. Nowadays, nanomotion detection is applied to perform rapid (1–3 hours) antibiotic [4], anticancer [5] and antifungal sensitivity tests as well to explore mitochondrial metabolism [7]. This presentation will explore various techniques for detecting nanomotion and discuss potential future applications.

1. Longo, G.et al. Rapid Detection of Bacterial Resistance to Antibiotics Using AFM Cantilevers as Nanomechanical Sensors. *Nature Nanotechnology* **2013**, *8*, 522–526, doi:10.1038/NNANO.2013.120.
2. Kasas, S.et al. Detecting Nanoscale Vibrations as Signature of Life. *Proceedings Of The National Academy Of Sciences Of The United States Of America* **2015**, *112*, 378–381, doi:10.1073/pnas.1415348112.
3. Willaert, R.G. et al. Single Yeast Cell Nanomotions Correlate with Cellular Activity. *Science Advances* **2020**, *6*, doi:10.1126/sciadv.aba3139.
4. Stupar, P.et al. Nanomechanical Sensor Applied to Blood Culture Pellets: A Fast Approach to Determine the Antibiotic Susceptibility against Agents of Bloodstream Infections. *Clinical Microbiology And Infection* **2017**, *23*, 400–405, doi:10.1016/j.cmi.2016.12.028.
5. Stupar, P.et al. Nano-Motion Analysis for Rapid and Label Free Assessing of Cancer Cell Sensitivity to Chemotherapeutics. *Med. Lith.* **2021**, *57*, 446, doi:10.3390/medicina57050446.
6. Villalba, M., I.et al. Nanomotion Spectroscopy as a New Approach to Characterize Bacterial Virulence. *Microorganisms* **2021**, *9*, doi:10.3390/microorganisms9081545.
7. Stupar, P.et al. Mitochondrial Activity Detected by Cantilever Based Sensor. *Mechanical Sciences* **2017**, *8*, 23–28, doi:10.5194/ms-8-23-2017.

THE POROSOME SECRETORY NANOMACHINE: DISCOVERY TO THERAPY

Bhanu Jena

Wayne State University, MI, USA

Life process is managed through secretion-mediated cellular communication. The discovery of a secretory portal—***the porosome*** nearly 30-years ago, has resulted in a paradigm-shift in our understanding of cell secretion. We now know that secretory vesicles transiently dock and fuse at porosomes via t-/v-SNARE proteins, and swell rapidly through aquaporin-mediated water transport to secrete. The result is the release of a measured portion of intra-vesicular contents into the extracellular milieu. Porosome-mediated secretion is present in all cells. Altered porosome proteins result in a wide range of secretory defects leading to disease. The porosome-mediated principles discovered and described, has turned out to be universal, operating similarly in all animal cells. A number of human hereditary diseases are caused by mutations in some of the nearly 30 proteins composing the porosome complex. The discovery of the porosome, in addition to providing a deep understanding of cell secretion, has also contributed to the establishment of a drug development platform for the treatment of a wide range of diseases resulting from secretory disorders such as Alzheimer's, Cystic Fibrosis and Diabetes. New and novel curative therapies developed for Alzheimer's and Cystic Fibrosis will be discussed.

GENE AND CELL THERAPIES FOR EPILEPSY

Merab Kokaia

Epilepsy Center, Lund University, Lund, Sweden

Gene and cell therapies are emerging as promising strategies for the treatment of epilepsy, a neurological condition affecting over 65 million individuals worldwide, with significant clinical and economic burdens. Current pharmacological treatments are insufficient for 30-40% of patients and often produce substantial side effects, highlighting the urgent need for alternative approaches.
This presentation outlines advanced strategies involving gene and cell therapies, aiming to restore the balance between excitatory and inhibitory neural networks disrupted in epilepsy. The traditional view of gene therapy involves introducing healthy genes to replace defective ones, while an alternative approach is amplifying beneficial functions. Using recombinant adeno-associated viral vectors (rAAV), the presented research has targeted the neuropeptide Y (NPY) system, specifically the Y2 receptors in the hippocampus, to reduce excitatory neurotransmitter release and consequently seizures. Preclinical studies demonstrated that combined gene therapies, such as rAAV-Y2 and rAAV-NPY, significantly delay seizure onset and reduce seizure frequency in translational models.
Moreover, the integration of advanced chemogenetic systems, such as Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) and Pharmacologically Selective Actuator Modules (PSAM), further refines therapeutic control over neuronal activity. Complementary cell therapy approaches, involving encapsulated cells engineered to produce neurotrophic factors like

GDNF or transplanting human embryonic stem cell-derived interneurons, have also shown efficacy in suppressing seizures.

The presentation emphasizes the translational potential of these therapies, forecasting clinical trial milestones within the next five years for direct gene therapies and stem cell therapies, and beyond five years for more advanced methods such as chemogenetics. These innovative strategies represent a significant step forward in addressing treatment-resistant epilepsy, offering hope for improved seizure control and quality of life for patients.

HUMAN REPROGRAMMED CELLS FOR RESTORATION OF STROKE-DAMAGED CORTICAL NETWORK

Zaal Kokaia

Stem Cell Center, Lund University, Lund, Sweden

Stroke is currently the third leading cause of disability-adjusted life-years and mortality worldwide. As the risk of stroke increases sharply with age, incidence, and prevalence are expected to rise even further as a result of an aging population. This disease affects about 3.5 million people in the EU, with 700 000 new cases yearly. More than half of the patients suffer significant residual impairments, causing huge economic and societal burdens. Acute clinical intervention, typically surgical removal or dissolution of the clot by administration of tissue plasminogen activator (tPA), aims to restore blood flow in the affected brain areas and are only possible within a very short time window after stroke onset. Stem cell therapy using human induced pluripotent stem (iPS) cell-derived neural precursors is a promising future therapy for stroke patients. Two main mechanisms have been proposed to give rise to improved functional recovery in animal models of stroke after the transplantation of these cells. First, the" bystander" effect, which could modulate the inflammatory environment by releasing different factors from grafted cells resulting in moderate improvements in the outcome of the insult. Second, the neuronal replacement and functional integration of grafted cells into the impaired brain circuitry. This will ultimately result in optimum long-term structural and functional repair. Our data show, that human skin-derived cortical progenitors can differentiate into cortical projection neurons and functionally integrate (forming afferent and efferent synaptic connections) not only into stroke-damaged rat cortical networks but also into organotypic cultures of the adult human cortex. The grafted cortical neurons respond to sensory stimulation of in live animals and importantly, also affect spontaneous behavior when inhibited by optogenetic stimulation. Stroke leads to the loss of oligodendrocytes and axonal demyelination which contributes to functional impairment. Also, for grafted neurons to become functional their axons should get myelinated. Our data show that human iPS cell-derived cells have the unique ability in addition to differentiating into functional neurons also to generate *bona fide* oligodendrocytes. The generated cells display the structural, molecular, and functional characteristics of human mature oligodendrocytes and can wrap both, grafted human cell- and host-derived axons from cortical neurons in different set-ups, after xenotransplantation into rat stroke-injured somatosensory cortex and the human adult cortical organotypic system. Our findings raise the possibility that injured neural circuitry might be restored by stem cell transplantation also in humans with stroke, which would have major clinical implications.

TRP CHANNELS IN ACUTE AND CHRONIC ITCH: EVALUATION OF HYPERALGESIA AND ALLODYNIA

Merab Tsagareli
Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Itch (pruritus) is an unpleasant sensation that provokes the desire to scratch away insects or plant spicules from the skin surface or dig out invasive parasites. While everyday acute itch reflects an adaptive mechanism to maintain the integrity of the skin, chronic itch can adversely affect the quality of life to the point of depression. In recent years, the role of various Transient Receptor Potential (TRP) channels and other receptors, including G-protein-coupled receptors (GPCRs) and protease-activated receptors (PARs), has been identified as critical in transducing itchy stimuli into action potentials that are conducted over "pruriceptive" primary afferent fibers into the nervous system. Roles for TRP channels have been elucidated in complex diseases of the nervous, intestinal, renal, urogenital, respiratory, and cardiovascular systems in diverse functions including pain and itch, headache, pulmonary function, oncology, neurology, visceral organs, and genetic diseases. Given the importance of TRPA1 and TRPV1 in mediating itch signaling, the investigation of these ion channels has been of considerable interest for their potential roles in contributing to acute and chronic pruritus. Beyond the known expression of TRP channels in the nerve endings of primary afferent neurons, TRP channels have been found in keratinocytes, epidermis, and mast cells. They are upregulated in affected skin in several dermatological pathologies associated with chronic itch, including dermatitis, psoriasis, eczema, and others. In this report, I will concentrate on the role of TRPV1 and TRPA1 channels in histaminergic and nonhistaminergic itch sensations, respectively, in mice.

DEEP BRAIN STIMULATION OF THE MEDIAL SEPTUM IMPROVES MEMORY IMPAIRMENT IN NATURALLY AGED RATS: BEHAVIORAL, IMMUNOHISTOCHEMICAL AND NEUROCHEMICAL STUDY

Gela Beselia[1,3], Maia Burjanadze[1], Revaz Solomonia[1,2], Lia Tsverava[1,2], Nino Chkhikvishvili[1], Mariam Chighladze[1], Temur Naneishvili[1], Barbare Nozadze[1], Manana Dashniani[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ilia State University, Tbilisi, Georgia;
[3]Petre Shotadze Tbilisi Medical Academy, Tbilisi, Georgia

Introduction and Objectives. The hippocampus, which provides cognitive functions, has been shown to become highly vulnerable during aging. One important modulator of the hippocampal neural network is the medial septum (MS). The present study attempts to determine how age-related mnemonic dysfunction is associated with neurochemical changes in the septohippocampal (SH) system, and investigate the effects of MS- deep brain stimulation (DBS) in naturally aged rats. Material and Methods. Behavioral and immunochemical experiments performed on young-adult, middle-aged and aged rats. Learning process and memory function were assessed using a Morris water maze (MWM). The expression levels of cholinergic, GABAergic and glutamatergic receptors

were assessed using Western blotting. Immunochemical experiments were performed to determine age-related changes in the number of cholinergic and GABAergic MS projection neurons and how these changes are associated with mnemonic dysfunction in rats. In the chronic MS-DBS experiment, aged animals received stimulation (60 Hz, 60 μs, 50 μA) 2 hr daily for a period of 2 weeks. Results. A comparison of expression levels of glutamatergic (NR2B, GluR1), GABAergic (α1 GABAA) and cholinergic (muscarinic M1 and α7 nACh) hippocampal receptors among young, aged and middle-aged rats sub-groups indicate a significant decline in the expression level of all these receptors in the hippocampus of middle-aged-impaired and aged rats in comparison to young-adult and middle-aged-unimpaired rats. MS-DBS restores the amounts of hippocampal neuroreceptors to levels comparable with the control group and improves cognitive impairment. Summary. Research into the causal mechanisms responsible for age-related dysfunction of the septo-hippocampal network is important for identifying new targets for the treatment of age-related memory decline. Understanding the role of MS-DBS can have important implications for age-related cognitive disorders in which the SH and consequently the memory systems are severely impaired as observed in natural aging.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG): Grant #-FR-23-18847

CITRULLINATED MYELIN BASIC PROTEIN ISOMER C8 MODULATES INFLAMMATION AND APOPTOSIS: IMPLICATIONS FOR AUTOIMMUNITY

Lali Shanshiashvili[1,2], Marika Chikviladze[1], Nino Mamulashvili[1], David Mikeladze[1,2]
[1]Ilia State University, Tbilisi, Georgia
[2] Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Introduction: Myelin basic protein (MBP) is a key structural component of the myelin sheath, critical for axonal function. It exists in various isomeric forms, and changes in their relative distribution are closely linked to the degree of myelination. In demyelinating diseases such as multiple sclerosis (MS), the citrullinated form of MBP is particularly abundant. Objectives: To investigate how MBP isomers, particularly the C8 isomer, affect inflammation, apoptosis, and immune regulation in macrophages. Materials and Methods: MBP was isolated and purified from bovine brain white matter. RAW 264.7 macrophages were cultured in DMEM with heat-inactivated fetal bovine serum. Following treatment with MBP isomers, macrophage polarisation was assessed by measuring inducible nitric oxide synthase (iNOS, M1 marker) and arginase-1 (M2 marker) using ELISA. The expression of key markers of inflammation (HMGB1, PPAR-γ), apoptosis (Bcl-2, Bad, P-Bad, caspase-3), immune regulation (CD200), and efferocytosis (Mer-TK) was also analysed by Western blotting. Results: The C8-citrullinated MBP isomer promoted a pro-inflammatory phenotype in macrophages, enhanced expression of pro-apoptotic markers, and reduced regulatory signals. These changes suggest a shift in immune homeostasis toward chronic inflammation and impaired apoptotic cell clearance. Summary: Our findings indicate that citrullinated MBP isomers, especially C8, modulate macrophage behaviour in ways that may promote autoimmune responses. Targeting MBP isomer-specific effects could provide new therapeutic approaches for MS and related disorders.

CYTOCHROME C AS A NON-CANONICAL MODULATOR OF NA,K-ATPASE: ISOFORM-SPECIFIC AND REDOX-DEPENDENT REGULATION

Gvantsa Chkadua[1,2], Eka Nozadze[1], Leila Tsakadze[1], Lia Shioshvili[1], Nana Arutinova[1], Marine Leladze[1], Sopio Dzneladze[1], Maia Javakhishvili[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Georgian National University, Tbilisi, Georgia

Na,K-ATPase is a pivotal membrane-bound enzyme responsible for maintaining sodium and potassium gradients across the plasma membrane, essential for neuronal excitability, osmoregulation, and secondary active transport. Beyond its classical role in ion transport, Na,K-ATPase also functions as a signaling molecule, with its activity tightly regulated by cardiotonic steroids (CTS), such as ouabain. While high concentrations of ouabain inhibit Na^+ and K^+ transport, low concentrations initiate distinct signaling cascades. The enzyme does not conform to traditional receptor categories, suggesting a unique role in cellular signal transduction.

In this in vitro study, we report for the first time that cytochrome c (Cytc), a mitochondrial protein traditionally associated with electron transport and apoptosis, modulates Na,K-ATPase activity in a concentration-dependent and subunit-specific manner. Cytc exhibits a biphasic effect, enhancing Na,K-ATPase activity at low concentrations (0.06 ng/ml and 6 ng/ml) and inhibiting it at higher concentrations (120 ng/ml). Importantly, Cytc selectively regulates the Na-activated form of the enzyme without altering the K-dependent form, indicating subunit/isoform specificity. Mechanistically, Cytc alters the enzyme's sensitivity to p-chloromercuribenzoic acid (PCMB), a thiol-reactive compound, indicating a shared redox-sensitive cysteine target. The observed changes in PCMB affinity in the presence of Cytc establish a redox-dependent mechanism of interaction. Furthermore, our data demonstrate that Cytc enhances both the affinity of Na, K-ATPase for ouabain and its maximal catalytic rate (Vmax), supporting a modulatory role in ouabain-induced conformational dynamics.

These findings suggest that Cytc, beyond its classical functions, acts as a non-canonical modulator of Na,K-ATPase. This novel interaction expands our understanding of redox regulation and enzyme signaling, offering insights into potential mechanisms of neuroprotection, apoptosis regulation, and redox-sensitive ion homeostasis in the brain.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) (FR-24-4786)

DECONVOLVING VISUAL IMPRINTING MEMORY IN CHICKS USING SINGLE-CELL TRANSCRIPTOMICS

Revaz Solomonia, Vincenzo Lagani, Zaza Khuchua, Lela Chitadze, Teimuraz Bokuchava, Veriko Bokuchava, Lia Tsverava

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
Ilia State University, Tbilisi, Georgia;
King Abdullah University of Science and Technology, Saudi Arabia

The specific gene expression programs activated in distinct brain cell subtypes during memory encoding, consolidation, and retrieval remain poorly characterized, particularly at single-cell resolution, even in brain regions known to be a memory store.

Visual imprinting is an experience-dependent form of learning that occurs during the early-life period, in which a young animal rapidly forms a strong and lasting attachment to a visual stimulus after brief exposure. The intermediate medial mesopallium (IMM) in the chick forebrain stores visual imprinting memory. We investigated learning-related molecular changes in the left IMM using single-nucleus RNA sequencing from strongly imprinted chicks and untrained controls. We characterized >30 cell clusters, with distinct transcriptional differences putatively linked to memory formation, nearly half of them in long non-coding (lnc)RNAs. Association of two lncRNAs and four proteins (FOXP2, RORA, LUC7L, ROBO1) with memory strength was demonstrated in PCR and immunoblotting experiments, with some correlations due to learning potential (a predisposition), while others resulted from imprinting training. One of the two lncRNAs, lncRNA-ENSGALG00010007489, an avian brain-specific transcript, was expressed in particular glutamatergic clusters. Its localization and role in imprinting were further investigated through quantitative multi-probe in situ hybridization. This study provides novel insights into transcriptional changes in chick IMM during memory formation at the single-cell level.

HORMESIS PRINCIPLE: ANALGESIC ACTION OF SMALL DOSES OF BLUNT-NOSED VIPER VENOM AND OREGANO ESSENTIAL OIL

Armen Voskanyan, Lilya Parseghyan, Armenuhi Moghrovyan, Sona Poghosyan, Anna Darbinyan

Leon A. Orbeli Institute of Physiology, Yerevan, Armenia

Introduction: Blunt-nosed viper venom in high doses induces severe pain, while low doses demonstrate analgesic effects, illustrating the hormesis principle. Similarly, essential oils, particularly from Origanum vulgare of the Armenian highlands (OVA), are recognized for their analgesic and anti-inflammatory properties. Objectives: This study aimed to investigate the mechanisms underlying the transition from nociceptive to analgesic effects of viper venom and to evaluate the antinociceptive and anti-inflammatory properties of OVA essential oil. Material and Methods: Pain behavior was studied in outbred white mice using various doses of Macrovipera lebetina obtusa (MLO) venom, starting from the LD50 dose and serial dilutions (1.0, 1/5, 1/10, 1/20, 1/30 of LD50), administered intraperitoneally and intraplantarly during formalin and hot plate tests. Additionally, MLO venom with inhibited phospholipase A2 (PLA2) activity was tested to

determine the enzymatic contribution to pain modulation. OVA essential oil was extracted by hydro-distillation, and its composition was analyzed using gas chromatography/mass spectrometry. The formalin and hot plate tests evaluated the oil's antinociceptive effects, and cytotoxicity was assessed via the methyl-thiazolyl-tetrazolium (MTT) assay in HeLa and Vero cell lines. Results: At 1.0 LD50, MLO venom produced strong nociceptive behavior, while the maximum analgesic effect was observed at 1/20 LD50. The enzymatic activity of PLA2 played a significant role in both the nociceptive and antinociceptive effects. OVA essential oil, with maximal β-caryophyllene (8.18%) and β-caryophyllene oxide (13.36%) content during blossoming, exerted significant antinociceptive and anti-inflammatory effects at a 4% solution (3.5 mg/mouse, P = 0.003). Cytotoxicity analysis revealed approximately 60% inhibition of cell viability at 2.0 μL/mL. Summary: Both small doses of blunt-nosed viper venom and OVA essential oil demonstrated pronounced antinociceptive effects, supporting the concept of hormesis. OVA essential oil, particularly harvested during the blossoming period, represents a promising candidate for developing pain-relieving preparations.

The work was supported by the Science Committee of MESCS RA, in the frames of the research project No. 21APP-1F003

ANALGESIC AND ANTI-INFLAMMATORY PROPERTIES OF BLUNT-NOSED VIPER VENOM COMBINED WITH OREGANO ESSENTIAL OIL

Anna Darbinyan, Lilya Parseghyan, Armenuhi Moghrovyan, Sona Poghosyan, Armen Voskanyan

Leon A. Orbeli Institute of Physiology, Yerevan, Armenia

Introduction: Natural compounds derived from plants and animals have been widely used to alleviate acute and inflammatory pain. Current research increasingly explores combination therapies, aiming to activate multiple mechanisms through the inclusion of several active components. Objectives: This study aimed to evaluate the analgesic and anti-inflammatory efficacy of a novel combined preparation consisting of Macrovipera lebetina obtusa (MLO) venom and Origanum vulgare essential oil (OVEO). We assessed the therapeutic efficacy, optimal dosing, and possible mechanisms underlying its action. Material and Methods: Male outbred albino mice were employed for testing, essential oil content analyzed using gas chromatography-mass spectrometry. Formalin, carrageenan, and hot plate tests were used to evaluate analgesic and anti-inflammatory effects. The involvement of cannabinoid (CB2) and opioid receptors was assessed using selective antagonists SR144528 and naloxone, respectively. Toxicity and side effects were also evaluated. Results: The ointment form of the combined preparation reduced inflammatory pain by 68% and paw edema by 36%. The analgesic effect was predominantly mediated by CB2 receptors (73%), with opioid receptors contributing to 64% of the effect. No significant adverse physiological side effects were noted. Summary: The combined MLO venom and OVEO ointment provides dual analgesic and anti-inflammatory effects through distinct mechanisms: reduced transmission of nociceptive impulses due to desensitization of nociceptive nerve fibers and activation of peripheral

cannabinoid and opioid anti-nociceptive systems. This preparation represents a promising therapeutic strategy for managing inflammatory pain, with no observed addictive potential.

The work was supported by the Science Committee of MESCS RA, in the frames of the research project No. 21APP-1F003.

ANTIMICROBIAL PEPTIDES: IMPLICATIONS FOR NEURAL AND MENTAL HEALTH

Malak Pirtskalava

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Antimicrobial peptides (AMPs) possess potent microbial-killing activity and are at the forefront of drug development for combating antibiotic-resistant pathogens. Research into their therapeutic potential is rapidly expanding. Meanwhile, neuropeptides (NPs) serve diverse functions, ranging from neurotransmission to growth regulation. Interestingly, many neuropeptides have demonstrated antimicrobial activity, raising a critical question: Why do neuropeptides exhibit antimicrobial properties? The answer lies in their shared structural and functional characteristics—both are membrane-active peptides. This similarity prompts another intriguing question: Can the antimicrobial potency of AMPs be harnessed to address brain disorders? Currently, the answer is partially yes. For example:

- LL-37, defensins, and humanin have been investigated for Alzheimer's disease.
- Melittin shows potential in Parkinson's disease.
- Dermcidin-derived peptides may be useful in multiple sclerosis.
- Tachykinins (e.g., Substance P) modulate serotonin/dopamine pathways, suggesting antidepressant potential.

The case of tachykinins highlights how AMPs can influence mental health, particularly through the gut-brain-immune axis. Mammals produce over 100 peptides involved in gut-brain communication, many of which exhibit antimicrobial properties. Given their presence in the gastrointestinal (GI) tract, these peptides may be influenced by gut microbiota changes and, in turn, modulate brain signaling—either directly or indirectly. Thus, targeting gut microbiota with AMPs could be an innovative strategy to improve mental health. For instance, β-lactam-derived AMPs have shown antidepressant effects in rodents and humans. However, it is crucial to note that AMPs can have dual effects—some may improve mental health, while others (e.g., broad-spectrum antibiotics) might disrupt microbial balance and worsen anxiety or depression. Therefore, when designing new antimicrobial agents, researchers must consider strategies that not only combat infections but also prevent or alleviate neuropsychiatric symptoms.

SUITABILITY OF EXPERIMENTAL MODELS OF HEMORRHAGIC SHOCK FOR RHEOLOGICAL STUDIES

Maia Mantskava[1], Nana Momtselidze[1], Giorgi Kuchava[1], Lena Davlianidze[1], Eka Arziani[2], Maia Gotsadze[2], Tamar Kandashvili[2]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Tbilisi State Medical University, Tbilisi, Georgia

One of the methodological tools for medical research is biological modeling. The task of modeling is to experimentally identify the properties and characteristic features of the disease under study. To create a useful model, it is necessary to select common essential features for both the original and the model. The area of our research is the study of rheological properties in experimental hemorrhagic shock. For this, the experimental model must meet the standards for rheological studies. In this regard, we studied the literature on pubmed (filters 2020-2025, keywords: using model, hemorrhagic shock). The data obtained showed that existing models, although they reflect the properties characteristic of hemorrhagic shock, do not meet the requirements of rheological studies. Modeling hemorrhagic shock by amputation of the tail has a component of traumatic shock, so it is not ideal. Puncture of the retroorbital venous plexus makes it possible to obtain only (Cocchetto and Bjornsson's model) a small amount of blood. The model was further improved (Grice's model), but the amount of blood is insufficient. Puncture in the lateral canthus (Sorg and Buckner's model) is more suitable, but very traumatic, which causes artifacts in rheology studies. The most successful model is the method that involves releasing blood into a reservoir connected by a system of tubes to the femoral artery, which is the best of the existing ones (Wiggers's model). Blood flows into the reservoir until the arterial pressure, decreasing during blood loss, is balanced by the hydrostatic pressure of the blood column in the reservoir. By changing the position (height) of the reservoir above the heart level, hypotension of any degree can be obtained. Although known methods of blood collection can reproduce hemorrhagic shock, and to some extent reflect the pathophysiological processes occurring in the body, they are not always acceptable for rheological studies. The development of new mathematical models of experimental hemorrhagic shock and the introduction of an in-silico approach to research will make it possible to study rheological properties in detail.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) (FR-24-389)

PSYCHOLOGICAL ASPECTS OF COMMUNICATING WITH PATIENTS ABOUT RADIATION RISKS

Ketevan Jariashvili[1,2,4], Salome Kiparoidze[1,3], Davit Nadareishvili[1,3,4], Manana Gvasalia[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Agency of Nuclear and Radiation Safety, Tbilisi, Georgia;
[3]New Vision University, Tbilisi, Georgia; [4]Radiation Safety Center, Tbilisi Georgia

The number and types of radiological procedures are increasing worldwide. The growing use of ionizing radiation in the medical field has become a matter of public interest. As public awareness

increases, patients, along with doctors and national regulatory authorities, are recognizing the importance of informed patient consent and comprehensive discussions about the benefits and risks involved in medical decision-making. Effectively communicating the elements of informed consent and clearly explaining the benefits and risks of procedures presents a significant challenge. Miscommunication or misunderstanding may lead patients to avoid necessary and appropriate imaging out of fear or misinformation, potentially resulting in harm. All medical decisions are, to some extent, influenced by both cognitive and emotional factors. Therefore, it is essential to integrate insights from psychology and cognitive neuroscience when developing new strategies to communicate medical risks. In the context of radiation medicine, it is particularly important to consider emotional and rational responses, anxiety and decision-making patterns, fear of the unknown and potential side effects, the perceived credibility of the information source, and a broad spectrum of emotions. To address these challenges, we drew upon existing literature in the psychology of radiation risk communication and applied commonly used methods in this field. Additionally, we incorporated feedback gathered from patients through questionnaires. Based on this, we began developing simple, practical strategies to enhance interactive communication with patients about the benefits and risks of radiological procedures. We plan to implement these strategies in the education, training, and retraining of healthcare professionals, as well as in their ongoing clinical practice.

IDENTIFICATION OF GLUTEN-SPECIFIC DNA MARKERS FOR ASSESSING THE ALLERGENICITY OF GEORGIAN ENDEMIC WHEAT

Nelly Datukishvili[1,2], Kakha Bitskinashvili[1], Tamara Kutateladze[1], Tamar Koberidze[2], Boris Vishnepolsky[1], Marina Karseladze[1]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Wheat (Triticum) is one of the oldest and most important food crops in the world. However, wheat belongs to potent allergens and causes significant health disorders. Georgia is an early center of wheat and is characterized by great diversity and endemism of ancient wheat. It is known that Georgian endemic wheat is less allergenic. The allergenicity of wheat is determined by gluten proteins. Therefore, the investigation of gluten in wheat species is important both for food safety assessment and health protection. This study aimed to develop new DNA markers of wheat gluten genes to characterize and compare endemic and modern species. Gluten proteins consist of two main groups, glutenins and gliadins. The study focused on the high molecular weight (HMW) glutenin subunit gene and the gamma- and omega-5 gliadin genes. Several sets of oligonucleotide primers targeting these genes were designed using bioinformatic tools. Various varieties of Georgian endemic wheat were studied. DNA markers were identified using the polymerase chain reaction (PCR) method. PCR products were evaluated by agarose gel electrophoresis. The best markers for the HMW glutenin subunit, gamma- and omega-5 gliadins genes were identified. It was found that gluten genes in Georgian endemic and modern wheat species differ according to DNA markers. Several gluten-specific DNA markers were identified, which do not exist in Georgian

endemic species. The results indicate that the new efficient PCR-based DNA markers allow accurate identification of wheat glutenin and gliadin and can be successfully used for gluten control in food.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) [Grant STEM-22- 637].

MODELING ALZHEIMER'S DISEASE THROUGH INACTIVATION OF COLLAPSIN RESPONSE-MEDIATOR PROTEIN 2

Afet Bakhshaliyeva, Arif Mekhtiev

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

Collapsin response-mediator protein 2 (CRMP2) is a protein that is involved in the process of autophagy of the neurons' debris. In the animals knock-down for the CRMP2-synthesizing genes brain ventricle's enlargement is detected. It is assumed that CRMP2 may play an important role in the pathogenesis of Alzheimer's disease (AD). Our earlier studies revealing the significant downregulation of anti-CRMP2 autoantibodies in the blood samples of the AD patients compared to its level of healthy individuals, confirmed this assumption. The aim of our current study was study of the neurochemical and behavioral signs of AD by using neonicotinoid insectiside actara. The studies were conducted on the 10-month-old Wistar male rats. In the first series of the study to define the optimal dose, 2 concentrations of the actara LD50 were used: group 1 accepted 1/20 dose of LD50, group 2 – 1/40 dose of LD50 in the form of bait for 75 days. Thereafter blood samples were taken from the animals and the level of CRMP2 was determined by an indirect immune-enzyme assay. The level of natural autoantibodies to CRMP2 in the blood serum of the rats receiving 1/20 dose of actara decreased by 44.8%, reflecting its expression in the brain subcortical structures. In the second series of the experiments, after the rats trained in the shuttle box was brought to 80% criterion of correct trials, they were given insecticide actara at a dose of 1/20 of LD50 as bait for 3 months, and finally, the level of memory retention was tested. According to the results, rats receiving insecticide actara showed a 50.3% decrease of memory retention. The obtained results give the grounds to elaborate a model of AD in the rats using neonicotinoid insecticide actara, which predispose for a more detailed study of the pathology and the development of adequate therapeutical approaches.

ALTERATIONS IN THALAMOCORTICAL HCN CHANNEL ACTIVITY BY MULTIPLE SCLEROSIS IN MURINE MODEL

Tengiz Oniani[1], Thomas Budde[1], Anna Junker[2]

[1]Institute of Physiology, Münster University, Münster, Germany;
[2]European Institute for Molecular Imaging, Münster University, Münster, Germany

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system (CNS), which is characterized by the progressive loss of mature oligodendrocytes. Considering the critical role of

thalamus in phathophysiology of MS, the degradation of myelin is associated with the abnormal thalamocritical (TC) rhytmicity. In this regard it becomes interesting if the de- and remyelination processes can affect the modulation of the hyperpolarization-activated cyclic nucleotide-gated cation (HCN) channels in TC neurons. To truthfully replicate de- and remyelinating processes of MS in murine model we used copper chelator (CPZ) as dietary supplement to mice standard chow. 35 days of 0.2% CPZ diet results into a general demyeliantion in brain of rodents, following which, the withdrawal of CPZ from diet, kick-starts the rapid remyelination process. This allowed us to research the changes in TC HCN channel activity both during de- and remyelination processes. Whole-cell voltage clamp recordings show that HCN channels elicit reduced currents in demyelinated TC neurons, whereas in early stages of remyelination they are characterized with over eliciting currents. Observed electrophysiological changes of HCN channel activity during de- and remyelination processes are also accompanied by the non linear changes of channel subtype protein expression, based on the immunofluorescence data. In vitro compound application of divalent cation chelators (EDTA; Tricine), water soluble derivative of CPZ (BiMPi) alongside divalent metal (Zinc; Copper) to native TC HCN channels show that observed changes of HCN channel activity are not mediated by the toxicity of the CPZ, or compounds copper chelating properties. This suggest that the previously displayed modulatory changes of HCN channel activity can be considered as a major hallmark of CPZ-induced de- and remyelination processes itself.
Disclaimer: Experimental data was acquired and published as part of presenters (Dr. Tengiz Oniani) PhD studies at the Münster University, Münster, Germany, while being part of RTG Chembion.

TRACE ELEMENTS-INDUCED NEUROTOXICITY IN WHITE RAT MODEL

Tamar Bikashvili[1,2], Lia Gelazonia[1], Mariam Mikadze[1], Marina Sardlishvili[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]New Vision University, Tbilisi, Georgia

The brain is a major target of environmental toxicants. A deficiency in or an excess of essential elements also could impair neuronal functions and cause severe neurological disorders. Environmental trace elements, manganese (Mn) and arsenic (As) are the focus of this research. Experimental animals were divided in groups and drank water for 3 months with manganese concentration of 20 mg/ml, water containing As at concentration 68 mg/L and 136 mg/L, accordingly. The both male and female rats and their offspring have been used for behavioral and morphological analyses. Intoxication with manganese compounds has a significant effect on the emotional state of an individual, this change is pronounced in both male and female rats. However, decreased locomotor activity was observed in female rats. Rats intoxicated with manganese ions lag behind control animals in learning and memory abilities. And learning disorders were more pronounced in male individuals. The accumulation of manganese ions from brain areas was particularly pronounced in the hippocampus and cerebral cortex. Changes in the number of neurons from hippocampal areas were noted in the CA3 field and dentate fascia. The protective role of some antioxidants against manganese-induced neurotoxicity were also studied. Resveratrol, as an antioxidant, has a positive effect on the changes caused by intoxication with manganese

compounds, but the effect was quite small. The antioxidant effect was better expressed when exposed to quercetin. Our studies on the effect of As exposure on CNS cells revealed high vulnerability of the cells from motor cortex of the offspring whose parents received As before and during pregnancy, as well as during lactation period. Such alterations, in cell number, however, was not found in animals, which received the same doses of As directly during postnatal development (starting from P21). The effect of Arsenic exposure on animal behavior, locomotor activity, and brain morphology was more dramatic during prenatal and early postnatal development.

RODENTS PROPIONIC ACID MODEL OF AUTISM: SYNAPTIC ARCHITECTURE OF SOCIAL BRAIN. ELECTRON MICROSCOPIC STUDY

Mzia Zhvania[1,2], Giorgi Lobzhanidze[2], Nadezhda Japaridze[2,3], Pikria Khomasuridze[1], Giorgi Kipiani[1]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[3]New Vision University, Tbilisi, Georgia

Autism spectrum disorder (ASD) is a neurodevelopmental disorder, characterized by social deficits, emotional disturbances, restricted interests, and stereotyped behavior. Although ADS is a common disorder, its precise etiology is not defined yet. Propionic acid (PPA), short-chain fatty acid and microbial metabolite generated in the gut, is actively involved in a number of neurodevelopmental pathologies, including ASD. Limbic areas, as the areas of social brain are among the most vulnerable regions to PPA treatment. Numerous biochemical, immune and morphological data indicate that PPA affect these regions. Previously we have shown that even single and relatively low dose of PPA (175 mg/kg) provokes short-term effects on social behavior (the main hallmarks of ASD), emotions and cognitive functions, as well as on the ultrastructure of the hippocampus, amygdala and prefrontal cortex in adolescent male Wistar rats. All these regions play important roles in social cognitions, social interactions and social memory. In the present study, we elucidate short-term (5 days after treatment) and medium-term effect (10 days after treatment) of the same dose of PPA on synaptic architecture of rat amygdala, hippocampus and prefrontal cortex. The measurable parameters of synaptic active zone (diameter and depth), presynaptic and postsynaptic mitochondria (the number, area, the distance from synapse active zone, the number of mitochondria with protrusions), synaptic vesicles (total number and the number of vesicles located in different synaptic vesicle pools) and porosone complex (diameter and depth) were evaluated. In almost all parameters, the time-dependent significant effects were revealed. The most affected was amygdala, where the increase of the diameter and the depth of synaptic active zone at both time points were found. Such findings indicate that social and emotional disturbances, which develop as a result of PPA treatment, are accompanied by significant changes in the synaptic architecture of brain responsible for social and emotional processing.

MYO-INOSITOL AS A PROMISING ANTIEPILEPTOGENIC DRUG: MULTIDISCIPLINARY STUDY

Georgi Gamkrelidze[1], Luka Kharkhelauri[1], Veriko Bokuchava[1], Lia Tsverava[1,2], Eka Lepsveridze[1], Vincenzo Lagani[1,3], Maia Burjanadze[2], Manana Dashniani[2], Merab Kokaia[4], Revaz Solomonia[1,2]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Epilepsy is one of the most widespread neurological diseases characterized with spontaneous recurrent seizures (SRS). Epileptogenesis is a multifaceted pathophysiological process that transforms a normal brain into an epileptic brain. Current antiepileptic drugs provide only symptomatic relief, suppressing SRS, but not curing the disease. Thus, revealing new drugs that oppose, modify or mitigate epileptogenesis is a significant challenge in modern neuroscience. In early studies in our laboratory, Myo-insitol (MI) was identified as a promising antiepileptogenic compound. We hypothesized that MI is endogenous antiepileptic substance that contributes to neuron excitability homeostasis in the forebrain. To test and elaborate this hypothesis, using kainic acid temporal lobe epilepsy model rats, we investigated different MI dose dependent, 30mg/kg, 60mg/kg and 120 mg/kg, effects on the behavioral and electrographic SRS in the hippocampus and on spatial learning and memory decline caused by epileptogenesis. In addition, we studied the MI optimal dose effect on transcriptome and epigenetic changes associated with epileptogenesis in the hippocampus. We found that MI had long lasting dose dependent inhibitory effects on behavioral and electrographic manifestations of epileptogenesis. The dose 60 mg/kg was identified as most effective and it had broad effect on gene expression and DNA methylation in the hippocampus. Importantly, MI reversed some of gene expression associated with epileptogenesis and related to ion channels and postsynaptic receptors. The obtained data are consistent with our stated hypothesis. The identified optimal antiepileptogenic dose of MI in rats is comparable with MI dose recommended to humans as organic supplement. Thus, MI offers promising treatment against epileptogenesis in humans.

ASSYST: A UNIVERSAL AUTOMATED TOOL FOR RELIABLE SEIZURE DETECTION POWERED BY RUNNING RHYTMOGRAM METHOD

Armen Sargsyan[1], Andreas A. Ioannides[2], Pablo Casillas-Espinosa[3], Gilles van Luijtelaar[4], Terry O'Brien[3]

[1]Orbeli Institute of Physiology, Yerevan, Armenia**;** [2]AAI Scientific Cultural Services Ltd., Nicosia, Cyprus; [3]Monash University, Melbourne, Australia;
[4]Radboud University, Nijmegen, Netherlands

Introduction and Objectives: Seizure detection in animal and human EEG recordings remains a challenging task, even in generalized epilepsies where the widespread epileptic activity should be more reliably observed. However, it continues to be difficult for fully automatic algorithms to

reliably detect seizures without generating high rates of false positives. EEG records often contain artifacts, which may be falsely detected as a seizure. This requires subsequent tedious visual revision of detection results. Despite the variety of artifact detection and removal methods described in the literature, this remains a demanding task. Material and Methods: Earlier we have developed a convenient interactive software, ASSYST, for reliable seizure detection in long-term EEG recordings, which showed high sensitivity for both rodent (>99%) and human (>95%) recordings and significantly reduced the processing time. We now enriched ASSYST with a new "running rhythmogram" algorithm for automatic distinction of seizures/SWDs from other not relevant events (e.g., artifacts) using the fact that seizures or SWDs consist of regularly repeating patterns - the spike-wave complexes. Preliminary testing of the method was performed on long-term EEG from four chronic epilepsy rat models: post-status epilepticus model of temporal lobe epilepsy; lateral fluid percussion injury model of post-traumatic epilepsy; and two genetic models of absence epilepsy – GAERS and rats of the WAG/Rij strain. Results: Recordings contained seizures/SWDs and artifacts. In 85% of recordings the method showed high (>97%) sensitivity and specificity for both seizures and artifacts. Two recordings contained long and strong ECG and instrumental artifacts that were difficult to segregate from the seizures since they had identical rhythmic structure. In these cases, the sensitivity dropped to 80%. Summary: The running rhythmogram is an effective method for distinguishing rhythmic patterns in EEG, such as seizures and SWDs, and can increase the sensitivity and specificity of a seizure detection algorithm. Further improvements might be needed to increase its robustness and universality.

EVALUATING THE FEASIBILITY OF AN AI-BASED ALGORITHM ENCEVIS AS AN ASSISTANT TO NEUROPHYSIOLOGISTS IN CLINICAL PRACTICE

Aleksandre Tsereteli, Natela Okujava

S. Khechinashvili University Hospital, Tbilisi, Georgia

Objective This study evaluated the performance of the ENCEVIS AI-based algorithm as a screening tool to predict the presence of ictal and/or interictal epileptiform discharges (IEDs) in EEG recordings. Methods This prospective study was conducted from 2019 to 2023 at Khechinashvili University Hospital, Tbilisi. EEG recordings over three hours were included; standard EEGs and recordings with EEG-negative seizures were excluded. Two independent EEG experts performed blinded visual analyses. In case of disagreement, a third neurophysiologist was consulted, and the final consensus served as the reference standard. ENCEVIS annotations were compared to this reference. Results A total of 267 EEG recordings were analyzed. Clinical events occurred in 54 patients (20.2%): 43 had epileptic seizures, 11 had non-epileptic events, and 2 had both. Overall, 114 seizures were recorded; ENCEVIS correctly identified 65 (57.0%, $p > 0.05$). Sensitivity increased with seizure duration: 12.5% for <10 seconds, 55.7% for 10–60 seconds, and 65.8% for >60 seconds ($p < 0.05$). ENCEVIS detected at least one seizure in 42 of 43 seizure-positive recordings (sensitivity: 97.7%), with a specificity of 48.2%, PPV of 26.6%, and NPV of 99.1%. The overall false detection rate was 0.29 events/hour. Interictal epileptiform discharges were visually confirmed in 162 recordings. ENCEVIS yielded 67 false positives, 4 false negatives, and 43 true negatives. For interictal detection, sensitivity was 97.4%, specificity 40.2%, PPV 69.3%,

and NPV 91.8%. Significance The ENCEVIS algorithm demonstrates high sensitivity in detecting EEG recordings with ictal and interictal epileptiform activity. However, its limited specificity necessitates neurophysiological review to validate positive findings. Its high negative predictive value highlights ENCEVIS's potential as a prescreening tool for identifying EEG recordings without ictal or interictal abnormalities, thereby reducing the workload on neurophysiologists.

INTERACTION BETWEEN SEIZURE AND THETA RHYTHM

Nini Nikabadze[1,2], Irine Bilanishvili[1], Maia Barbakadze[1], Ketevan Balarjishvili[1], Giorgi Andronikashvili[1], Nadejda Khizanishvili[1], Zaqaria Nanobashvili[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ilia State University, Tbilisi, Georgia

Recently it was shown by us that combined stimulation of hippocampus and dorsomedial hypothalamus resulted in suppression of the electroencephalographic seizure reactions and, respectively, manifestations of behavioral seizures reduced. It is expected, that augmentation of inhibitory processes in hippocampal neurons in the course of dorsomedial hypothalamus stimulation can trigger mechanisms preventing the development of epileptiform activity. Because of two important characteristics of the hippocampus—theta rhythm and epileptogenesis—these appear to be interrelated in respect of their cellular substrates, and as far as theta rhythm may modulate hippocampal excitability, a study of the functional relationship between theta rhythm and seizure activity was endeavored. The purpose of this study is to test this proposal by determining the effects on seizures of induction or suppression of hippocampal theta activity. There were two main goals in our study: 1) Changes in convulsive electrical activity of the hippocampus in different stages of sleep and wakefulness of the animal. 2) Changes in electrographic convulsive reactions during theta-rhythm and/or desynchronization of the electrical activity of the hippocampus caused by stimulation of the hypothalamus. Our findings show that: 1) the frequency of hippocampal interictal epileptiform dischargers increased with the transition from the awake state to drowsiness and a slow-wave sleep phase. After the animal came from slow-wave sleep to paradoxical sleep, epileptiform activity completely disappeared; 2) at threshold stimulation of hypothalamus when electrohippocampogram shows augmentation of the theta rhythm there is a significant reduction of seizure durations. When at hypothalamus stimulation instead of theta rhythm the electrical activity is desynchronized, there occurs a considerable intensification of seizure activity. Therefore, seizure-theta antagonism in our experiments could be interpreted as an adjustment of the inhibitory mechanisms when the theta rhythm is evoked.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) Grant – FR-23-1938

SIGMA-1 RECEPTOR AGONISTS COUNTERACT PARA-CRESOL-INDUCED DEPRESSIVE-LIKE BEHAVIOR: ROLE OF DOPAMINE TRANSPORTER DYSREGULATION IN A GUT-BRAIN AXIS MODEL

Elene Zhuravliova[1,2] Natia Okriashvili[1], Natalia Kiknadze[1], Nana Narmania[1,2], Tamar Barbakadze[1,2], David Mikeladze[1,2]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

The gut-brain axis has emerged as a key player in the pathophysiology of neuropsychiatric disorders, including major depressive disorder (MDD), autism, and ADHD. A growing body of evidence links gut microbiota dysbiosis with altered brain function, partly through microbial metabolites that influence neurochemical pathways. Clostridium difficile, a known gut pathogen, produces p-cresol, a metabolite that readily crosses the blood-brain barrier and has been implicated in central nervous system dysfunction.

Para-cresol has been shown to disrupt dopaminergic signaling by altering the function and expression of the dopamine transporter (DAT), a critical regulator of synaptic dopamine availability. Given the central role of dopamine in mood regulation, DAT dysregulation may underlie the behavioral consequences of gut-derived neurotoxins. Furthermore, traditional antidepressants, such as SSRIs, often fail to address dopaminergic imbalance, particularly in treatment-resistant depression.

Sigma-1 receptors (S1Rs), endoplasmic reticulum-associated chaperones, have emerged as modulators of dopamine homeostasis and neuroprotection. In this study, we used a para-cresol-induced rat model to assess the effect of S1R activation on depressive-like behavior and DAT function. Behavioral assays revealed that para-cresol significantly increased immobility in the forced swim test and reduced grooming and exploratory behavior. Co-administration of the selective S1R agonist PRE-084 reversed these effects and restored behavioral parameters to baseline. Preliminary molecular analyses indicate that para-cresol exposure downregulates striatal DAT expression, while PRE-084 treatment normalizes DAT levels, suggesting a mechanistic link between S1R activation and dopamine transporter regulation. These findings highlight the involvement of DAT dysregulation in microbiota-related depression and suggest that Sigma-1 receptor agonists may exert antidepressant effects through the restoration of dopaminergic balance. This mechanism may represent a promising therapeutic pathway for SSRI-resistant depression.

THE ROLE OF INTEGRINS IN THE DEVELOPMENT OF HYPOXIC-ISCHEMIC PROCESSES IN NEURONAL CELLS

Tamar Barbakadze, Elisabed Kvergelidze, Elene Zhuravliova, Nana Narmania, Maia Sepashvili, David Mikeladze

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
Ilia State University, Tbilisi, Georgia

Thyroid hormones (TH) play a critical role in the development and differentiation of both neurons and glial cells, as well as in synaptogenesis and myelin sheath formation. They are also implicated in the pathogenesis of several neurological disorders. Beyond their classical nuclear receptor-mediated actions, TH can signal through the αvβ3 integrin receptor located on the plasma membrane, modulating the transcription of signaling proteins that influence cell adhesion and survival in various neurological conditions. TH has demonstrated neuroprotective effects in the context of brain hypoxia; however, the precise intracellular mechanisms underlying these protective actions remain poorly understood. Hypoxic or ischemic conditions can trigger neurodegeneration and impair synaptic plasticity. We hypothesized that thyroid hormones, acting through αvβ3 integrin, may regulate hypoxia-induced cellular responses via downstream signaling pathways, thereby enhancing neuronal cell survival. In this study, we examined the effect of TH on the αvβ3 integrin-mediated JAK2/STAT5 signaling pathway in differentiated PC-12 cells under hypoxic conditions. We employed immunoprecipitation, electrophoresis, and western blotting techniques to analyze cells treated with or without T3 (3,5,3'-triiodo-L-thyronine), in the presence or absence of αvβ3 integrin-blocking antibodies. Our results show that T3 activates the JAK2/STAT5 pathway through αvβ3 integrin signaling and suppresses SHP2 activity in hypoxic PC-12 cells. This activation correlates with previously reported downregulation of the palmitoyltransferases ZDHHC2 and ZDHHC9, resulting in reduced palmitoylation and phosphorylation of the Fyn tyrosine kinase. In conclusion, our findings provide novel evidence that T3 exerts protective effects under hypoxic conditions via αvβ3 integrin-dependent activation of the JAK2/STAT5 pathway, suppression of SHP2, and modulation of Fyn kinase post-translational modifications.

TARGETING THE UB/SDF1/CXCR4 AXIS: A MULTIMODAL APPROACH TO UNDERSTANDING CELLULAR REGENERATION AND PATHOLOGY

Rusudan Sujashvili[1,3], Irine Ioramashvili[1,2], Giorgi Javakhishvili[3]

[1]Ivene Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ilia State University, Tbilisi, Georgia;
[3]The University of Georgia, Tbilisi, Georgia

Extracellular ubiquitin has been relatively understudied, and its roles and mechanisms of action in cellular processes remain unclear. After thoroughly reviewing existing data, we selected disease models involving liver regeneration, myocardial infarction (MI), and cytostatic- and radiation-induced cytopenia. Both endogenous and exogenous extracellular ubiquitin were examined using various methods, including cytology, histochemistry, immunoblotting, ELISA, statistical analysis,

and bioinformatics. Through long-term investigation, we established a significant influence of extracellular ubiquitin on cell cycle, and we characterized its interaction with the membrane receptor CXCR4 and its ligand SDF1. Our findings indicate that extracellular ubiquitin regulates the proliferation of both healthy and pathological cells. Furthermore, the study identified the prognostic potential of ubiquitin in MI and confirmed the involvement of the Ub/SDF1/CXCR4 signaling axis in the regulation of cellular activity. Bioinformatic analyses revealed that the Ub/SDF1/CXCR4 complex may target metabolic pathways such as MAPK, PI3K, Wnt, and Sonic Hedgehog (SHH) through coupling with G-protein subunits and activation of second messengers. This research is ongoing to further elucidate the Ub/SDF1/CXCR4 signaling mechanisms. The objective of this presentation is to provide a comprehensive overview of our research on ubiquitin, conducted over the period from 2006 to 2025.

VITAMIN D DEFICIENCY IN TYPE 2 DIABETES MELLITUS: META-ANALYTIC INSIGHTS (2020–2025) INTO ITS IMPACT ON CARDIOVASCULAR RISK, LIPID PROFILE, INFLAMMATORY MARKERS, OBESITY PARAMETERS AND DIABETIC MICROVASCULAR COMPLICATIONS

Nino Sakhanberidze[1,2], Maia Mantskava[1,2], Nana Momtselidze[1], Giorgi Kuchava[2], Manana Namoradze[1], Nino Charkviani[1]

[1]Tbilisi State Medical University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Vitamin D deficiency represents one of the significant challenges in modern biomedicine. Experimental, clinical and epidemiological data show a relationship between vitamin D levels and the development of cardiovascular diseases, decreased bone density, metabolic syndrome, malignant neoplasms, autoimmune conditions and infections. Currently, the role of the vitamin D-hormonal system in various metabolic processes has been studied, along with the therapeutic use of vitamin D preparations to correct its insufficiency and deficiency. Our interest is focused on how vitamin D deficiency affects the condition of patients with type 2 diabetes mellitus. We analyzed meta-analysis data on PubMed (filters: keywords: diabetes, vitamin D, 2020-2025). It was found that vitamin D has a blood pressure–lowering effect in patients with type 2 diabetes mellitus. Vitamin D significantly reduced serum levels of total cholesterol and low-density lipoproteins, but had no effect on triglycerides and only a minimal effect on high-density lipoproteins. A systematic review and meta-analysis confirmed that vitamin D deficiency is associated with increased body mass index in patients. At the same time, the inclusion of vitamin D in weight loss programs among a heterogeneous group of participants led to a significant decrease in body mass index and waist circumference, but did not affect overall weight loss. In patients, vitamin D led to a significant decrease in high-sensitivity C-reactive protein levels, but did not affect TNF-α and IL-6. Vitamin D reduced certain markers of chronic low-grade inflammation in patients; Vitamin D deficiency increases the risk of developing diabetic retinopathy and a relationship was established between vitamin D deficiency and the development of diabetic peripheral neuropathy.

TRP CHANNELS IN PAIN MODULATION

Ivliane Nozadze, Gulnaz Gurtskaia, Natia Tsagareli, Gulnara Gedevanishvili, Elene Abzianidze, Merab Tsagareli

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

The Transient Receptor Potential (TRP) channel superfamily is comprised of a large group of cation-permeable channels, which display an extraordinary diversity of roles in sensory signaling and are involved in a plethora of animal behaviors. These channels are activated through a wide variety of mechanisms and participate in virtually every sensory modality. Although the physiological functions of most TRP channels are not well known, their wide distribution indicates important biological roles and activation mechanisms. TRP channels are best recognized for their contributions to sensory transduction, response to temperature, nociceptive stimuli, touch, osmolarity, chemical substances such as pheromones or odorants, pungent natural compounds, and other stimuli from both within and outside the cell. This data indicates that the specific and selective inhibition of TRP channels can be used to relieve pain, and thus these channels represent promising targets for the development of further generation of novel analgesic drugs. In this report, we are concentrating on up-to-date review information and our experimental data on the role of TRP channels in acute thermal and mechanical pain modulation.

TOLERANCE TO NSAIDS IN BRAIN LIMBIC AREAS OF RATS

Gulnaz Gurtskaia, Natia Tsagareli, Ivliane Nozadze, Gulnara Gedevanishvili, Elene Abzianidze, Merab Tsagareli

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

The ability to detect noxious stimuli is essential to an organism's survival and well-being. The nervous system, by special receptors, detects and interprets a wide range of environmental and endogenous stimuli, as well as varied mechanical, thermal, and chemical irritants. When intense, these stimuli activate pain receptors (nociceptors), generating acute pain, and in the setting of persistent injury, both peripheral and central nervous system (CNS) components of the pain transmission pathway exhibit tremendous plasticity, enhancing pain signals and producing hypersensitivity and pain chronification. Emotional distress is an intrinsic and the most disruptive and undesirable feature of pain behavior. Pain perception is characterized as a complex process, dependent not only on the regulation of nociceptive sensory systems but also on the activation of mechanisms that control emotional functions in the brain limbic areas, such as the hypothalamus, amygdala, hippocampus, insular, and cingulate cortices. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most widely used analgesics. They have analgesic, antipyretic, and, at higher doses, anti-inflammatory actions. However, a few recent studies have demonstrated that these non-opioid drugs, in the case of prolonged use, elicit the opioid-like effect, tolerance, which, alongside the drug withdrawal syndrome, may entail serious adverse effects. The brain limbic system is involved in the affective-emotional aspects of pain. Here are collected data of the study of brain mechanisms of non-opioid induced antinociceptive tolerance to NSAIDs. This review provides up-to-date literature information and experimental findings on antinociceptive tolerance to non-opioids in brain limbic areas, such as the central amygdala, anterior cingulate, and agranular insular cortices.

ATTENTION DISTRIBUTION ACCORDING TO THE SIZE, COLOR, AND LOCATION OF STIMULI IN THE VISUAL SPACE

Manana Khomeriki, Natela Lomashvili
Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Visual attention allows individuals to select the information most relevant to ongoing behaviour. Attention mechanisms serve two critical roles. First, attention can be used to select behaviourally relevant information and/or to ignore irrelevant or distracting information. Second, attention can modulate or enhance the selected information according to the perceiver's state and goals. With attention, perceivers are more than passive receivers of information. They become active seekers and processors, able to interact intelligently with their environment. Among the characteristics of visual stimuli, size can refer to the spatial extent of an item. Searching for the largest item is particularly efficient. Regarding colour, it has long been accepted as a pre-attentive feature. The aim of our research was to determine the importance of three characteristics of a visual object – size, colour, and location in the visual field in the process of attention distribution under central and peripheral vision conditions. In the no-text experiment (without additional information), when foveal information is scarce, attention distribution based on the size of the stimuli is more refined, and such stimuli are detected faster than in the text experiment (with additional information), where foveal information plays a more significant role. In both the no-text and text experiments, yellow and red stimuli are detected faster than green and blue. We assume that when perceiving a scene, the eye begins moving from the upper left corner to the lower left area, then to the lower right, and finally to the upper right during the no-text series, when focal information is scarce. Apparently, regardless of stimulus parameters and the intensity of the information flow, stimuli located in the upper left corner of the scene are perceived faster. This may be due to the habitual left-to-right reading pattern, or one can also pay attention to the phenomenon of pseudoneglect, which is often left-sided.

EFFECTS OF RADON VAPOR EXPOSURE ON BEHAVIOR AND ELECTROLYTE BALANCE IN AGGRESSIVE RATS: A CASE STUDY

Marina Nikolaishvili, Aleksandre Tarkhnishvili, Giorgi Andronikashvili, Tea Gurashvili, Ketevan Phevadze, David Natadze, Khatuna Dondoladze

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Our study investigates the behavioral and electrolyte balance changes in three aggressive rats exposed to radon vapor. The aim of the study is to explore the biological changes induced by low doses of ionizing radiation in the organism. Methodology: For the study, three aggressive rats were selected using Iumatov's method. Blood samples were taken from the rats to determine the electrolyte concentrations of potassium, sodium, and calcium. The grooming cycle was also studied in an open field. Two weeks after blood collection, the rats were taken to Tskaltubo, where they were exposed to radon vapor in a radonized bath/swimming pool room for 5 days, 24 hours a day (total of 120 hours). The radon concentration was 37 Bq/m3. After the exposure to radon vapor,

blood samples were taken again to study the changes in electrolyte concentration, and the grooming cycle was examined once more. Results: As indicated by the results, after inhalation of radon vapor, potassium concentration increased in the blood of all three rats. Regarding the grooming test, radon exposure enhanced the super stereotypical, syntactic, and rostral grooming behavior.

Electrolyte	Before Exposure (mmol/L)	After Exposure (mmol/L)
Calcium (Ca)	2.23	2.59
Potassium (K)	5.87	12.93
Sodium (Na)	137.7	131.8

Conclusion:
Our study shows that low doses of radon vapor exposure affect the behavior and electrolyte balance of aggressive rats. The inhalation of radon led to an increase in potassium concentration in the blood, indicating a shift in the electrolyte balance within the organism.

THE IMPACT OF THE BIAS OF VISUAL ATTENTION TO THE VISUAL HALF-FIELD ON THE FLUENT READING IN LEFT-TO-RIGHT AND RIGHT-TO-LEFT READERS

**Giorgi Tsiklauri, Amiran Kerashvili, Mahmoud Ali Khaled,
Maksoud Aly Loura, Maya Roinishvili, Lela Roinishvili, Malkhaz Makashvili**

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Most left-to-right readers, both adults and children, of both sexes, demonstrate a bias to the left visual half-field (BLV) and in relatively rare cases - a bias to the right visual half-field (BRV) in tasks on visual attention. In order to find if BRV and BLV have an impact on the quality of fluent reading, the study was conducted in the civil schools 32 and 175, Tbilisi, Georgia. Total Participants, 105 school second-graders, left-to-right readers in native Georgian language, performed a Star-cancellation task. Based on the sidedness of the first cancellation, and the total number of targets cancelled on the left and the right side, participants were considered to have BLV or BRV. Teachers were asked to assess the reading ability of participants by grading from 50 to 100. Successful fluent reading was found to associate with BLV, while pupils with BRV were found to have some reading difficulties. If BRV is associated to fluent reading difficulties in left-to right readers, should we expect a reversed effect in right-to-left readers? To answer this question, the study was conducted in 60 school second graders, right-to-left readers in native Arabic (Al Dhabiania Private School, Abu Dhabi and Rak Modern Private School, Ras Al-Khaimah, UAE). The study design was the same, as in case of Georgian participants. No association between the quality of fluent reading and BLV/BRV was found in female participants. Male participants demonstrating BRV were found to have higher fluent reading scores than male participants with BLV. In conclusion, bias of attention to the visual half-field is suggested to have an impact on the quality of fluent reading in primary school pupils. Pupils demonstrate better fluent reading in case, when the direction of attentional bias to the visual half-field coincides to the direction of reading in native language.

OXIDATIVE AND ANTIOXIDATIVE ACTIVITY OF ORGANISM AFTER CONDITIONS OF HYPERTHERMIA-INDUCED HORMESIS AND ITS DISRUPTION BY HIGH TEMPERATURE

Nino Sikharulidze[1], Marina Devdariani[1], Ia Kvachakidze[1], Marina Nebieridze[1], Lena Davlianidze[1], Lali Gumberidze[1], Babry Oren[2], Nodar Mitagvaria[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia
[2]BAO Health Resource Corporation, Tarzana, USA

It is known that oxidative stress, to varying degrees, can be responsible for the initiation or progression of various diseases (cancer, diabetes, Alzheimer's, Parkinson's, autism, cardiovascular diseases). Therefore, it is of particular importance to determine the number of free radicals and antioxidants in the body in order to assess the severity of oxidative stress. Directly related to oxidative stress is the emergence of the phenomenon of hormesis, which has a "dose-dependent" effect. It involves stimulation of the process at low doses of the stress factor, and inhibition of the process at high doses. The main goal of the study was to study the oxidative (ROMs) and antioxidant (PAT) statuses developed in the body under conditions of hyperthermia-induced oxidative stress of varying intensity. Oxidative stress was assessed using the free radical analysis system FRAS 5, the d-ROMs test (measures the concentration of free radicals) and the PAT test (measures the concentration of antioxidants and scavengers). The study found that increasing hyperthermia conditions lead to an increasing effect on the generation of free radicals (ROMs) and the oxidative stress index (OSI), obtained as a function of temperature; while the concentration of antioxidants (PAT) fluctuates within the normal range. We assume that the majority of free radicals generated during 400C hyperthermia are superoxide and hydrogen peroxide, which activate hormesis mechanisms, while high-grade hyperthermia (up to 450C) results in severe oxidative stress, which increases the likelihood of the formation of free radicals such as hydroxyl radical and peroxynitrite, which directly cause cellular damage, and therefore, the hormesis phenomenon is inhibited.

NEUROPROTECTIVE SYNERGY OF DEXAMETHASONE AND SEABUCKTHORN OIL IN HIGH-ALTITUDE BRAIN INJURY: EVIDENCE FROM RAT BRAIN HISTOLOGY

Ruzanna Shushanyan[1,2], Anna Grigoryan[1,2], Tamara Abgaryan[1,2], Anna Karapetyan[1,2]

Research Institute of Biology, Yerevan State University, Yrevan, Armenia

Acute hypoxia, a condition characterized by insufficient oxygen supply to tissues, can lead to significant damage to brain tissue and functionality, resulting in cerebral edema. Dexamethasone is commonly used as a pharmacological intervention to mitigate inflammation and oxidative stress during hypoxia-induced brain edema. Sea Buckthorn seed oil (SBT), derived from the berries of Hippophae rhamnoides L., has gained attention for its potential therapeutic properties, including anti-inflammatory, antioxidant, and cytoprotective effects, which may provide additional protective benefits in hypoxia-related cerebral edema. This study aims to evaluate the combined therapeutic impact of SBT oil and Dexamethasone in a preclinical rat model of hypoxia-induced brain injury. Hypoxic damage to the brain was induced by a decompression chamber (7620m, 24h) in the rat

model to mimic the development of cerebral edema. The simulated edema was evaluated through histological and morphometric analysis. The results show that the brain water content (BWC) increased following hypoxic injury, while after SBT oil and Dexamethasone pretreatment, it dropped significantly ($p<0.05$). The histomorphological analysis demonstrated cytotoxic vacuolation of neuronal cells in the cerebral cortex and hippocampus, along with vessel congestion and fibrin deposits within erythrocyte clots. After SBT+DEXA pretreatment, the number of pyknotic and damaged neurons observed in brain regions decreased ($p<0.05$). The SBT seed oil pretreatment also resulted in significantly improved hypoxic tolerance in the animals, offering a potential complementary therapy to corticosteroids—a more holistic approach to managing hypoxia-induced brain injury. Furthermore, it may highlight the therapeutic benefits of combining natural products with conventional drugs to enhance the hypoxic tolerance of the brain.

EFFECTS OF PROLONGED SOCIAL ISOLATION ON MEMORY AND DEPRESSIVE BEHAVIOR IN RATS OF VARYING SOCIAL STATUS

Tamar Matitaishvili[1], Tamar Domianidze[1], George Burjanadze[2], Mariam Shengelia[2], Nato Menteshashvili[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

The COVID-19 pandemic and its accompanying quarantine measures have heightened interest in the cognitive and behavioral consequences of chronic social stress induced by prolonged social isolation. The impact of stress varies based on individual neurophysiological characteristics, including social status. Prior research indicates that dominant rats exhibit greater resilience to short-term stress, whereas submissive rats are more vulnerable to cognitive deficits. The present study aimed to investigate the effects of prolonged social isolation on short-term memory and depressive behavior in rats of varying social status. The study involved 60 white adult rats, divided into experimental and control groups, each consisting of 3 males and 2 females. Experiments performed on male rats only. Social status was determined through behavioral observation during competition for food and water, classifying individuals as dominant or submissive. Rats in the experimental groups underwent a 30-day isolation procedure in individual cages. Cognitive performance was assessed via the Y-maze test, while depressive and anxiety-like behaviors were evaluated using the "forced swim" and "elevated cross maze" tests. Serotonine levels in the hypothalamus and hippocampus were measured using an immunoenzyme analyser (ELISA). Statistical analysis was conducted via two-way ANOVA. Results showed a significant decrease in spontaneous alternation behavior in the Y-maze among both dominant and submissive rats subjected to isolation. Depressive behaviors were observed in rats of both social statuses. The anxiety levels were particularly high in submissive rats, which showed increased serotonine concentration in the hypothalamus. Our findings suggest that prolonged social isolation induces short-term memory deficits and depressive behavior, regardless of social status; however, submissive rats appear to be more vulnerable to anxiety-related responses. These findings highlight the importance of considering individual social profiles in future research on stress-related psychopathologies.

This work is supported by Shota Rustaveli National Science Foundation of Georgia, grant FR--23-2770

ACTIVITY OF BRAIN ENERGY METABOLISM ENZYMES IN NEURODEGENERATIVE DISORDERS IN THE AGING PROCESS

Abiyeva Elnaz

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

In the process of aging biological mechanisms are damaged under the influence of both internal and external factors. As a result, age-related pathologies develop and the probability of death increases. With aging, the processes of cell decay prevail over cell regeneration. Aging leads to a weakening of metabolism and changes in the work of individual functional systems. Processes known as neurodegeneration begin in the brain, leading to progressive loss of neuronal structure or function. This damage to neurons eventually leads to cell death and neurodegenerative diseases. Since energy metabolism in the brain is at a very high level, the activities of the body must be directed primarily to meet and maintain the needs of the brain. The brain is the first to react to a decrease in the intensity of bioenergetic processes, which is manifested primarily by a decrease in the activity of energy metabolism enzymes, including succinate dehydrogenase. During the experiments, a neurodegenerative experimental model was created on old male and female white rats (bilateral removal of the olfactory bulb by aspiration) and the dynamics of succinate dehydrogenase enzyme activity in the brain structures of animals was studied. Males aged 6 months kept under normal vivarium conditions were taken as a control. During the experiment, a decrease in the activity of succinate dehydrogenase in the brain structures of both male and female rats was observed. Moreover, the inhibition of the enzyme activity was more pronounced in female rats. The decrease in the activity of the enzyme studied by us can be explained by the weakening of metabolism in old animals and changes in the activity of some functional systems.

MALATE DEHYDROGENASE ACTIVITY IN THE BRAIN OF OLD RATS AS A RESULT OF OLFACTORY BULBECTOMY

Vafa Mammedkhanova

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

The brain's capacity for neuroplasticity decreases with age. The aging process of the organism depends on human genetics by about 20% and more than 80% on epigenetic factors (sleeping, nutrition, physical activity, ecology, etc.). One of the irreversible signs of aging is age-related changes in the brain. It is impossible to stop these processes, but it is possible to slow them down and make them smoother. In the present study, we examined malate dehydrogenase activity in mitochondrial and cytosolic fractions of brain structures (hypothalamus, cerebellum, sensori-motor, orbital, limbic cortex and hippocampus) of aged rats (≈24-28 months old), as a result of bilateral bulbectomy. Comparison of the obtained data allowed us to conclude that the hippocampus is most susceptible to pathological changes manifested as a result of removal of olfactory bulbs, at the same time, more striking changes were observed in the mitochondrial fraction of the rat brain. It is known that mitochondria are involved in ATP synthesis, fatty acid metabolism, ion transport and other processes necessary for normal functioning and survival of the cell. Mitochondrial dysfunction is

accompanied by the development of severe cellular pathology. They play a crucial role in the metabolism of all mammalian cells, including brain neurons, and abnormalities in mitochondrial structure and function can lead to age-related neurodegenerative diseases. This predetermines the need to study the mechanisms of development of structural and functional disorders of mitochondria in the development of neurodegenerative diseases. Currently, a whole area of research is devoted to the development of "mitochondrial medicine", where MCH themselves are the target of therapeutic actions.

OXIDATIVE AND BEHAVIORAL CHANGES INDUCED BY ISOLATION IN DOMINANT AND SUBMISSIVE RATS

Tamar Domianidze, Tamar Matitaishvili, Nodar Mitagvaria, lena Davlianidze, Lali Gumberidze, Nato Menteshashvili

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

The investigation of psychogenic stress, particularly that resulting from social isolation, is becoming increasingly relevant due to its role in the development of mental disorders. Stress primarily affects behavior and cognitive functions, with its impact varying depending on the individual characteristics of the nervous system. The objective of our study was to assess the behavioral and oxidative changes resulting from short-term isolation in dominant and submissive rats. The experiments were carried out on groups of adult white laboratory rats, each consisting of three males and two females. Hierarchical relationships within the groups were determined through conflict situations with high food and thirst motivation. Following the identification of dominant-submissive relationships, the rats were subjected to 14 days of social isolation in individual cages. In order to study behavior of animals, we used "open-field" and "elevated cross maze" tests. Oxidative status was measured by analyzing oxidative (Reactive Oxygen Metabolites - d-ROM) and antioxidative (Plasma Antioxidants - PAT) indicators in blood plasma using the FRAS5 analyzer (H&D, Italy). Statistical analysis of the data was performed using the Student's t-test. The results from the behavioral tests conducted post-isolation indicated that both dominant and submissive rats exhibited increased emotional tension, fear, and anxiety, with these effects being more pronounced in submissive rats. Oxidative stress levels (d-ROM) increased in both dominant and submissive rats, but they remained within the lower range according to established oxidative stress criteria. Additionally, all animals showed a slight, non-significant increase in antioxidant (PAT) levels following isolation-induced stress. In conclusion, the findings suggest that the stress caused by short- term isolation led to behavioral and oxidative changes in all experimental animals. However, submissive rats were more sensitive to isolation stress. Additionally, a correlation was observed between the intensity of behavioral and oxidative stress changes.

ADAPTATION OF GLUTAMINE SYNTHETASE ACTIVITY TO THE LIGHT DEPRIVATION AS A MANIFESTATION OF NEUROPLASTICITY IN RATS

Esmira Efendiyeva, Venera Khairova, Nazaket Aliyeva

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

Neuroplasticity is a fundamental property of the brain that ensures its ability to adapt in response to environmental changes. One of the key biochemical indicators reflecting metabolic and plastic restructuring in the brain is the activity of the glutamine synthetase (GS) involved in the regulation of glutamate and ammonia metabolism. The aim of the present study was to reveal the changes in GS activity in brain structures of rats subjected to complete light deprivation. The experiment was performed on twelve-month-old rats, which were kept in constant darkness for 14 days. A control group kept under standard lighting conditions. At the end of the exposure the animals were removed from the experiment by decapitation. GS activity was determined in the cytosol fraction of the cortex, cerebellum, hippocampus, hypothalamus, midbrain, and medulla oblongata spectrophotometrically using an appropriate kit. The results obtained showed a significant increase in GS activity in all brain structures in animals under dark regime compared to the control. The most increase in GS activity was observed in the cortex, hippocampus, and cerebellum, which is probably related to the high concentration of glutamatergic neurons in these structures, as well as to the participation of specialized Bergmann glia in the cerebellum, characterized by a developed system of terminal outgrowths and active participation in metabolic regulation. The increase in GS activity under conditions of light deprivation can be regarded as a biochemical manifestation of neuroplastic processes aimed at the adaptation of neuronal and glial systems to new conditions of functioning.

ELECTRON TRANSFER AND THERMAL STABILITY OF CYTOCHROME C UNDER PROLONGED GLYCATION BY GLUCOSE AND LACTOSE: SIMILARITIES AND DIFFERENCES

Maia Makharadze[1], David Vashakidze[1], Tinatin Dolidze[1], Sophio Uchaneishvili[1], Dimitri Khoshtariya[1,2]

[1]I.Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]I. Javaxishvili Tbilisi State University, Inst. of biophysics and bionanosciences, Tbilisi, Georgia

The electron transfer efficiency and global thermodynamic stability of horse heart cytochrome c (Cyt C), in potassium chloride buffered solutions containing either monosaccharide-glucose or disaccharide-lactose, during long-term (more than three weeks) glycation period were explored. The oxidation and reduction reaction rates of Cyt C at a modifier-coated gold electrode, as well as, the thermodynamic stability of dissolved protein was determined at different stages of the glycation process using, respectively, the cyclic voltammetric and micro-calorimetric methods. The obtained volatammetric experimental results indicate that long term glycation of Cyt C by glucose and lactose produces distinct effects on the functional properties of Cyt C: the glucose- glycated Cyt

C retains electron transfer activity at least up to 25 days, while glycation with lactose, in contrast, leads to a sharp deterioration of the redox activity of Cyt C one week after the beginning of the glycation period. Meanwhile, according to micro-calorimetric (that is the protein's thermal melting) experimental data, in above mentioned both cases, assessments of a thermal stability of Cyt C revealed increase in the global stability of glycated (by glucose and/or by lactose) protein in the same period of time. Taking into account the similarity for effects of global(thermodynamic) stabilization of Cyt C by glycation with glucose and lactose, we may propose that reasons for the different impact of glycation on electron transfer ability of Cyt C in cases of glucose and lactose stem from the different local spatial geometry of a docking complex formed in the course of a non-enzymatic glycation process involving the protein amino groups near the heme-binding active center moiety and structurally and commpositionally different reducing sugars (Glucose and lactose).

ELECTROMAGNETIC RADIATION AND ISOENZYME SPECTRUM OF LACTATE DEHYDROGENASE IN THE BRAIN OF RATS

Khalida Panakhova, Samira Madjidova

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

Electromagnetic radiation (EMR) in its effect on humans and animals has reached a critical level. Numerous studies have shown significant physiological changes in living organisms caused by EMR. The effect of EMR on the central nervous system (CNS) is one of the most important aspects of this problem: of particular interest is the developing brain under the influence of electromagnetic fields. Lactate dehydrogenase (LDH CF 1.1.1.27) and its isoenzymes, which play an important role in the energy exchange occurring in the structures of the CNS, controls one of the main pathways of glycolysis - the conversion of pyruvate into lactate. The aim was to study the LDH isoenzyme spectrum in tissue homogenates and subcellular fractions (mitochondria, cytosol) of various regions of the cerebral cortex of one-month-old rats exposed to a single (25 minutes) EMR at birth. As a result of the conducted studies, it was found that the activity of the aerobic (LDH1,2) fraction was 106% and 118% ($p<0.001$) of the control level in the mitochondrial fraction in the limbic region, and in the cytosol fraction in the hypothalamus, respectively. An increase in the activity of the anaerobic (LDH 4,5) fraction from the control level was observed in the tissue homogenate of the limbic region and hypothalamus. Thus, this indicator was 121% and 105% ($p<0.001$) of the control value, respectively. In the cerebellum, a significant increase in the activity of the LDH 4,5 fraction from the control level was observed at all levels of the cell studied. Thus, changes in the LDH isoenzyme spectrum as a result of the influence of EMR lead to changes in the dynamics of enzymatic reactions in tissues and cellular compartments of brain regions, the main energy source for cells, and adaptive-compensatory reactions.

THE EFFECT OF 30-DAY PROTEIN FEEDING IN ANIMALS ON THE FORMATION OF MEMORY TRACES OF CONDITIONED PASSIVE AVOIDANCE REFLEXES

Samira İbrahimova

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

One of the main models used in memory research is the conditioned passive avoidance reflex (CPAR). The development of this reflex may depend not only on the ability to learn and recall a skill but also on various other factors. The aim of this study is to investigate the effect of protein nutrition on the formation of the conditioned passive avoidance reflex in animals with different types of nervous systems. Each group was trained in the conditioned passive avoidance reflex (CPAR) based on rats' innate preference for darkness, a well-developed instinct in this species. During CPAR training, the latency of the first entry into the dark chamber was nearly the same in control animals, regardless of whether they were stress-resistant and stress-sensitive. The memory retention test was conducted 24 hours after training, in the light chamber. During this test, the rats—both stress-resistant and stress-sensitive—mostly remained in the light chamber, avoiding the dark chamber with the electrified floor where the aversive stimulus had been previously administered. On day 30 of protein nutrition, training of experimental stress-resistant and stress-sensitive animals proceeded similarly to that of control animals. Testing for the reproduction of the conditioned passive avoidance reflex (CPAR) revealed that experimental animals from both groups entered the dark compartment of the chamber. This suggests that protein nutrition inhibited the formation of passive avoidance behavior. Behavioral analysis showed a significant decrease in both behavioral and autonomic indicators by day 30. However, stress-resistant animals primarily exhibited grooming behaviors, whereas stress-sensitive animals predominantly displayed freezing responses. These findings indicate that protein nutrition in 3-month-old stress-resistant and stress-sensitive animals enhances innate self-preservation behaviors, which in turn interferes with the development of conditioned reflex activity.

THE SHINE-THROUGH PARADIGM: A SENSITIVE MARKER FOR SCHIZOPHRENIA SPECTRUM DISORDERS

Maya Roinishvili[1,2], Simona Garobbio[3], Janir Ramos da Cruz[3], Ophélie Favrod[3], Albulena Shaqiri[3], Andreas Brand[3], Michael H. Herzog[3], Eka Chkonia[4]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Institute of Cognitive Neurosciences, Free University, Tbilisi, Georgia;
[3]BMI, EPFL, Lausanne, Switzerland; [4]Medical State University, Tbilisi, Georgia

Introduction: The shine-through paradigm, a visual backward masking task (VBM), has proven to be a sensitive endophenotype for schizophrenia. In this paradigm, the vertical vernier is followed by a 25-element grating mask, reducing target discriminability. Our research examines how

schizophrenia and related disorders, including bipolar disorder and depression, exhibit unique deficits in this paradigm. Objectives: We aimed to assess the shine-through paradigm as an endophenotype for schizophrenia and explore its relevance in other psychiatric conditions. The study focused on whether masking deficits are specific to schizophrenia or present across its spectrum, as well as the neural and genetic correlates of these deficits. Methods: We used the shine-through paradigm to assess masking performance in patients with schizophrenia, schizoaffective disorder, bipolar disorder, and depression, along with their non-affected relatives and healthy controls. Behavioral performance was compared across groups, and neurophysiological data were collected using the electroencephalography (EEG) to examine N1 component amplitudes at 200 ms. In schizophrenia patients, the associations between masking performance and the single-nucleotide polymorphisms (SNPs) of the cholinergic nicotinic receptor gene were also tested. Results: Schizophrenia and bipolar patients showed significant masking impairments and reduced N1 amplitudes compared to controls. These deficits were consistent across schizophrenia spectrum disorders but absent in depressive patients, who had reduced N1 amplitudes, though stronger than those in schizophrenia. Unaffected siblings exhibited higher N1 amplitudes than controls, suggesting evidence for a neural compensation mechanism. Genetic analysis revealed a correlation between a cholinergic SNP (rs904952) and masking deficits in schizophrenia. Atypical medications improved performance. Summary: Impairments in the shine-through paradigm across schizophrenia spectrum and bipolar disorder seem linked to attention and neuromodulation dysfunctions rather than visual deficits. Depressive patients' ability to stabilize target representations contrasts with schizophrenia and bipolar patients, who may struggle to enhance neural responses. These findings connect genetics, neural processing, and behavior, offering insights into the pathophysiology of psychiatric disorders. They suggest that the shine-through masking paradigm is a potential endophenotype of psychosis.

SHORT- AND LONG-TERM EFFECT OF TOLUENE CHRONIC EXPOSURE ON SYNAPTIC ARCHITECTURE IN ADOLESCENT MALE WISTAR RATS. ELECTRON MICROSCOPIC STUDY

Nino Pochkhidze[1,2], Mzia Zhvania[1,2], Nadezhda Japaridze[1,3]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ilia State University, Tbilisi, Georgia;
[3]New Vision University, Tbilisi, Georgia

Toluene, a water-soluble aromatic hydrocarbon and volatile inhalant, is usually used as an industrial solvent and added to crude oil to produce benzene. As solvent, toluene is also present in cleaners, pharmaceuticals, glues and other household and industrial products. Toluene-containing substances are known to have demonstrative addictive properties. Millions of people inhale toluene vapors to gain a “toluene high”. Central nervous system is one the most vulnerable to toluene vapors: long-lasting neurological damage, learning and memory disorders, cerebellar dysfunction or leukoencephalopathy were described. Toluene abuse misuse is higher during adolescence.

Moreover, the majority of adults who abuse toluene, started as teenagers. However, compared to other abused drugs, limited research has been carried out regarding the impact of toluene on the adolescent brain. Earlier, we reported that 40 days' toluene exposure (2000 ppm/3-5 min) produces short (immediately after treatment) and long-term (90 days after treatment) consequences on hippocampus-dependent recognition memory and spatial memory (tested in open field and Morris water maze) and the morphology (light and electron microscopic studies) of the hippocampus in adolescent male Wistar rats. Now, using the same experimental design, we elucidate the effect of toluene chronic exposure on synaptic architecture of the CA1 area. Concretely, using corresponding software and one-way ANOVA, on electron micrographs the area of presynaptic terminals, the length and diameter of synaptic active zone, the number and area of presynaptic mitochondria, total number of synaptic vesicles, the number of vesicles docked with plasma membrane and the depth and diameter of porosome complex were measured. Significant effects on the area of presynaptic terminals, the length of active zone, the area of presynaptic mitochondria and the number of synaptic vesicles were found. The most alterations were developed immediately after 40 days' treatment. The data indicate altered neurotransmission and correspondingly to the changes in neuroplasticity.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) Grant #-YS-24-194

ASSESSMENT OF THE SMELL OF LONG – LIVERS IN THE POSTCOVID PERIOD

Farida Bagirova

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

It is known that the new coronavirus infection COVID-19 affected all groups of the population. Its negative impact was reflected in both the psycho-emotional, psychophysiological and neuropsychiatric status of patients (A.I. Melekhin, 2021). It has been shown that the new coronavirus infection COVID-19 in some cases leads to hypo- or anosmia. A number of authors (X. Meng et al., 2020) believe that anosmia can occur independently without other clinical manifestations of the disease and be the main criterion in the diagnosis of a new coronavirus infection. It was revealed that the restoration of smell in all people occurs differently. Earlier, we interviewed people of elderly and senile senile age living in Baku and registered at the Gerontological Center as having suffered and not suffered from COVID-19. We also noted isolated cases of lack of restoration of smell even 2 years after infection. Moreover, if hyposmia was observed in almost all persons we interviewed, both elderly and senile, in the postcoid period, then anosmia was less common. It seemed interesting to us to study the effect of COVID-19 on the sense of smell of long- livers in the postcoid period. A survey of long- livers infected with COVID-19 showed that hyposmia was rare and recovery occurred within 4-5 days. Anosmia was not detected in these long- livers. Thus, the absence of anosmia in long- livers, one of the risk factors for the development of postcoid syndrome, indicates that they have strong immunity.

CHANGES IN THE BLOOD LEUKOCYTE FORMULA OF WHITE RATS EXPOSED TO NON-IONIZING ELECTROMAGNETIC WAVES

Mushgunaz Abbasova

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

Introduction: Electromagnetic radiation is currently widely used in almost all areas of medicine. It is known that under the influence of low-power electromagnetic radiation, the metabolic and functional properties of a number of biological systems can be significantly changed. The abstract is devoted to identifying changes in the leukocyte formula of white rats exposed to non-ionizing electromagnetic waves. Aim: Study of blood leukoformula in rats exposed to chronic decimeter-range electromagnetic radiation. Materials and methods: Rats weighing 250-300 g were subjected to total exposure to EMR with a power flux density of 10 μW/cm2 for 4 weeks, 20 min/day, 6 days/week. Specific absorption rate (SAR) values were estimated at 5 mW/kg. Animals were divided into experimental and control groups. The experimental group was divided into 4 subgroups of 10 animals each, which were exposed to EMR (frequency 460 MHz, apparatus "Volna-2") for 1, 2, 3 and 4 weeks. Results: According to the microscopic analysis, it was found that in those irradiated for 7 and 14 days, there was a breakdown of leukocytes, vacuolization of lymphocytes, and lymphocytes of various sizes, while in those irradiated for 21 and 28 days, there was a breakdown of erythrocytes, aggregation of platelets, and atypical lymphocytes. At the same time, the number of lymphocytes increases in the experimental groups (7, 14, 21, 28 days) compared to the control group. The number of monocytes and eosinophils decreases in the experimental group compared to the control group. When it comes to neutrophils, the number of segmented neutrophils decreased in the experimental group compared to the control group, while the number of band neutrophils increased. Conclusion. These effects could be due to the stimulatory effects of radiation on cell division in bone marrow cells. But the effects of radiation on living systems require further research.

THE EFFECT OF ELECTROMAGNETIC WAVES ON THE BLOOD LEUKOFORMULA OF PUPPIES AT DIFFERENT PERIODS OF PRENATAL DEVELOPMENT

Aynur Guliyeva

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

Introduction: This study is devoted to identifying changes in the leukocyte formula of rat pups born to mothers exposed to non-ionizing electromagnetic radiation of the decimeter wavelength range during different periods of pregnancy. Aim: The aim of this study was to evaluate hematological parameters of peripheral blood in rat offspring after exposure to electromagnetic radiation during intrauterine development. Materials and methods: Experiments were conducted on 20- and 30-day-old rat pups born to female Wistar rats exposed to EMR during different pregnancy stages. The

"Volna-2" device (Russia), commonly used in clinical physiotherapy, was employed. It is a tube-based EMR generator that allows controlled exposure with a frequency of 460 MHz (±1%). Exposure lasted 20 minutes daily during: embryonic period (days 1–6 of pregnancy), pre-fetal period (days 7–16), fetal period (days 17–21). Each age group (20-day-old and 30-day-old) had three subgroups of 8 pups each, corresponding to the three exposure periods. Control pups were from non-irradiated mothers kept in identical vivarium conditions. Results: The data obtained for all 3 periods of irradiation - the embryonic, prenatal and fetal periods - showed that the offspring of irradiated animals have an increased number of lymphocytes and a reduced number of monocytes and neutrophils compared with control animals. The exception is an increased level of neutrophils in 30-day-old rats exposed during the embryonic period. Prolymphocytes are found in 30-day-old rats exposed during the fetal period of development. The indicators of the leukocyte formula in offspring exposed to non-ionizing EMR in intrauterine development are characterized by lymphocytosis, which, apparently, can be considered typical for the chronic action of this physical factor. Conclusion: Thus, the influence of electromagnetic radiation on peripheral blood indices-indirect markers of physiological disturbances such as slowed redox processes, weakened immunity, and lowered reactivity ultimately impacts overall organism vitality and longevity.

PHOSPHATE-ACTIVATED GLUTAMINASE ACTIVITY IN A RAT MODEL OF STREPTOZOTOCIN-INDUCED NEURODEGENERATION

Leyla Gadirova

Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

Neurodegenerative diseases are characterized by a progressive course and remain difficult to treat effectively. Despite ongoing advances in neuroscience, the pathogenic mechanisms underlying neurodegeneration are still not fully understood. Experimental animal models are widely used to explore these mechanisms. To investigate the pathogenic mechanisms of neurodegeneration, particularly glutamatergic system disruption, we used an animal model involving intracerebroventricular administration (ICV) of streptozotocin (STZ), which induces Alzheimer's-like cognitive and morphological impairments and replicates key metabolic features of the disease. In the context of altered brain metabolism, glutamate has received particular attention. As an excitatory neurotransmitter in the brain, glutamate plays a dual role. It is essential for synaptic transmission and plasticity, but in excess, it can lead to excitotoxicity and neuronal death. This study examined age-related changes in phosphate-activated glutaminase activity in various brain regions using the STZ model of neurodegeneration in aged Wistar rats. The animals were divided into three groups: an intact group, a control group that underwent a sham operation involving bilateral saline ICV injections under calypsol + xylazine anesthesia, and an experimental group that received 5 µL STZ, 3 mg/kg, ICV. Three months following the injections, the animals were decapitated for analysis. The activity of phosphate-activated glutaminase was measured using the phenol-

hypochlorite method in the visual, sensorimotor, orbital, and limbic cortices, as well as in the hippocampus, midbrain, cerebellum, and medulla oblongata. Following the STZ administration, varying degrees of sensitivity to the neurotoxic agent were observed across different brain regions. The study demonstrated significant alterations in glutaminase activity, particularly in the hippocampus, hypothalamus, and cerebral cortex areas. These changes observed during the progressive neurodegenerative process indicate altered glutamine hydrolysis, resulting in the production of glutamate and ammonia, both of which are known to exert neurotoxic effects and may contribute to ongoing neuronal damage.

REVOLUTIONIZING HEMORHEOLOGY THROUGH ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING

Maia Mantskava, Giorgi Kuchava, Nana Momtselidze

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

The intricate flow behavior of blood, governed by its unique rheological properties, plays a pivotal role in cardiovascular health and disease. Traditional methods for analyzing and predicting blood flow dynamics, such as computational fluid dynamics, often face limitations in computational cost and real-time applicability. The burgeoning fields of Artificial Intelligence (AI) and Machine Learning (ML) offer transformative solutions, providing powerful tools for analyzing complex hemorheological data, predicting flow patterns, and ultimately improving clinical decision-making. This abstract explores the significant impact of AI and ML on the study of blood flow rheology. We delve into how ML algorithms are being employed to predict crucial hemodynamic parameters, including velocity profiles, pressure gradients, and wall shear stress, with enhanced speed and efficiency compared to conventional methods. Furthermore, we highlight the potential of AI in analyzing vast datasets of patient-specific information, enabling personalized predictions of blood flow and facilitating tailored treatment strategies for cardiovascular conditions. The application of AI and ML extends to the analysis and interpretation of blood flow data for diagnostic purposes. We discuss how these technologies can identify subtle patterns indicative of disease markers and contribute to improved risk stratification for major adverse cardiovascular events. The integration of AI with medical imaging techniques, such as CT scans and angiograms, allows for the extraction of valuable information about vessel geometry and flow characteristics, further enhancing the predictive capabilities of ML models. Moreover, AI and ML are instrumental in modeling the complex non-Newtonian behavior of blood and the intricate interplay between blood flow and vessel wall mechanics. These advanced modeling techniques offer a more comprehensive understanding of cardiovascular physiology under both healthy and pathological conditions. While the integration of AI and ML in hemorheology presents significant opportunities, challenges such as data availability, model interpretability, and seamless integration into clinical workflows must be addressed. Nevertheless, ongoing research and development in this interdisciplinary field hold immense promise for revolutionizing the diagnosis, treatment, and management of cardiovascular diseases, ultimately leading to improved patient outcomes.

WHITE LABORATORY RATS AFTER ACUTE SINGLE STRESS SOUND EXPOSURE TO ULTRASTRUCTURAL CHARACTERISTICS OF GLIAL-CAPILLARY CONTACTS IN THE ORBITAL CORTEX

Maya Sultanli
Academician Abdulla Garayev Institute of Physiology, Baku, Azerbaijan

Introduction: To date, the electron microscopic features of the structure of the glial-capillary barrier (GCB) in the orbital cortex (OC) in white laboratory rats under normal conditions and under various extreme influences have not been sufficiently studied. Purpose: The aim of this study was an electron microscopic examination of glial-capillary contacts in the orbital (prefrontal) cortex of white laboratory rats on a normal and low-protein diet after a single acute stressful sound effect. Materials and methods. The experiments were performed on sexually mature white male laboratory rats weighing 170-210 g, exposed to a special chamber with a continuous 2-minute 120-dB sound effect. After the exposure, the animals were divided into 2 groups: stress-resistant (12) and stress-unresistant (18). The control group consisted of 12 intact animals on a normal balanced diet. The animals were withdrawn from the experiments on the 10th and 30th days by air embolization. Ultrathin sections of epon-araldite blocks of the OC samples were examined on a JEM-1400 electron microscope (JEOL, Japan). Results of the study. It was established that the hemocapillary bed of the OK of a white laboratory rat consists of a chaotic wide-meshed network of capillaries with a continuous basement membrane. Sound stress exposure initiates pericapillary edema with parallel compaction of the matrix of glial processes, focal rupture of their contacts with the surface of the hemocapillary, focal fragmentation of part of the astrocytic "legs", partial vacuolization of the cytoplasm, swelling of the nucleus of endotheliocytes and vacuolization of the glial ectoplasm with extreme variability of the diameter of the lumen of the capillaries. These disorders are maximally expressed by the 10th day of the experiments in animals in the stress-unstable group, especially with a low-protein diet. Some of the changes identified in the specified group remain even by the 30th day from the beginning of the experiments. In animals of the stress-unstable subgroup, an ambiguous correlation of some ultrastructural disorders of the GCB with the composition of food was found, however, this circumstance requires separate study. Conclusion. The correlation of some changes in glial-capillary contacts with acute sound stress against the background of low-protein food can serve as a manifestation of the irreversible nature of morpho-functional disorders occurring in the orbital cortex of experimental animals.

AUTHENTICATION OF OILS USING NOVEL PCR APPROACHES

Tamara Kutateladze[1], Kakha Bitskinashvili[1], Boris Vishnepolsky[1], Tata Ninidze[1,2], Kakha Karchkhadze[2], Nelly Datukishvili[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ilia State University, Tbilisi, Georgia

Oil authentication is important for food quality and safety assessment, proper labeling, consumer information, and health protection. Oilseed crops such as sunflower, corn, soybean, and rapeseed are widely used in food production, but they are recognized as important allergens. This study

presents novel nested polymerase chain reaction (PCR) approaches for the reliable detection of these plants in foods and oils. The work included: design of new PCR primers, extraction of genomic DNA, development of PCR systems, evaluation of genomic DNAs and PCR products by agarose gel electrophoresis. Seeds, flours, and various processed foods, including cold-pressed and refined edible oils, were investigated. Efficient nested and double PCR methods were developed that target species-specific genes such as sunflower helianthinin, soybean lectin, maize zein, and rapeseed acetyl-CoA carboxylase. The new triplex PCR has enabled the simultaneous identification of sunflower, soybean, and corn. Testing of various food products has shown that new PCR methods are useful for the accurate, fast and inexpensive detection of oilseeds in foods and oils.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) [Grant AR-22- 636].

THERMAL AND MECHANICAL SENSORY AND PAIN ASSESSMENT IN HEALTHY STUDENTS

Irina Kvachadze, Tamar Gvasalia, Tamar Giorgobiani, Merab Tsagareli

Tbilisi State Medical University, Tbilisi, Georgia

Objectives. Studies of pain mechanisms in normal, pain-free individuals provide a degree of experimental control not found in studies of clinical pain and open a window to the experience of pain that is not available in controlled studies with laboratory animals. In this study, we report findings of cold and heat sensations, thermal pain thresholds, mechanical pressure thresholds, and pressure pain thresholds in healthy student volunteers. Materials and Methods. Forty undergraduate student volunteers (22 male and 18 female) with a mean age of 21±2 years participated in the study. Contact thermal stimuli were delivered using a computer-controlled stimulator (Medoc Ltd, Israel). Mechanical pressure threshold and pain sensation were obtained using a computerized pressure algometer (AlgoMed, Medoc Ltd, Israel) in kilopascals (KPa). The mean values for each of the responses for detection of thermal and mechanical pressure sensation thresholds and thermal and mechanical pain thresholds were calculated. Results. There are significant differences between the cold sensation threshold and the cold pain threshold ($P<0.001$) and between the warm sensation threshold and the heat pain threshold ($P<0.001$), which is correct for these indices. At the same time, we did not find gender differences for either the thermal sensation threshold or the thermal pain threshold. There is a statistical difference between the pressure threshold and pressure pain threshold groups ($P<0.001$). Here we found gender difference values either for the pressure stimulus threshold ($P<0.01$), and for the painful pressure threshold ($P<0.001$). Thus, our study confirmed significant variability across trials and individuals, which appeared greater at lower heat and mechanical pressure intensities. Conclusions. While we have shown gender differences in mechanical pressure assessment, additional studies and a collection of more data are needed to determine gender differences between male and female groups in assessment of temperature intensities in healthy human subjects.

A GENERAL VIEW OF PAIN PERCEPTION IN ATHLETES

Liana Kakiashvili[1,2], Ketevan Ebralidze[2], Merab Tsagareli[2], Irina Kvachadze[2]
[1]Georgian State University of Physical Education and Sport, Tbilisi, Georgia;
[2]Tbilisi State Medical University, Tbilisi, Georgia

Pain is almost synonymous with sport. For many athletes, pain is an everyday experience, and success is often achieved despite pain. However, pain can restrict the ability to concentrate on performance and take away the opportunity to compete. It can even end sporting careers. Therefore, the relationship between pain and sport is filled with challenges for sportsmen. One consequence and response that sport researchers have focused on is the pain associated with injury. Sport medicine professionals have directed the major part of their research and rehabilitation attention towards the physical recovery, but psychological factors are also very important for injured athletes. In western European countries, e.g., in Germany, about two million sport-related accidents are reported every year, while in the United States, the number of people who get injured each year participating in a range of sports, exercise, and recreational activities is estimated to be up to 25 million. Sport injuries are probably the most dreaded experience athletes might face during their sporting careers. Traditionally, sports medicine professionals have directed the major part of their research and rehabilitation attention towards the physical recovery of injured athletes. One consequence and response that sport researchers have focused on is the pain associated with injury. Pain is seen as a pervasive and debilitating obstacle for the injured athlete because it threatens and alters the athlete's ability to participate in sport. Pain also has an impact on the rehabilitation programs. Thus, an adequate understanding of injury pain requires knowledge of not only its biological substrates but also its psychological aspects. Talking to athletes about their injury is an important part of injury diagnosis and rehabilitation, as it is thought that this interaction can increase adherence to rehabilitation programs and reduce recovery time.

THERMAL PAIN SENSATION DURING DIFFERENT SATIETY LEVELS IN MALES AND FEMALES ACROSS OVARIAN-MENSTRUAL CYCLE

Tamar Gvasalia, Giorgi Chichinadze, Merab Tsagareli, Irina Kvachadze
Tbilisi State Medical University, Tbilisi, Georgia

Objectives. Sex hormones play an important role in the reproductive system, but also in thermoregulation, somatosensory control, and pain sensation. In addition to sex, feeding status is also an essential factor for pain perception. Metabolic factors and glucose levels may play a role in the sensation of pain. In this work, we report an evaluation of thermal pain thresholds induced by heat and cold stimulation in males and females during primary (pre-resorption) and secondary (metabolic) satiety. Materials and Methods. The study sample comprised 50 volunteer students (mean age 20,5 ± 2,5). Menstrual cycle phases were determined using questionnaires and calendar methods. Thermal pain sensitivity was assessed using the computer-controlled device Pain & Sensory Evaluation combined system PATHWAY (Medoc, Ltd, Israel), in which probands were given heat/cold stimuli, and thermal sensitivity and pain thresholds were simultaneously detected. The mean values for each of the responses for detection thermal sensation thresholds and thermal

pain thresholds were calculated. Results. The obtained data showed that pain perception seems to be affected by changing satiety levels. Moreover, in both sensory-motor satiety and metabolic satiety, the heat pain threshold was significantly higher in males than in females in the follicular and luteal phases of the ovarian-menstrual cycle. Finally, these findings can result in altered approaches in patient-care services. Assessing whether the patient is in primary or secondary satiety can assist physicians in improving pain management tools and diminishing the risks of pain chronification. Conclusions. To actively use the results in clinical medicine, it is compulsory for investigation within the field to continue, which can become essential for creating an algorithm to manage chronic pain. This can be life-changing for healthcare workers to prevent disabilities caused by chronic pain, which in turn can improve the quality of life of patients with chronic illnesses.

DOSE-DEPENDENT EFFECTS OF MYO-INOSITOL ON KAINIC ACID INDUCED EPILEPSY

Eka Lepsveridze[1], Georgi Gamkrelidze[1], Lia Tsverava[1,2], Luka Kharkhelauri L[1], Vincenzo Lagani V[1,3], Revaz Solomonia [1,2]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[3]King Abdullah University, Thuwal, Saudi Arabia

Objectives: Epilepsy is one of the most devastating neurological diseases remaining the challenge for the modern neuroscience and neurology. Many patients are resistant to pharmacotherapy, since most of the currently available drugs are suppressing the major symptom - spontaneous recurrent seizures (SRS), rather than coping with causes, occurring during epileptogenesis. In previous studies we have shown that Myo-inositol (MI) is a potent antipeileptogenic compound which shows SRS suppressing effect even after several weeks of treatment termination; moreover, it alters important biochemical changes taking place upon epileptogenesis. However, it is always of great importance to find the best treatment dose for pharmacological compound. Materials and Methods: Our current study aimed to identify this dose and further characterize MI effects on kainic acid model of temporal lobe epilepsy. Experiments were performed on adult rats and 3 different doses of MI - 30, 60 and 120 mg/kg have been tested. The treatment lasted for 4 weeks and the duration and frequencies of electrographic SRS and spatial learning and memory efficiency were scored 8 weeks after kainic acid induced status epilepticus (SE). Results: Experiments have revealed that the most effective dose for reduction of electroencephalographic SRS comprise 60 mg/kg of MI. The same dose improved spatial learning and memory deficit associated with KA induced epilepsy. Conclusions: Our results are important step forward to translational research, that can lead to the development of the new drug with beneficial effects on epileptogenesis.

THE EFFECT OF VENTRAL TEGMENTAL AREA ACTIVATION ON THE COURSE OF LOCAL AND GENERALIZED CONVULSIVE REACTIONS INDUCED BY HIPPOCAMPAL STIMULATION

Maia Barbakadze[1], Irine Bilanishvili[1], Nini Nikabadze[2], Ketevan Balarjishvili[1], Giorgi Andronikashvili[1], Nadejda Khizanishvili[1], Zaqaria Nanobashvili [1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2] Ilia State University, Tbilisi, Georgia

Emotional disturbances in patients with epilepsy can be: ictal - which accompany seizures, periictal - which develop after the seizures, preictal - which develop before the onset of seizures, and interictal - which develop between seizure manifestations. It should be noted that 1) In patients with temporal lobe epilepsy, emotional disorders may develop 1-2 days or several hours before the onset of seizures. 2) Some antiepileptic drugs enhance and/or induce the development of affective emotional states. 3. In patients suffering from epilepsy, the use of antidepressants against emotional disorders increases the seizure incidents. It is especially noteworthy that pre- and interictal emotional disorders in patients with epilepsy can have both negative and positive manifestations. The relation between emotions and epileptic activity relies largely on exiguous clinical investigations. Consequently, the empiric and/or neurophysiological evidence for the possible relation between emotions and epileptic activity remains poorly known to date. Therefore, the influence of stimulation of the ventral tegmental area in the development of convulsive reactions caused by irritation of the hippocampus was studied. It was shown that electrical stimulation of the ventral cover causes blocking of local convulsive reactions of the hippocampus. Stimulation of the ventral tegmental area also inhibits the development of epileptogenic foci by irritation of the hippocampus in the presence of an already formed epileptogenic focus. The results obtained may be caused by the potentiation of dopaminergic neurons in the ventral tegmental area. It is also possible that neurons of the reticular nucleus of the thalamus participate in the blockade of seizure responses. It has been shown that activation of neurons of the reticular nucleus of the thalamus leads to a blockade of the development of generalized seizure responses.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) Grant – FR-23-1938

PRENATAL EXPOSURE TO DI(2-ETHYLHEXYL) PHTHALATE ALTERS THE ASSOCIATION OF GLUTAMATERGIC PROTEINS WITH PTEN IN THE HIPPOCAMPUS OF MALE OFFSPRING RATS

Natalia Kiknadze, Elene Zhuravliova, Davit Mikeladze
Ilia State University, Tbilisi, Georgia

Phthalates are common chemicals recognized for their harmful effects on human health. Prenatal exposure to these substances has been associated with potential disruptions in brain development and heightened risk for cognitive and behavioral problems. Although the impact of phthalates on learning, memory, and hippocampal functions has been widely studied, the specific molecular

mechanisms through which they affect synaptic activities remain largely undefined. Our research evaluated the effects of prenatal exposure to di(2-ethylhexyl) phthalate (DEHP) in male rats. Immunoprecipitation experiments revealed that prenatal DEHP exposure led to decreased binding of the scaffold protein NHERF1, NMDA receptor subunits (NR1, NR2A, and NR2B), the AMPA receptor subunit (Gria1), metabotropic glutamate receptor 5 (mGluR5), and excitatory amino acid transporter-2 (EAAT-2) with PTEN (phosphatase and tensin homolog protein) in the offspring's hippocampus, while the overall levels of these proteins remained stable. Furthermore, our results indicated that prenatal phthalate exposure resulted in lower protein phosphatase activity, reduced autophosphorylation of calcium/calmodulin-dependent protein kinase II (CaM kinase II), decreased protein kinase A (PKA) activities, and increased Akt kinase activity in the hippocampi of young rats. These findings imply that the PTEN protein interactome's sensitivity to phthalates at glutamatergic postsynapses may affect synaptic plasticity in excitatory neurons within the hippocampus of offspring, following the DEHP exposure of their parental rats during gestation.

ANXIOLYTIC EFFECT OF LEMON BALM (MELISSA OFFICINALIS) INFUSION AND ITS COMPARISON WITH DIAZEPAM IN BEHAVIORAL MODELS IN RATS

Giorgi Andronikashvili[1], Mikheil Okujava[1,2], Tea Gurashvili[1,3], Tamila Bagashvili[1,4], Ketevan Gogeshvili[1].

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ilia State University, Tbilisi, Georgia; [3]Alterbridge University, Tbilisi, Georgia;
[4]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

Introduction: The Elevated Plus Maze (EPM) and grooming microstructure analysis are validated methods for assessing anxiety in laboratory animals. Aim To evaluate the anxiolytic effect of lemon balm infusion in rats and compare it with diazepam.

Materials and Methods: Twenty-four adult male rats were divided into three groups (n=8): Control (water/food), Lemon balm (30 mg/kg, orally, for 10 days), and Diazepam (0.25 mg/kg, intraperitoneally, 1hour prior). Similar material was used for the Plexiglas cages. Tests•EPM test (5minutes): entries and time in open/closed arms. Indices: –In: proportion of entries into open arms – It: proportion of time spent in open arms • Grooming analysis (5 minutes, individual Plexiglas boxes): total episodes, fragmentation, sequence integrity. Statistics IBM SPSS 21 was used for data analysis. Results: In the EPM, lemon balm significantly increased both times spent and entries into open arms ($p<0.05$), similar to diazepam. No significant difference was found between the two treatments. In grooming, total episodes did not differ ($p>0.05$), but both lemon balm and diazepam groups showed reduced fragmentation and sequence disruption ($p<0.05$). Their effects were roughly equivalent. Conclusions: Lemon balm shows anxiolytic properties similar to diazepam. Grooming microstructure is a sensitive indicator of anxiety. Lemon balm may be aviable alternative for treating anxiety with fewer side effects.

BIOINFORMATIC INSIGHTS INTO UBIQUITIN AND SDF1/CXCR4 AXIS AFTER IRRADIATION

Irina Ioramashvili[1,2], Rusudan Sujashvili[1,3]
[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Ilia State University, Tbilisi, Georgia;
[3]The University of Georgia, Tbilisi, Georgia

Building on our recent discovery and initial presentation of the involvement of ubiquitin conjugates in regulating the SDF1/CXCR4 axis during post-radiation recovery, we now provide further validation through bioinformatic analyses and comprehensive literature review. To deepen our understanding of how radiation-induced changes in ubiquitin conjugate levels influence gene expression and tissue repair mechanisms, we specifically examined the interplay between ubiquitin conjugates, SDF1, and CXCR4. Our findings strengthen the hypothesis that the SDF1/CXCR4/ubiquitin conjugation serves as a critical mediator of radiation responses and cellular proliferation, with extracellular ubiquitin acting as a key regulatory mechanism in signaling cascades in damaged cells triggered by irradiation. Upon SDF1 binding to CXCR4, conformational changes in the receptor activate signaling through various G protein subunits, leading to the engagement of multiple pathways, including MAPK, PI3K, Wnt, and Sonic Hedgehog (SHH). Particularly, the Ras/Raf/MEK/ERK cascade—central to MAPK signaling—triggers phosphorylation of key regulatory proteins like c-Myc and RSK, promoting cell cycle progression, proliferation, and differentiation. Activation of ERK and AKT pathways further leads to NFκB accumulation, which inhibits apoptotic signaling and supports survival mechanisms after radiation. We suggest that radiation exposure alters signaling dynamics, potentially by modulating the balance between free and conjugated forms of investigated proteins. These findings not only validate but also reinforce the robustness of our earlier observations, highlighting the potential of targeting the ubiquitin-SDF1/CXCR4 axis to promote tissue regeneration and control abnormal proliferation in pathology. Our study provides a solid foundation for advancing therapeutic approaches to mitigate radiation-induced tissue damage.

THE EFFECT OF TOLUENE ON MOTOR CORTEX PYRAMIDAL NEURONS IN DIFFERENT AGED RATS

Lia Gelazonia, Mariam Mikadze, Marina Sardlishvili, Tamar Bikashvili

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Abuse of toluene-containing volatile inhalants has become widespread among adolescents, young people and adults. It is clear that toluene shares common cellular mechanisms and have similar actions to other drugs of abuse. Prolonged or high-level exposure to toluene may lead to neurological symptoms such as tremors, muscle weakness and impaired coordination, all of which are controlled by the motor cortex. Exposure to toluene may have a specific effect on pyramidal

neurons in the motor cortex, as these neurons play a critical role in the control of voluntary motor movements. The effects of toluene on neurons may vary depending on several factors, including the level and duration of exposure, the age of the exposed individual, and individual susceptibility. The effects of toluene on the morphology of neurons in the motor cortex were studied in adolescent (P28–30) and adult (P110–120) male rats of different ages. Experimental rats were exposed to toluene vapor at a concentration of 2000 ppm for 3–4 min per day for 40 days. The number of pyramidal neurons in the motor cortex and their fine structure were studied. The results showed that in adults there are fewer changes in the fine structure of neurons, mainly affecting the mitochondria, where individual cristae are damaged. The changes were much more pronounced in rats that inhaled toluene at the age of one month. Here there were changes in the structure of synapses, severe damages of mitochondria, which leads to degenerative changes in neurons and ultimately to neuronal death. Statistical analysis showed that the number of pyramidal neurons in adolescents decreased by 45% in the experimental rats exposed to toluene compared to the control rats. The same cannot be said for morphological analysis of adult rats, in which the number of these neurons was only slightly reduced as a result of exposure to toluene.

INOSITOLS AND TRAUMATIC BRAIN INJURY BIOMARKERS – TIME DEPENDENT STUDIES

Nino Oganezovi[1], Eka Lepsveridze[1], Vincenzo Lagani[1,2], Giorgi Gamkrelidze[1], Lia Tsverava[1,3], Revaz Solomonia[1,3].

[1]Ilia State University, Tbilisi, Georgia, [2]King Abdullah University, Thuwal, Saudi Arabia;
[3]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Traumatic brain injury (TBI) represents a spectrum of brain injuries, which remains an unsolved health problem globally. TBI is often followed by a number of severe, long-lasting complications, which are accompanied by changes in expression of some compensatory or damage-related biochemical markers, such as SOD1, PSD95 and GFAP. We have previously shown that Myo-inositol has a long-term effect on TBI induced transcriptomic and epigenetic changes. However, nothing is known about early effects of Myo-inositol or other biologically active inositols as Scyllo-inositol and D-chiro inositol on TBI induced biochemical changes. Using controlled cortical injury model of TBI we aimed to evaluate the effects of inositol isomers on the expression of the important biochemical markers of TBI. Expression of biochemical markers were studied in neocortical and hippocampal samples on the 7th and 14th days after TBI by SDS gel electrophoresis, western immunoblotting approach. Our results indicate the time-dependent and region-specific changes of potential biomarker protein molecules after TBI. Some of these changes could be reversed by inositol treatment in a way that could weaken the TBI induced pathological molecular changes.

PREVENTION OF KAINIC-ACID INDUCED EPILEPTOGENESIS BY MYO-INOSITOL: TRANSCRIPTOMIC AND EPIGENOMIC STUDIES

Lia Tsverava[1,2], Vincenzo Lagani [1,3], Luka Kharkhelauri [1], Natia Nadirashvili [1], Eka Lepsveridze[1], Giorgi Gamkrelidze[1,3], Revaz Solomonia[1,2]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Centre of Experimental Biomedicine, Tbilisi, Georgia;
[3] King Abdullah University of Science and Technology.

Objectives: Epilepsy is a severe neurological disease characterized by spontaneous recurrent seizures (SRS). A complex pathophysiological process referred to as epileptogenesis transforms a normal brain into an epileptic one. Our previous studies have revealed highly promising antiepileptogenic properties of a myo-inositol (MI) on kainic acid (KA)-induced epileptogenesis. The favourable effects persisted for four weeks post-treatment, indicating long-lasting effects of MI. Materials and Methods: In the present study, we have investigated the effects of 60 mg/kg MI injections for 28 days on KA-induced epilepsy. Dose was chosen based on our prior study which revealed the best effects for 60 mg/kg MI. Comparative changes in DNA methylome and transcriptomes were studied in the hippocampal samples extirpated 8 weeks after KA induced SE from three groups of rats: (i) Control + Saline; (ii) KA+Saline and (iii) KA+MI. Results: Based on research We have: 1. created comprehensive map of long-term DNA methylation changes after SE in the hippocampus; (ii) identified differences by methylation sites between the groups; (iii) characterized transcriptome changes; (iv) provided association between DNA methylation sites and gene expression. Our study revealed that SE induces profound changes in gene expression (including genes involved in seizure induction and development, such as voltage-gated Na+ channel subunits, collagen6 and collagen8 subunits, etc.) and DNA methylation pattern (affecting histone deacetylase, Zinc finger, RAB6B, RAS oncogene family member, Prpf38b etc. genes). Conclusions: MI treatment specifically alters these changes, which could lead to the prevention of epileptogenesis by modification of specific molecular pathways.

INFORMATION INTAKE AND RETENTION ON RADIORESISTANCE RESEARCH IN LABORATORY WHITE MICE

Mikheil Gogebashvili, Sophio Kalmakhelidze, Anastasia Avalishvili, Nino Gunia, Nazi Ivanishvili
Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Recent advancements in medical technology have increased the use of radiation-based diagnostic and therapeutic procedures, underscoring the importance of understanding their potential biological impacts, particularly on cognitive functions. As global populations age, there is heightened concern regarding radiation exposure and its effects on memory and learning. This study investigates the influence of acute gamma irradiation on cognitive performance and emotional behavior in laboratory white mice, emphasizing differences in radiation dose and prior cognitive training. Mice were subjected to doses of gamma radiation from a Cesium-137 source (1.1 Gy/min) with

experimental groups receiving 2 Gy or 4 Gy. Each dose group was further divided into trained and untrained subgroups. Cognitive and emotional behaviors were evaluated through the Open Field Test and Morris Water Maze test over a 21-day period. Results demonstrated a dose-dependent regularity. Mice exposed to 4 Gy exhibited significant deficits in both emotional regulation and spatial memory, with untrained mice showing prolonged latencies to locate the hidden platform. Notably, mice with prior training in the MWM performed substantially better than untrained counterparts, suggesting that pre-acquired information, or memory retention, is more resistant to radiation-induced impairment than the acquisition of new information following exposure. In contrast, at 2 Gy, both trained and untrained mice initially showed impairments; however, over subsequent days, their performance improved and approached baseline levels, indicating that the damage caused by this dose was within the recovery capacity of repair mechanisms. No similar recovery was observed in the 4 Gy groups, implying that higher radiation doses induce more severe, possibly irreversible, cognitive deficits. These findings suggest that information retained from prior training—exhibit greater resilience to radiation damage than the initial acquisition of new information. This differential radiosensitivity underscores the importance of cognitive preconditioning and may inform strategies to mitigate radiation-related cognitive risks.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) [grant number FR-24-12700]

RADON AS A FACTOR OF CHRONIC RADIATION EXPOSURE TO HEMATOPOIESIS

Harry Grebenchuk[1], Eremia Tulashvili[2], Sophio Kalmakhelidze[1], Nazi Ivanishvili[1], Mikheil Gogebashvili[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Nodar Kekelidze Materials Research Scientific-Research Institute;
Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

Radon, a radioactive gas, poses a serious threat to human health, particularly with long-term exposure in enclosed spaces. It is formed through the decay of uranium and thorium, which can be present and accumulate in living areas, creating significant health risks. In recent decades, interest in studying the effects of radon on the human body has grown, driven by an increase in diseases such as lung cancer linked to radon exposure. The primary focus of most research has been on the lungs—the main target of radon's radioactive impact. According to the World Health Organization, radon, alongside smoking, is one of the leading causes of lung cancer. However, in this context, considerably less attention has been paid to the secondary effects of radon after it enters other organs through the lungs. In our study, we conducted analyses and calculations of the radiation dose to critical organs. One of the key findings relates to the long-lived decay product of radon, radioactive lead-210 (^{210}Pb), which tends to accumulate in bone tissue. As ^{210}Pb decays, it produces polonium-210 (^{210}Po), which emits alpha particles with an energy of 5.3 MeV, irradiating the bone marrow.

We attempted to calculate the energy released in this process in relation to radon concentration in the external environment, using numerical modeling to simulate the transfer and accumulation of decay products in bone tissue. We also assessed the radiation dose to bone marrow based on established radioactive decay equations and their correlation with radon activity. As a result of this analysis, we developed an information-logical model describing the radiation effects of radon decay products on bone marrow and the associated impact on hematopoiesis.

LONG-LASTING EFFECTS OF MYO-INOSITOL ON IONOTROPIC GLUTAMATERGIC RECEPTOR EXPRESSION IN KAINIC ACID INDUCED EPILEPSY

Veriko Bokuchava[1], Lia Tsverava[1,2], Georgi Gamkrelidze[1], David Dzneladze[2], Revaz Solomonia[1,2]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Epilepsy is chronic neurological condition characterized by abnormal spontaneous electrical activity in brain, resulting in unprovoked seizures. Nearly 1% of population is suffering from this disorder. The management of disease typically involves anti-seizure medications (ASM), which only aims to weaken the symptoms of disease. In our early studies, we have shown the promising antiepileptogenic capabilities of Myo-inositol (MI) on kainic acid (KA) induced temporal lobe epilepsy model. MI exerted positive effect on behavioral and electrographic spontaneous recurrent seizures (SRS), learning and memory decline and molecular changes associated with epilepsy. All the previous experiments were carried out on initial effective concentration of MI (30mg/kg). Later, we examined dose-dependent comparative effects of MI, where 60mg/kg turned to be the most effective concentration according to all parameters. Additionally, we assessed the transcriptional profile of Control+Saline, KA+Saline, KA+MI (60mg/kg) treated group in hippocampus, which revealed nearly hundreds of differentially expressed transcript. Among them, ionotropic kainite receptor subunit 3 (GRIK3) and NMDA type ionotropic receptor subunit 3a (GRIN3a) was significantly upregulated in MI treated group, as compared to others. In the current study we aimed to validate RNA-seq data. With this objective, we performed quantitative PCR, which confirmed the expression patterns obtained from RNA-seq. We speculate that the decrease of GRIK3 and GRIN3A mRNA in KA treated group, in contrast to control, might be the result of compensatory mechanism against hyperexcitability of neuronal networks, which is reversed by influence of MI.

RADIATION-INDUCED MODULATION OF HIPPOCAMPAL NA,K-ATPASE ACTIVITY

Eka Nozadze[1], Leila Tsakadze[1], Lia Shioshvili[1], Nana Arutinova[1], Marine Leladze[1], Sopio Dzneladze[1], Maia Javakhishvili[1], Gvantsa Chkadua[1,2]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Georgian National University, Tbilisi, Georgia

Introduction: Ionizing radiation (IR) is a well-established source of oxidative stress in biological systems, primarily through the generation of reactive oxygen species (ROS), which can modify cellular macromolecules and impair enzymatic function. This study examined the impact of whole-body irradiation (1 Gy and 5 Gy) on hippocampal Na,K-ATPase activity in mice. Objectives: We aimed to assess the dose- and time-dependent effects of irradiation on hippocampal Na,K-ATPase activity. To elucidate the redox mechanisms underlying enzyme activity changes. Material and Methods: Age- and weight-matched male and female mice (10 weeks old) were subjected to whole-body irradiation at doses of 1 Gy and 5 Gy. Hippocampal tissue was harvested at one and two weeks post-exposure. Na,K-ATPase activity was quantified by measuring ouabain-sensitive ATP hydrolysis. Kinetic assays were conducted using p-chloromercuribenzoate (PCMB) to evaluate redox-sensitive thiol modifications. Vmax and Ki values were calculated to infer catalytic capacity and sensitivity to PCMB. Results: Na,K-ATPase activity increased significantly one week after 1 Gy (by 45%) and 5 Gy (by 129%) exposure. At two weeks, enzyme activity declined but remained above control levels. Vmax values were unchanged, indicating preserved catalytic function. However, Ki for PCMB increased at two weeks, consistent with oxidative modification of thiol groups and conformational changes in the enzyme. This suggests a transition from reversible redox modulation to progressive oxidative impairment. Furthermore, the role of endogenous ouabain, a cardiotonic steroid with affinity for Na,K-ATPase, may contribute to these effects by triggering intracellular signaling pathways that amplify mitochondrial ROS production—a proposed feed-forward mechanism termed the "Na,K-ATPase oxidant amplification loop." This model offers a plausible explanation for the delayed decline in enzyme activity despite initial stimulation. Conclussion: These findings underscore a redox-sensitive, time-dependent regulation of hippocampal Na,K-ATPase in response to IR and suggest that early adaptive responses may be overtaken by progressive oxidative damage. Given the enzyme’s essential role in maintaining neuronal ion homeostasis and excitability, these radiation-induced changes may underlie impairments in cognitive function and increase vulnerability to neurodegenerative processes.

SINGLE NUCLEI RNA-SEQ ANALYSIS OF VISUAL IMPRINTING MEMORY IN CHICKS: MEMORY-SPECIFIC CHANGES OF DIFFERENTIALLY EXPRESSED GENE PRODUCTS: RORA, LUC7L, ROBO1, FOXP2

Lela Chitadze[1], Vincenzo Lagani[1,2] Teimuraz Bokuchava[1], Veriko Bokuchava[1], Lia Tsverava[1,3], Natia Nadirashvili[1], Brian McCabe[4], Zaza Khuchua[1], Revaz Solomonia[1,3]

[1]Ilia State University, Tbilisi Georgia; [2]King Abdullah University Thuwal, Saudi Arabia;
[3]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[4]University of Cambridge, UK

A comprehensive understanding of the fundamental mechanisms of learning and memory remains elusive to neuroscientists. Despite many important discoveries, how memory is encoded and maintained at the molecular level remains an open question. Visual imprinting in domestic chicks is a rapid and robust form of learning that underlies recognition memory formation. Converging evidence indicates that the intermediate medial mesopallium (IMM) of the chick's forebrain is crucial for visual imprinting memory. With precise knowledge of memory trace localization and other properties, imprinting represents one of the most complete phenomena for the neuronal study of memory. Different learning- and memory-related molecular changes during visual imprinting mainly take place in defined types of IMM cells; however, the cell-type-specific changes are poorly studied. We investigated learning-related molecular changes in the left IMM using single-nucleus RNA sequencing from strongly imprinted chicks and untrained controls. We characterized >30 cell clusters and revealed transcriptional differences between groups. Among them, for further study, we examined two transcription factors (FOXP2, RORA) a splicing regulator (LUC7L), and an axon guidance protein (ROBO1) in learning performance using quantitative immunoblotting to determine whether the observed differences were specifically related to memory rather than being mere side effects of the training procedure. LUC7L, FOXP2, and RORA proteins showed strong correlations between preference score and their expression levels, indicating changes directly attributable to learning during training. ROBO1 exhibited associations that likely reflect learning capacity, suggesting a predisposition to learn that existed prior to training.

SINGLE NUCLEI TRANSCRIPTOMIC PROFILE OF MEMORY AFTER VISUAL IMPRINTING IN CHICKS- STUDYING QUANTITATIVE CHANGES OF DIFFERENTIALLY EXPRESSED LONG NON CODING RNAS ENSGAL00010007489 AND ENSGAL00010026609

Teimurazi Bokuchava[1], Lela Chitadze[1], Vincenzo Lagani[1,3,] Brian J. McCabe[4], Zaza Khuchua[1], Revaz Solomonia[1,2]

[1]Ilia State University, Tbilisi, Georgia; [2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia; [3]King Abdullah University, Thuwal, Saudi Arabia, [4]University of Cambridge, Cambridge, UK

The learning process of visual imprinting, causes newly hatched chicks to learn the characteristics of first conspicuous moving object they encounter and later develop preferences for that specific object. Intermedial and medial mesopallium is the region in chick's forebrain, where information about imprinting stiumuls is stored. Single-nucleus RNA sequencing has been employed to study

transcriptomic changes of left IMM on a single cell level between good learner and untrained chicks. Bioinformatic analysis was conducted on >30 cell clusters, in which long non coding RNAs (lncRNA) contributed for almost a half of significant transcriptomic changes between experimental groups. An avian brain specific LncRNA ENSGAL000100007489 has shown to be upregulated in unique subtype of glutamatergic neurons, whereas upregulation of lncRNA ENSGALG00010026609 was observed in all major cell types of left IMM. Quantitative characterization of these lncRNAs revealed upregulation of ENSGAL000100007489, to be consequence of the imprinting training, whereas increase in amounts of ENSGALG00010026609 reflects preliminary capacity existed before training - namely predisposition to learn. Expression of ENSGAL000100007489 is strictly brain tissue specific, showing no levels in heart, lung, muscle and liver tissues. Subcellular distrubution of ENSGAL000100007489 shows to be at least 100 times higher in nuclear, compared to cytoplasmic compartment. Contrary to ENSGAL000100007489, the expression of lncRNA ENSGALG00010026609 was present in all analyzed tissues and was localized in both- nuclear and cytoplasmic fractions of left IMM.

KNOWLEDGE, AWARENESS, AND ATTITUDES TOWARDS EPILEPSY AMONG SECONDARY SCHOOL TEACHERS IN GEORGIA

Marina Lazariashvili[1,2], Marika Megrelishvili[2], Nino Gogatishvili[1,4], Giorgi Kuchukhidze[3], Sofia Kasradze[1,4]

[1]Institute of Neurology and Neuropsychology (INN), Tbilisi, Georgia
[2]Ilia State University (ISU), Tbilisi, Georgia
[3]Christian Doppler University Hospital, Paracelsus Medical University, Salzburg, Austria
[4]Caucasus International University (CIU), Tbilisi, Georgia

Background: The stigma of epilepsy among school teachers often creates significant problems for children and adolescents with epilepsy in relationships with their teachers, which hinders the educational process and reduces the quality of life of individuals with epilepsy. In order to implement the proper intervention measures in this group of society, it is necessary to assess the level of awareness on epilepsy-related issues among teachers. Purpose: To study knowledge, awareness and attitudes towards epilepsy among secondary school teachers. Methods: The study was carried from 1st September to 30th November, 2024 in three secondary schools located in different parts of Tbilisi, Georgia. We used the Georgian version of the "Questionnaire for Knowledge, Attitudes, and Perceptions (KAP) on epilepsy", which was adapted from the original Chinese version and previously was used in Georgia. The KAP questionnaires were distributed among school teachers; study subjects had the opportunity to fill them out anonymously and return to the researchers. Results: 180 questionnaires were distributed, 141 were returned, and 135 of them were appropriately completed, on the basis of which the data analysis was performed. Out of the 135 participants, aged between 27 and 66 years (SD 45 years), 78 (57.7%) were male. Almost all respondents (n=132; 97.7%) had heard of epilepsy and less than half of them (n=60, 44.4%) believed that epilepsy is a form of mental illness, or psychiatric disease (n=23; 17%). 40 (29.6%)

schoolteachers would not allow their children to marry a person with epilepsy. Conclusion: There is a serious lack of knowledge about epilepsy among school teachers; more action is needed to raise their awareness and create an adequate social and learning environment for children with epilepsy in schools.

This Study was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG (PHDF-24-271*) and internal scientific grant of CIU (# CIU-FR-127-22)*

PEPTIDYL ARGININE DEIMINASE-2 EXPRESSION RATE BY THE ACTION OF MYELIN BASIC PROTEIN CHARGE ISOMERS

Nino Mamulashvili[1], Marika Chikviladze[1], Lali Shanshiashvili[1,2], David Mikeladze [1,2]

[1]Ilia State University, Tbilisi, Georgia;
[2]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Posttranslational modifications of arginine to citrulline occur frequently in positively charged proteins such as histones or myelin basic protein (MBP). Peptidyl arginine deiminase (PAD) is the enzyme that initiates this modification, and its abnormal activation is linked to autoimmune diseases like rheumatoid arthritis and multiple sclerosis. The precise mechanisms that cause PAD activation and the pathological processes that lead to hypercitrullination are not fully comprehended. In this study, we investigated the interaction between PAD and various charged isomers of MBP, each exhibiting different levels of posttranslational modification. We evaluated the binding between PAD and these MBP isomers through immunoprecipitation experiments. The anti-Citrulline detection Kit was used to determine the degree of citrullination of charge isomers of MBP. According to our findings, MBP in its phosphorylated states (C3 and C4) had a greater affinity for PAD than the unmodified (C1) and fully citrullinated forms (C8). Our study revealed that PAD only undergoes autocitrullination in the presence of the unmodified C1 isomer, and this process was slowed down by creatine, which contains guanidine. The presence of other isomers did not lead to autocitrullination for PAD. Furthermore, we discovered that the unmodified isomer of MBP C1 has methylated arginines that were not affected by PAD pretreatment. We have observed that the activation of PAD can be initiated by the increased phosphorylation of central threonines in the original MBP, leading to enhanced citrullination of the proteins and subsequent myelin sheath disruption. Understanding the order of posttranslation modification may pave the way for new therapeutic approaches to treat demyelinating diseases.

WORK ENDURANCE AND LOCOMOTOR ACTIVITY OF CHRONICALLY EXPOSED RATS

Tea Museliani, Gogi Jikia, Levan Tsitskishvili

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Introduction: In recent years, interest has grown regarding the effects of electromagnetic fields (EMF), particularly concerning the potential neurophysiological and behavioral outcomes of chronic exposure. Findings from experimental studies on animal models suggest that chronic EMF exposure may be associated with alterations in the functional state of the central nervous system, manifesting in reduced motivation, energy efficiency, and cognitive performance. Of particular concern are changes in indicators of work capacity, such as physical endurance, locomotor activity, and learning ability. Objectives: To investigate the influence of chronic non-ionizing radiation on the work endurance and locomotor activity of rats. Materials and Methods: The study involved 20 adult male rats divided into two groups: experimental and control (n = 10 per group). Rats in the experimental group were exposed to a low-frequency electromagnetic field (EMF) at 1800 MHz. The exposure was administered daily for two months, from 8:00 a.m. to 10:00 p.m. A specific program triggered a signal every 10 minutes for a duration of 10 seconds. In order to evaluate the work endurance and locomotor activity of the animals, the rotarod test was used. Results: The experiment demonstrated that the muscles of the exposed rats remain contracted, enabling them to grip the rod more tightly and stay on it longer, thus covering greater distances than compared to those in the control group. Exposed rats maintain their position on the rotarod until muscle relaxation occurred, leading to a fall. In contrast, control rats exhibited more flexible movement patterns on the rotarod, and their falls were primarily due to physical fatigue. These findings may be explained by an increased level of acetylcholine in the exposed rats. Summary: Chronic electromagnetic radiation represents a potential risk factor that affects the physical work endurance and behavioral performance of rats.

OXYTOCIN AND ELECTROMAGNETIC THERAPY: HORMONE-DEPENDENT EFFECTS ON STRESS

Nato Bukia[1,2], Marina Butskhrikidze[1], Lamara Machavariani[1], Melitsa Svanidze[3], Mariam Siradze[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Caucasus International University, Tbilisi, Georgia;
[3]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

According to the World Health Organization, mental health disorders affect over 970 million individuals globally. Chronic stress and sedentary behavior are recognized as major contributing factors. This study investigates the effects of electromagnetic stimulation (EMS) and oxytocin (OXY) on corticosterone (CORT) levels in immobilized male and female rats—both intact and

gonadectomized—to assess the modulatory role of peripheral sex hormones in stress responses. Methods: Rats underwent daily 2-hour immobilization for 20 days. After each immobilization session OXY was administered intranasally (18 IU), and EMS was applied for 10 days using experimentally defined parameters. CORT levels were assessed using ELISA. Data were statistically processed by factorial analysis (ANOVA). Results: Baseline measurements showed higher CORT levels in females compared to males. Immobilization significantly increased CORT secretion in both sexes, with a more pronounced effect in gonadectomized rats, underscoring the role of sex hormones in HPA axis regulation. A single dose of OXY effectively prevented stress-induced CORT elevation in intact rats but was less effective in gonadectomized ones. EMS alone had minimal impact after a single session; however, repeated EMS sessions significantly reduced CORT levels. The most notable reduction occurred when OXY was combined with EMS, especially in intact rats, indicating a synergistic effect dependent on the presence of sex hormones. Conclusion: These findings highlight the anxiolytic properties of OXY and the therapeutic potential of EMS in mitigating stress-induced neuroendocrine responses. The combined influence of OXY, EMS, and sex hormones appears crucial in restoring HPA axis balance following chronic stress. This study lays the groundwork for future research into non-pharmacological interventions for stress-related disorders and emphasizes the importance of sex hormone status in treatment approaches.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) N FR-22-1319

NEUROPROTECTIVE EFFECTS OF HERNIARIN AGAINST IONIZING RADIATION-INDUCED COGNITIVE AND BEHAVIORAL DEFICITS

Sophio Kalmakhelidze[1,2], Diana Museridze[1], Lali Gegenava[1], Nino Ghvinadze[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Tbilisi State Medical University, Tbilisi, Georgia

The increased use of ionizing radiation in medical diagnostics and therapy has raised concerns about unintended exposure to healthy tissues, especially the central nervous system (CNS), which is particularly sensitive to oxidative stress. Ionizing radiation produces free radicals that can directly or indirectly damage DNA, leading to metabolic disruptions and neurotoxicity. Acute exposure to high doses of radiation can trigger bystander effects in the CNS, resulting in decreased neurogenesis in the hippocampus, neuroinflammation, and subsequent cognitive impairments, such as memory deficits and anxiety-like behaviors. Herniarin, a naturally occurring simple coumarin found in various fruits and vegetables, has antioxidant properties and may provide neuroprotection against radiation-induced damage. Materials and methods: Male mice were exposed to whole-body γ-irradiation using 137Cs at 5 Gy (dose rate: 1.1 Gy/min) via a “Gamma-Capsule-2” system. Herniarin (20 mg/kg) was administered intraperitoneally for five consecutive days before irradiation and again one-hour post-exposure. Behavioral assessments included the Morris Water Maze (MWM) to evaluate spatial learning and memory, and the Open Field Test to measure

locomotor activity and anxiety-like behaviors. Histological analysis was conducted to quantify neuronal density in the CA1 and CA3 regions of the hippocampus, dentate gyrus, and entorhinal cortex at early and late post-irradiation periods (days 90 and 180). Results: Early post-irradiation analysis showed no significant neuronal loss between control and irradiated mice. However, late-phase evaluation revealed pronounced neuronal depletion: a 62% reduction in the dentate gyrus and a 67% reduction in the entorhinal cortex, CA1, and CA3 regions. Herniarin-treated mice maintained neuronal counts comparable to controls. Behavioral testing at three- and six-months post-irradiation demonstrated significant spatial learning and memory deficits in irradiated mice, while Herniarin treatment ameliorated these impairments. Conclusion: Exposure to a 5 Gy dose of ionizing radiation induces persistent behavioural and morphological deficits in mice, primarily through oxidative stress mechanisms. Herniarin administration mitigated these effects, preserving both neuronal integrity and cognitive function. These findings support the potential of Herniarin as a neuroprotective agent against radiation-induced CNS damage.

RLS AND OTHER SLEEP DISORDERS AMONG YOUNG PEOPLE OF GEORGIA

Ketevan Mamasakhlisi[1], Sofia Kasradze[1,2], Birgit Högl[3]

[1]Institute of Neurology and Neuropsychology, Tbilisi, Georgia;
[2]Caucasus International University, Tbilisi, Georgia;
[3]Medical University of Innsbruck, Innsbruck, Austria

Problem: Restless legs syndrome (RLS) is cause insomnia and other sleep/wake disturbances, they impact on human health. Aim: To analyze the specificity of association of RLS sings with other sleep/wake cycle disorders and mood disorders among young populations of Georgia. Methods: The study was conducted among students and young lecturers of two universities in Tbilisi, who agreed to fill out all the questionnaires, namely: Restless legs syndrome diagnostic criteria (2014) and RLS Rating Scale, the Epworth sleepiness scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and Beck anxiety inventory. Results: A total 90 beneficiaries participated in the study; out of them 15 (16.7%) were with a high probability of RLS (F/M-9/6). In comparison to people without RLS-like symptoms (n=75) the subjects with a high probability of RLS (n=15) showed more frequently ESS scores higher than 12.5, indicating daytime sleepiness (46% - 23.5%, respectively), dissatisfaction with sleep quality was three times frequent (60% - 19.2%, respectively), and severe insomnia was more common (7% and 1.2%, respectively). People with RLS two-should often were revealed the moderate to severe anxiety than those without RLS (60% and 30%, respectively). In contrast, depression was more common in the control group (21.1%) than in those with RLS (13.3%). Conclusion: About 17% of young people living in Georgia have a high probability of RLS; Subjects with RLS significantly more frequent have excessive daytime sleepiness, poor sleep quality, severe insomnia, and anxiety, which necessitates the exclusion of RLS in the presence of such disorders. Limitations: The study is based solely on questionnaires. In a next step, we plan to conduct face-to-face expert interviews.

CHARACTERIZATION OF MICROPLASTICS IN HUMAN TISSUES: CASE STUDIES AND RESEARCH PERSPECTIVES

Ekaterine Mikautadze

European University, Tbilisi, Georgia

Introduction: Microplastics (MPs), which are plastic particles smaller than 5 mm in size, are well-known environmental pollutants. Recent studies have identified their presence in various human tissues, raising concerns about potential health consequences. Objectives: The aim of this study was to synthesize data from recent case studies to assess the presence and distribution pathways of microplastics in human tissues. Material and Methods: A review of published case studies investigating microplastic contamination in human tissues was conducted. The reviewed studies used various analytical techniques to detect and characterize microplastics in biological samples. Results: The synthesis of the collected data revealed the detection of microplastics in various human tissues. In particular, microplastics were found in liver tissues of individuals with cirrhosis, suggesting a possible link between liver pathology and microplastic accumulation. Microplastics were also found in all placenta samples analyzed, suggesting potential exposure during pregnancy. The presence of microplastics was detected in 17 placentas using laser direct infrared (LD-IR) spectroscopy. Microplastics were detected in all placenta samples and 11 types of polymers were identified. A case series was reviewed in which microplastic samples were collected from 15 heart surgery patients. Notably, studies have identified intravenous infusion sets as a source of microplastic contamination, highlighting the need for screening of medical device manufacturing. Summary: The presence of microplastics in important human tissues highlights the need for further research into their health implications. A key area for future research is the formation of a "protein corona"—a layer of biomolecules that adheres to microplastic surfaces upon entry into the human body. This crown may influence the biological identity, cellular uptake, and potential toxicity of microplastics. Understanding the dynamics of protein corona formation and its impact on microplastic behavior in human tissues is essential for assessing health risks and developing mitigation strategies.

THE IMPACT OF EDUCATIONAL LEVEL ON QUALITY OF LIFE IN GEORGIAN PEOPLE WITH EPILEPSY

Tamar Jishkariani[1,2,3], Ketevan Mamasakhlisi[1,2], Gvantsa Museridze[2], Marika Megrelishvili [3], Sofia Kasradze[1,2]

[1]Caucasus International University, Tbilisi, Georgia;
[2]Institute of Neurology and Neuropsychology, Tbilisi, Georgia;
[3]Ilia State University, Tbilisi, Georgia

Introduction: The quality of life (QoL) for people with epilepsy (PWE) is significantly influenced by education and employment. Higher education often correlates with better QoL through improved self-advocacy, social support, and access to resources. Employment offers financial stability and social integration, though PWE frequently face workplace stigma and discrimination. Seizure

control and comorbidities also pose challenges. Aim: To assess the the QoL in PWE depending on educational level in Georgian population. Methods: This study, conducted from May 2023 to May 2024 at the Epilepsy Center of the Institute of Neurology and Neuropsychology (EC-INN) in Tbilisi, Georgia, assessed QoL in 351 PWE (median age 31, 155- female) using the adapted QOLIE-31 questionnaire. Indicators of patients' education, employment, marital status, satisfaction with their own health and social relationships were evaluated. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (Armonk, NY: IBM Corp). Results: Results showed varied educational attainment: 44.2% had a university degree, while 5.4% had incomplete primary education. Over half (53.6%) of participants were unemployed. Education level significantly associated with all QOLIE-31 domains ($p<0.001$), however, post-hoc analysis showed significant difference only between no or primary education and Student or university degree of education. Female sex was associated with lower QOLIE 31 scores in Overall quality of life ($p=0.001$), Emotional well being ($p=0.023$), Social functioning ($p=0.001$) and QOLIE 31 overall score ($p=0.013$) domains. Conclusion: In summary, higher educational attainment and stable employment have the potential to improve the quality of life for people with epilepsy, but challenges like stigma, seizure control, and comorbidities must also be addressed. A supportive, inclusive society that accommodates the needs of people with epilepsy can greatly enhance their QoL, regardless of education or employment status.

Study was supported by Fundamental research Grant of the Caucasus International University, Tbilisi, Georgia (# CIU-FR-125-22) and Shota Rustaveli National Science Foundation of Georgia (SRNSFG) "PHD program's grant" (#PHDF-23-1911)

THE IDENTIFICATION AND COMPARATIVE CHARACTERISATION OF THE ENDOGENOUS GROWTH INHIBITORY FACTOR FROM VARIOUSLY TRANSFORMED HUMAN NERVE CELLS

Irina Modebadze[1], Aleksandre Kordzadze[2], Ekaterine Bakuradze[1], Levan Rusishvili[1], Manana Berulava[3], Diana Dzidziguri[1]

[1]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia;
[2]The First University Clinic of TSMU, Tbilisi, Georgia;
[3]Sokhumi State University, Tbilisi, Georgia

The study of the mechanisms regulating proliferation remains a current and important issue, as the disruption of this regulation is associated with the development of many diseases, including cancer. Numerous growth factors are involved in cell proliferation. However, most descriptions focus on proliferation-stimulating factors, while comparatively less information is available about growth-inhibiting factors. One of such inhibitory endogenous factors has been identified in the various cells of an adult rat. It does not exhibit species specificity but is characterized by tissue specificity, which is only expressed to terminally differentiated cells. In order to use these proteins for therapeutic purposes, it is necessary to determine their effectiveness, as the cause of tumor is generally a

disruption of the cell proliferation controlling mechanisms. Therefore, studying the regulation of cell proliferation in nervous tissue is particularly interesting, since it is known that terminally differentiated nervous tissue does not exhibit active proliferation. The quantitative and qualitative analysis of the components of the thermostable protein complex (TPC) isolated from human brain cells with varying degrees of transformation has been conducted. It has been shown that thermostable protein complexes isolated from benign (adenohypophysis) and malignant (glioblastoma) tumor brain cells differ by the quantitative amount of active component (calmodulin). It has also been established that the thermostable protein complex derived from the does not inhibit the proliferation of the cells in adolescent rats, which is explained by the minor content of active components in it. At the same time, it has been shown that the stimulating effect on the proliferation of liver cells in adolescent rats by the thermostable protein complex derived from the glioblastoma is due to the high amount of androgen receptors in these cells and the major content of the active component (calmodulin) in the complex that functionally binds to receptors.

KAINIC ACID STATUS EPILEPTICUS - INDUCED CHANGES IN THE HIPPOCAMPUS AND HYPOTHALAMUS ALTER THE EFFECTS OF EXOGENOUS OREXIN-A IN THE HIPPOCAMPUS

Tsira Kapanadze[1], Ekaterine Bakuradze[1], Gia Kutelia[1,2], Butsiko Chkhartishvili[1], Nanuli Doreulee[1]

[1]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia;

[2]Vladimer Chavchanidze Institute of Cybernetics, Georgian Technical University, Tbilisi, Georgia

We studied behavioral, electrophysiological and morphological changes in the brain of kainic acid status epilepticus (KA-SE) rats and evaluated changes in the effects of Orexin-A on the stimulus-evoked activity in the hippocampus of the epileptic rats compared to the age-matched naive animals as a control group. The KA-SE animals showed significant changes in open field and impaired learning in the T-maze and passive-avoidance tests, indicating changes in emotional and cognitive abilities. In vivo electrophysiological recordings revealed that KA-SE in the CA1 significantly decreased the amplitude of electrically evoked potentials (EEPs). In the control rats, the EEPs amplitude was significantly increased in the CA1 and decreased in the CA3 following Orexin-A application. Orexin-A exerted no effects on the evoked responses in the CA1/CA3 fields of the KA-SE animals. Orexin-A had no significant effects on the paired-pulse facilitation of EEPs in both the control and KA-SE groups indicating postsynaptic locus of its action. Hematoxylin eosin and immunocytochemical staining of brain slices revealed KA-SE related changes in cytoarchitectonic organization of the hippocampus and hypothalamus, namely a reduced total number of neurons in both hippocampal fields, the reduced number of Glutamic Acid Decarboxylase-positive cells (GAD) in the CA3 and the Orexin-B positive neurons in the hypothalamus, respectively. Loss of GAD-positive neurons in CA3, which are main target of Orexinergic innervation, can provide an explanation for the loss of Orexin modulation of evoked synaptic potentials in KA-SE rats. These results shed more light on different role of Orexins in hippocampus under normal and pathological conditions.

GLIOMA–NEURON SYNAPSES: REDEFINING TUMOR–BRAIN INTERACTIONS

Jugal Kishore[1,2], Mzia Zhvania[1,3]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Georgian National University, Tbilisi, Georgia;
[3]Ilia State University, Tbilisi, Georgia

Recent advances in neuro-oncology have identified the formation of functional synaptic connections between malignant glioma cells and neurons, particularly in high-grade gliomas such as glioblastoma multiforme. These glioma–neuron synapses permit tumor cells to receive excitatory neuronal input, promoting tumor proliferation, local invasion, and therapeutic resistance. This synaptic integration signifies a major conceptual shift in the understanding of glioma biology, wherein tumors are no longer regarded as isolated cellular masses but as active components of the neural circuitry. While the existence of such synaptic interfaces has been substantiated through both experimental models and human tissue analyses, their implications for clinical neurosurgery remain insufficiently addressed. Key questions emerge regarding the extent to which these connections influence tumor margins, seizure activity, neuroplastic adaptation, and postoperative outcomes. Furthermore, the possibility of intraoperatively identifying and modulating these synaptic structures remains a subject of considerable interest. This abstract introduces a conceptual framework in which glioma–neuron synapses are viewed as integral elements of a broader functional tumor connectome. Such a model necessitates a reevaluation of surgical planning and resection strategies, incorporating electrophysiological mapping, advanced imaging techniques, and emerging neuromodulatory approaches. The recognition of glioma synaptic integration may inform novel surgical and adjuvant interventions, ultimately enhancing precision in tumor removal while preserving neurological function. In conclusion, the study of glioma–neuron synapses offer a promising frontier in neuro-oncology, with significant implications for neurosurgical decision-making. A deeper understanding of this phenomenon may facilitate the development of innovative strategies that bridge molecular neuroscience with patient-centered surgical care.

BEHAVIORAL BIOMARKERS OF TRAUMATIC FEAR MEMORY

Gia Kutelia[1,2], Roza Bukia[1,2], Manana Chikovani[1], Nanuli Doreulee[1]

[1]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia;
[2] Vladimer Chavchanidze Institute of Cybernetics, Georgian Technical University, Tbilisi, Georgia

In our study we focused on the identification of specific behavioral changes of post-traumatic stress disorder (PTSD) in mice models. Fear conditioning models of PTSD were created with the combination of the contextual fear conditioning (CFC) and single intraperitoneal injection of corticosterone. Mice with only CFC were considered models of normal fear memory. During model formation, animals were placed in CFC box for 5 minutes and presented with painful footshocks with the corticosterone (5mg/kg)/solvent injection at the end. Additionally, 2 control groups were created: CFC(-) + corticosterone(+) and CFC(-) + corticosterone(-). Behavioral patterns of fear

memories were analyzed in an open field with the program Videotrack (Viewpoint, France) 3 days after CFC in the same CFC box or in a new box. Fear (freezing duration) and exploratory/relaxed reactions of experimental animals were assessed. During CFC, several auditory stimuli were presented, which weren't followed by footshocks. Fear conditioning to auditory stimulus and to the context were evaluated separately. After recording, 5 days of exposure therapy was conducted for the evaluation of the resistance of the memory types. For statistical analysis t-test was applied. Obtained results show that mice from normal and PTSD-associated fear memory groups both have increased fear and decreased exploratory/relaxed reactions to context and auditory stimulus after CFC. Interestingly, exposure therapy works in both groups and restores pre-CFC reactions to context, however to auditory stimuli it functions only in animals with normal fear memory and does not work in PTSD-associated fear memory group. Moreover, freezing duration to auditory stimulus increases with the decrease of exploratory/relaxed activities over the time in PTSD-associated group. Our findings could once more indicate the importance of corticosterone in PTSD development, where it promotes more therapy resistant type of pathological fear memory. This memory type is conditioned to the stimulus, which doesn't indicate threat. As time passes, the pathological aspect of fear memory enhances and doesn't fade compared to normal fear memory. To conclude, results of our study demonstrated another way of differentiation normal and PTSD-associated fear memory types, which could be used as a behavioral biomarker of PTSD animal models.

EXOGENOUS CORTICOSTERONE CHANGES THE EXPRESSION OF GENES INVOLVED IN TRAUMATIC MEMORY FORMATION

Rusudan Ansiani[1], Gia Kutelia[1,2], Giorgi Ugulava[1], Zurab Kuchukashvili[1], Keti Silagava[1], Tamazi Giunashvili[1], Nanuli Doreulee[1]

[1]Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia;
[2]Vladimer Chavchanidze Institute of Cybernetics, Georgian Technical University, Tbilisi, Georgia

Traumatic memory serves as a fundamental mechanism in the development of trauma and stress-related disorders, including Post-Traumatic Stress Disorder (PTSD). In exploring its biological basis, three brain structures are of particular interest: the hippocampus, which supports the formation of new memories; the amygdala, which regulates the emotional context of memory; and the anterior cingulate cortex (ACC), which functions as a "gate" between the hippocampus and the cortex, facilitating the consolidation of short-term memory into long-term storage. Our study aimed to examine the effects of the stress hormone corticosterone on behavioral outcomes in animal models of traumatic memory and to explore how these behavioral changes correlate with the expression of genes involved in memory processing. We focused on NR3C1, NR3C2, and Fkbp5—genes encoding glucocorticoid and mineralocorticoid receptors and their regulatory signaling molecules. Animal models of trauma and stress were developed using varying doses of corticosterone in combination with contextual fear conditioning (CFC). The experimental groups included: 1). CFC(–) + corticosterone(–); 2). CFC(–) + corticosterone(+) (20 mg/kg); 3). CFC(+) + corticosterone(+) (20 mg/kg); 4). CFC(+) + corticosterone(+) (chronic); 5). CFC(+) + corticosterone(-). Behavioral assessments were conducted using the Videotrack system (Viewpoint,

France). Animals were tested in both contextual fear conditioning and open field chambers. We evaluated exploratory activity, freezing duration, and the number of center crossings in the open field. Using these models and quantitative real-time PCR (qPCR), we measured the expression levels of the selected genes two hours after exposure to the traumatic event and analyzed the effects of both single and repeated corticosterone administration. Our findings revealed statistically significant differences between experimental and control groups and identified distinct patterns indicating how corticosterone modulates the synthesis of key proteins involved in the consolidation of traumatic memory.

This work was supported by Shota Rustaveli National Science Foundation of Georgia (SRNSFG) (FR/22-26152)

ANTIDEPRESSANT AND ANTIMICROBIAL ACTIVITY OF THE SELECTIVE SEROTONIN REUPTAKE INHIBITORS IN DEPRESSIVE AND NON-DEPRESSIVE RATS

Nino Rogava[1,2], Neli Maglakelidze[1], Khatuna Bezhanishvili[1], Zaur Lomtatidze[2], Nargiz Nachkebia[1]

[1]Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Sokhumi State University, Tbilisi, Georgia

Introduction: Searching for non-antibiotic agents with antimicrobial activity, antidepressants particularly, is very topical, because unlimited uses of antibiotics, contributed to the development of "resistance" and new infectious diseases. Espetially interesting was the question - whether the antimicrobial activity of antidepressants can be dependent on their effectiveness in restoring sleep disturbances in animal models of depression. Problem is important because antidepressants are supposed to restore disturbances characteristic for MDD - sleep disorders among them, and they mustn't worsen sleep and general condition during depression. Method: Antibacterial and antidepressive action of Selective Serotonin Reuptake Iinhibitors (SSRIs), Stimuloton (sertraline) - Group I, Fluoxetine - Group II, was studied in High immobilisation (depressive) and low immobilisation (non-depressive) rats selected by forced swim test. Epidural stainless still screws were implanted stereotaxically under anesthesia in white wild rats (250-300 g). After recovery and 3day baseline recordings both groups received chronic, 10-day, systemic SSRIs (10 and/or 15 mg/kg). EEG registration was started immediately and lasted continuously for 6 hours daily. Statistical processing was made by Students'-test. Antimicrobial activity of SSRIs was studied in vivo on the microflora of fecal masses of the colon, collected from non-depressive and depressive rats whithout antidepressant treatment (control data). In non-depressive and depressive rats (experimental group) the microflora of the large intestine was examined after preliminary chronic SSRIs treatment. Results: In depressive rats sleep latency was increased twice, nonREM sleep was fragmented and superficial, its incidence was raised. REM latency was also raised with significant elevation of its incidence. SSRIs exhibited high anti-depressive efficacy, manifested in a sharp weakening of disturbed sleep patterns.

LONG-LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTION OF THE BRAIN MUSCARINIC CHOLINERGIC SYSTEM ON LEARNING AND MEMORY AND ADULT HIPPOCAMPAL NEUROGENESIS

Melano Shavgulidze, Neli Maglakelidze, Nino Rogava,
Khatuna Bezhanishvili, Nargiz Nachkebia
Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Introduction: Work was intended to explore the dysfunction of the brain muscarinic cholinergic system (MChS) as the main factor for changes in adult hippocampal neurogenesis and cognitive disorders alike to major depressive disorder (MDD) in animal models. Basic information about MChS participation in neurogenesis and cognitive disorders is obtained from post-mortem studies and immune-toxic lesions, followed by neurodegeneration and sprouting interfering identification of net effects. Therefore, we thought that it is essential that the effects of early postnatal dysfunction of the brain MChS explore in animal models where the early postnatal functional modification of MChS can be reached without any damage to the nerve cells by the exogenous factors. Methods: We used for the first time, the early postnatal antagonization of M1-M5 choline receptors in the rat pups by means of the nonselective antagonist, scopolamine. White inbred rats (n=15 in each group) were used. EPDMCHS was produced by a new method, which includes early postnatal blocking of M1-M5 muscarinic acetylcholine receptors in the rat pups, using subcutaneous injection of Scopolamine during postnatal days 7-28. Control rat pups received the same volume as Saline. Researches were started in adult age (2.5–3 months). We thought that the procedure, as a result, will have adult age relatively pure effects of early postnatal dysfunction of MChS on the formation of declarative and non-depletion memory and endogenous adult hippocampal neurogenesis. Results and conclusion: It wkalas shown for the first time that EPDMCHS exerts long-lasting effects manifested in adult age in the impairment of hippocampal neurogenesis and significant deterioration of spatial long-term declarative memory in the MWM. The possible causal link between the EPDMCHS and two types of resulting disorders is underlined.

SLEEP DISTURBANCES AND DYSREGULATION OF ANTIOXIDATIVE STATUS IN VPA-MODELS OF AUTISM AND PREVENTIVE EFFICIENCY OF MICROENCAPSULATED GRAPE SEED OIL

Khatuna Bezhanishvili, Olga Mchedlidze, Neli Maglakelidze, Nino Rogava,
Darejan Kharadze, Tina Omiadze, Nargiz Nachkbia

Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia

Introduction. The aim was to microencapsulate grape seed oil (MCGSO) in biodegradable wall materials and to study their antioxidative efficiency in Valproic Acid (VPA) animal models of autism. The problem is topical since: 1) antioxidative dysregulation is considered as one of factors of pathogenesis of Autism spectrum disorder and 2) MCGSO is the only way to use it in preclinical studies, in the form of unspoiled products. Therefore, we studied for the first-time possible antioxidant efficacy of safe, controlled use of MCGSO in VPA-models of autism on sleep

disturbances and concentration of reactive oxygen metabolites in blood plasma. Methods: Mature white, wild rats subjected prenatally: 1) to Valproic Acid - VPA-models of Autism and 2) to Saline with the same volume, Sal-control. Antioxidant efficacy of two-week dosed use of MCGSO was studied in both groups of rats: a) by the intraperitoneal injection; b) as a dosed food additive. EEG registration of sleep was started on 10.00 p.m. until 16.00 a.m. daily. Statistical processing was made by Students'-test. Results: We found that in VPA-models of autism: sleep latency is significantly longer; NonREM sleep is superficial with frequent awakenings; REM sleep latency is four times longer; its incidence is lower and content of reactive oxygen metabolites in the blood plasma is significantly higher than in Sal-controls. High efficiency of MCGSO in reducing the content of reactive oxygen metabolites and prevention of described sleep disturbances in VPA-models of autism was showed for the first time. Since GSO is rich in phenolic compounds with antioxidant effects, we believe that its effectiveness is based on this mechanism. Conclusion: It was shown for the first time that MCGSO exerts high antioxidative efficiency in reducing the content of reactive oxygen metabolites in the blood plasma and in the correction of sleep disturbances described in VPM-models of autism.

THE RESULTS OF 3-MONTH PSYCHOLOGICAL TRAINING IN CHILDREN WITH ADHD

Lasha Chantadze[1,2], Nutsa Zhamureli[2], Luka Katcharava[2], Ketevan Darsavelidze[2], Keteven Aptsiauri[1], Manana Gugushvili[1], Irma Khachidze[1,2]

[1]Ivane Beritashvili Center for Experimental Biomedicine, Tbilisi, Georgia;
[2]Georgian National University, Tbilisi, Georgia

Various psychological interventions have been used to address ADHD, but none have established strong empirical support as standalone treatments. This preliminary study evaluated the effects of a three-month cognitive training program—Cognitive Computer Tests (CCT) and Cognitive Paper Exercises (CPE) on attention and executive functioning in children with ADHD. 25 children (ages 7–11; 7 females, 18 males) with predominantly inattentive-type ADHD participated. Interventions were conducted in accordance with ethical guidelines. CCT sessions (twice weekly) aimed to improve different types of attention such as: Selective, Sustained, Focused, Divided and Vigilance. CPE tasks (daily) focused on selective and sustained attention. Neuropsychological assessments were conducted pre-and post-intervention. Computer-based assessments (NCAT) were mesuring different aspects of attention. Paper-based tools (NPAS) included the Vanderbilt and ASEBA (CBCL) parent/teacher rating scales were measuing more bahvioral and innatention problems of children In the CCT tests, the results showed a significant improvement in correct answers in only 1 test and reduced reaction times were shown in 2 tests ($p < .05$). CPE tasks showed trends of improvement but lacked statistical significance. NCAT results showed increased correct responses on the tests of divided, selective and sustained attention ($p < .05$) Parent ratings on CBCL and NICHQ showed reduced inattention ($p < .05$); teacher ratings on CBCL also showed improvement.

Conclusion: While executive function changes were limited, combining CCT and CPE showed potential benefits over standalone approaches. Best outcomes in ADHD treatment remain with integrated methods, including pharmacotherapy and cognitive-behavioral strategies.

The work is supported by Shota Rustaveli National Science Foundation of Georgia; Research grant #FR-22-1991

THE INFLUENCE OF CYB5-REDUCTASE INHIBITION ON THE CHOLINERGIC SYSTEM, EPILEPTIFORM ACTIVITY, AND BEHAVIORAL PATTERNS

Natia Adamashvili, Sergo Gegechkori, Nata Melkadze, Mariam Qurasbediani, Nanuli Doreulee

Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

Epilepsy is one of the most common chronic neurological conditions, characterized by an imbalance between the excitatory and inhibitory neurotransmitter systems of the brain. Many forms of epilepsy are recognized for their resistance to different types of antiepileptic drugs. For more effective treatment of this pathology, we need a better understanding of the mechanisms that are involved in the development of epilepsy. There is growing concern that the cholinergic system may play a crucial role in establishing relations between the brain's excitatory and inhibitory neurotransmitter systems. A bibliographical review indicates the excitatory function of GABA in the early postnatal period. Therefore, we can assume that changes in the functioning of the acetylcholine system during the early postnatal period can influence the course of excitatory/inhibitory processes in the brain. Acetylcholine itself is produced by binding two compounds: choline and acetyl-CoA, with the latter being a product of aerobic glycolysis. For the normal functioning of numerous enzymes involved in glycolysis, it is necessary to associate them with a suitable substrate. This is achieved through the crucial ability of the liver P450 system to distinguish between exogenous and endogenous substrates, which directly depends on the presence of an additional cofactor protein, cyb5r3. Thus, at the initial stage of the research, our interest lay in studying the influence of changes in the level of the cofactor protein cyb5r3 on the cholinergic system and the process of forming kainic acid-induced epileptiform discharges in the brain, specifically in the early postnatal period. Inhibition of Cyb5-reductase during early postnatal development had an impact on the brain's cholinergic system and epileptiform activity induced by kainic acid in the rat brain dorsal hippocampus. So far, the results have shown that both the frequency and duration of kainic acid-induced epileptiform discharges were reduced in animals in which the activity of the liver P450 system was selectively inhibited by cyb5r3. Following these results, our interest extended to studying the behavioral patterns of animals with Cyb5-reductase inhibition. By this point, changes in the neurotransmitter spectrum due to cyb5r3 inhibition were evident in the behavioral parameters of different animal groups, including control and experimental animals.

THE VALUE OF NMDA- GLUTAMATE RECEPTORS IN THE STRUCTURE OF SLEEP-WAKEFULNESS CYCLE

Olga Mchedlidze, Eka Chkhartishvili, Eter Chijavadze, Marina Babilodze, Nargiz Nachkebia

Ivane Beritashvili Center for Experimental Biomedicine, Tbilisi, Georgia

Introduction: Structural and functional relation between NMDA glutamate receptors' specific binding and phencyclidines' sites is very important for a possible modulation of NMDA receptors' function. It has been found that "REM-on" neurons are not only of cholinergic nature, but glutamatergic neurons can also be of the "REM-on" type. Therefore, we have had the interest what would happen with sleep cycles structure in the case when NMDA receptors function is modulated. In this connection, we studied the effects of Trihexyphenidyl, which is the structural analog of phencyclidine, on the various phases of sleep-wakefulness cycle. Method: Stainless steel electrodes were implanted into cats' cortical and subcortical regions of the brain for EEG registration of sleep-wakefulness cycle, lasted 12 hr daily. Trihexyphenidyl was injected 0.5 mg/kg (i.p.) before starting of EEG recording at 10:00 a.m. Statistical processing was made by Students' t-test. Results: During slow wave sleep the amplitude of delta waves increased significantly. Moreover, modulation of NMDA receptors function by antagonizing of phencyclidines' sites resulted in an increase of both the latency of slow wave and paradoxical sleep, decrease in its incidence and total time. Trihexyphenidyl resulted in dissociated triggering of paradoxical sleep signs and sharp dissociation between its electroencephalographic and vegetative parameters. REM and PGO waves appeared against at the background of active waking which was an indicator of animals' hallucinogenic state. This indicates that the NMDA glutamate receptors must be involved in paradoxical sleep modulating mechanisms and realization of this function is possible only in the case when the phencyclidines' site is not in the blocked state. Conclusion: The normal functioning of the NMDA glutamate receptors' phencyclidines' sites appears to be the mechanism which inhibits dissociated triggering of the sign's characteristic exclusively for paradoxical sleep and/or hinders hallucinogenic state. NMDA glutamate receptors have a paradoxical sleep modulating effect.

ANTINOCICEPTIVE TOLERANCE TO CANNABINOIDS IN ADULT MALE MICE

Merab Tsagareli[1,2], Maia Jonsson[2], Giorgi Chichinadze[2], Zaza Dumbadze[2], Irina Kvachadze[2]

[1] Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia;
[2]Tbilisi State Medical University, Tbilisi, Georgia

Objectives. Numerous studies show the potential effectiveness of endocannabinoids for the relief of pain and neurological disorders. However, global targeting of the endocannabinoid system has also been associated with unwanted outcomes, including deleterious effects on cognitive and emotional functions, the development of tolerance and dependence, and withdrawal symptoms after

drug cessation in humans. The main aim of the present study was to determine whether male mice develop tolerance to delta-9-tetrahydrocannabinol (THC) and cannabinolic acid (CBNA)-induced antinociception with long-term treatment. Material and Methods. Studies were conducted in male mice weighing 30-50 g. Delta-9-THC (250 μg/kg) and CBNA (2.5 mg/kg) were injected intraperitoneally (i.p.) repeatedly over five consecutive days. Using behavioral tests, we recorded thermal paw withdrawal latencies (sec) and mechanical paw withdrawal thresholds (g). All data are presented as mean ± SEM. Post-hoc comparisons between vehicle-treated and THC- or CBNA-treated mice were made using the Tukey-Kramer or Dunnett's multiple comparison tests. Results. We found that systemic (i.p.) administration of THC and CBNA resulted in strong antinociception on the first day of the experiment. However, over the next four days, the behavior indices of antinociception to mechanical and thermal stimuli gradually decreased, indicating the development of tolerance following systemic administration of these drugs. Thus, the two main components of cannabis, THC and CBNA, are characterized by the development of tolerance in mice as a result of their repeated i.p. administration. Conclusions. Further studies are needed to better understand the neuronal and molecular mechanisms underlying the development of tolerance upon repeated cannabinoid exposure regarding agonist-induced downregulation of cannabinoid receptors and their intracellular trafficking. Such information is required to optimally develop effective cannabinoid agonists that lack antinociceptive tolerance.

Author's Index:

Ivane Beritashvili Center of Experimental Biomedicine
14, Levan Gotua Str, Tbilisi, Georgia