16th INTERNATIONAL CONFERENCE OF
THE LITHUANIAN NEUROSCIENCE ASSOCIATION

29th November 2024, Vilnius, Lithuania

Life Sciences Center,
Sauletekio av. 7, Vilnius, Lithuania

LITHUANIAN NEUROSCIENCE ASSOCIATION

Life Sciences Center

16th International Conference of
the Lithuanian Neuroscience Association

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16th International Conference of the Lithuanian Neuroscience Association

29 November 2024

Life Sciences Center, Sauletekio av. 7, Vilnius, Lithuania

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15:35	GRZEGORZ GRZEŚK *(Nicolaus Copernicus University in Toruń, Poland)*, **Off-target effects of SGLT2 inhibitors, from diabetology to cardiology and neurology**
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Oral presentations

The Shadows of the Subplate

Zoltán Molnár

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The lowermost cell layer of the cerebral cortex that contains interstitial white matter cells in humans has great clinical relevance (Kostovic and Rakic, 1990). These neurons express higher proportions of susceptibility genes linked to human cognitive disorders than any other cortical layer and their distribution is known to be altered in schizophrenia and autism (Hoerder-Suabedissen et al., 2013; Bakken et al., 2016). Despite these clinical links, our current knowledge on the adult layer 6b is limited. These cells are the remnants of the subplate cells that are present in large numbers and play key role in the formation of cortical circuits but a large fraction of them die during postnatal development (Molnár et al., 2020). The adult population that remains in all mammals to form interstitial white matter cells in human or layer 6b in mouse display unique conserved gene expression and connectivity (Hoerder-Suabedissen et al., 2018). We study their input and output using combined anatomical, genetic, and physiological approaches. Selected cortical areas, relevant for sensory perception, arousal, and sleep (V1, S1, M1, prefrontal cortex) are studied using genetic and chemogenetic methods. Our data suggest that 6b is not just a developmental remnant cell population in the adult, but a layer that plays a key role in cortical state control, integrating and modulating information processing (Guidi et al., 2016; Meijer et al., 2022; Zolnik et al., 2023; Messore et al., in preparation).

Breaking Habits: Advancing the Research of Neurodevelopmental Disorders with Drosophila

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Our brains are constantly bombarded with sensory stimuli, yet must be shielded from information overload. One critical protective mechanism is habituation, a fundamental and conserved form of learning that enables a decreased response to repeated, irrelevant stimuli, allowing us to focus on what truly matters. Deficits in habituation are common in individuals with intellectual disability (ID) and autism spectrum disorder (ASD)—two major, often co-occurring neurodevelopmental disorders. These deficits are associated with sensory processing issues and clinical severity. Both ID and ASD are frequently caused by mutations in single genes, and to date, over 1,800 monogenic causes have been identified. These genes provide valuable entry points for investigating underlying mechanisms and identifying treatment targets. However, studying so many genes using traditional, low-throughput mouse models is challenging. This calls for a high-throughput model with translatable readouts, where fruit fly *Drosophila* offers a unique opportunity.

We have developed a high-throughput habituation assay based on the suppression of the fly's jump response to a light-off stimulus, termed the light-off jump habituation. Using this assay, we demonstrated that, similar to human ID/ASD individuals, habituation is broadly impaired in *Drosophila* models of monogenic ID/ASD. This makes light-off jump habituation a promising tool for investigating cognitive dysfunction in ID and ASD.

So far, we have identified over 100 ID/ASD-associated genes that, mostly upon loss of function, affect habituation. These genes converge on a few molecular pathways, including RAS-MAPK, GABAA receptor, GABAB receptor-cAMP, and inhibitory neuron function. Through circuit-specific manipulations, we are examining the roles of these pathways within the light-off jump circuit, with a particular focus on inhibitory potentiation—a crucial element of sensory information filtering and altered inhibitory function in ASD. Our ultimate goal is to address circuit-level mechanisms and correct habituation deficits in ID/ASD models using pathway- and mechanism-specific drugs.

The insights gained from *Drosophila* can be directly translated to clinical treatment trials using established human habituation protocols, facilitating the development of effective therapeutic strategies.

Neuropeptide Control of Social Behavior: a Vasopressin Story

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One of the largest sex differences in brain neurochemistry is the expression of the neuropeptide arginine vasopressin (AVP) within the vertebrate social brain. While AVP has long been implicated in social behavior, the exact anatomical substrate of AVP's control of social behavior is unclear. We have recently demonstrated using lesion, RNA knockdown, and optogenetic approaches, that the AVP-expressing cells in the bed nucleus of the stria terminalis (BNST), the major source of sexually-differentiated AVP in the brain, primarily drive male investigation of other males in mice. The effect of BNST AVP cells on male-male social interest may be due, in part, to action on the lateral septum (LS), a major output of BNST AVP cells and an area that strongly expresses vasopressin 1a receptor (V1aR). Stimulation of BNST AVP cells terminals in the LS increased male, but not female, social investigation as well as increasing male anxiety-like behavior, effects that could be blocked by V1aR antagonist. Stimulation of BNST AVP terminals ex vivo phasically increased, then decreased LS cell activity (V1aR-dependently), mimicking the timeline of in vivo increase in social investigation, suggesting that AVP-V1aR mediated inhibition of LS permits high levels of social investigation in males. Using a newly developed V1aR-cre driver mouse line, we have preliminarily data indicating that V1aR+ LS cells receive their strongest inputs from ventral hippocampal CA1 and project primarily to the diagonal band of Broca, lateral habenula, lateral hypothalamus, and supramammillary nucleus, all areas that also receive steroid-sensitive, sex-different AVP fibers and express substantial amounts of V1aR. Consequently, BNST AVP cells may modulate contextual information (from hippocampus) to alter activity of an interconnected AVP-sensitive circuit and ultimately facilitate sex-specific social approach and investigation. As disorders of social behavior, such as autism, often show sex differences in prevalence, this work suggests that sex differences in the neurochemical underpinnings of social behavior may contribute to sex differences in disorders of social behavior and communication.

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Multiscale modeling and application to personalized whole-brain modeling

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Complex systems are found throughout biology, from molecules and cells to entire ecosystems. The human brain is a prime example, with a vast network of cells and structures that control and coordinate body activities and functions. This complexity arises from numerous interactions at the sub-cellular level, the diversity of cell types, the intricate connections between them, and the dynamic nature of brain activity.

To study the brain's complexity, scientists create various models at different scales and levels of description. These models can be personalized, generative, and adaptive, using data from an individual's brain for research and clinical purposes. This talk introduces the concept of virtual brain twins and describes their key elements. A possible standard approach for creating personalized whole-brain network models, using individual brain imaging data to tailor the models, will be presented. By developing these detailed and individualized models, the goal is to enhance understanding of brain function and improve neurological diagnosis and treatment. In particular, an example of an application for Parkinson's disease, using The Virtual Brain, available on the EBRAINS platform will be detailed.

Preclinical Drug Development for Neurodevelopmental Disorders: new Insights from Chromosomal Copy Number Variant (CNV) Mouse Models and Deep Phenotyping

Neil Dawson

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Neurodevelopmental disorders, such as autism and schizophrenia, are common and have a significant detrimental impact on sufferers and their carers. There is an urgent need to further understand the complex neurobiology of neurodevelopmental disorders in order to identify new therapeutic strategies. Recent advances in our understanding of genetic risk for these disorders offers a unique opportunity to further elucidate the neurobiology of the disorders and to develop aetiologically relevant preclinical rodent models for drug validation. In this talk, Dr Neil Dawson will highlight recent advances made in his research undertaking deep phenotyping in transgenic rodent models of chromosomal copy number variants (CNVs) that substantially increase the risk of developing neurodevelopmental disorders. These studies not only provide insight into the biological basis of neurodevelopmental disorders but have also identify potential novel therapeutic strategies that require further development and validation.

Off-Target Effects ff SGLT2 Inhibitors, from Diabetology to Cardiology and Neurology

Grzegorz Grześk, Alicja Nowaczyk, Elżbieta Grześk, Jacek Nowaczyk

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Sodium-glucose cotransporter 2 inhibitors (SGLT2i) constitute a class of pharmacological agents initially developed to modulate glycemic control in individuals with type 2 diabetes mellitus. The approval of the first SGLT2 inhibitor in the early 2010s marked a significant advancement in diabetes management by facilitating glycosuria through inhibition of renal glucose reabsorption, leading to a reduction in blood glucose levels.

Subsequent clinical investigations, including pivotal trials such as EMPA-REG OUTCOME, have elucidated the cardioprotective benefits of SGLT2i, demonstrating their capacity to substantially lower the incidence of adverse cardiovascular events, including hospitalizations due to heart failure and cardiovascular mortality. Although the precise mechanisms remain an area of ongoing research, current evidence suggests that SGLT2i contribute to favorable hemodynamic modulation via plasma volume reduction and decreased cardiac preload, alongside enhancements in renal function and myocardial energetics. This has established SGLT2i as integral components of heart failure management, applicable even in non-diabetic populations.

Emerging research further suggests that SGLT2i may confer neuroprotective effects, which could extend their therapeutic potential to neurological disorders such as Alzheimer's disease and ischemic stroke. Mechanistic studies propose that SGLT2i improve cerebral glucose metabolism, attenuate oxidative stress, modulate inflammatory pathways, and enhance cerebrovascular function. These findings indicate that SGLT2i may influence central nervous system health through multifactorial actions, potentially mitigating neurodegenerative processes.

Thus, SGLT2 inhibitors exemplify a paradigm shift in pharmacotherapy, transitioning from their original role in glycemic control to a broader application encompassing cardiovascular and possibly neuroprotective benefits. Continued investigation into their molecular and physiological mechanisms is crucial to expanding their clinical indications and optimizing therapeutic strategies aimed at comprehensive chronic disease management.

The Role of Cannabinoid Type 2 Receptors, Physical Exercise, and Adult Hippocampal Neurogenesis in a Model of Depressive-Like Behavior

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Chronic stress is a major risk factor for neuropsychiatric conditions such as depression. Adult hippocampal neurogenesis (AHN) has emerged as a promising target to counteract stress-related disorders given the ability of newborn neurons to facilitate endogenous plasticity. Recent data sheds light on the interaction between cannabinoids and neurotrophic factors underlying the regulation of AHN, with important effects on cognitive plasticity and emotional flexibility. Since physical exercise (PE) is known to enhance neurotrophic factor levels, we hypothesised that PE could engage with cannabinoids to influence AHN and that this would result in beneficial effects under stressful conditions. We therefore investigated the actions of modulating cannabinoid type 2 receptors (CB2R), which are devoid of psychotropic effects, in combination with PE in chronically stressed animals. We found that CB2R inhibition, but not CB2R activation, in combination with PE significantly ameliorated stress-evoked emotional changes and cognitive deficits. Importantly, this combined strategy critically shaped stress-induced changes in AHN dynamics, leading to a significant

increase in the rates of cell proliferation and differentiation of newborn neurons, overall reduction in neuroinflammation, and increased hippocampal levels of BDNF. Together, these results show that CB2Rs are crucial regulators of the beneficial effects of PE in countering the effects of chronic stress. Our work emphasises the importance of understanding the mechanisms behind the actions of cannabinoids and PE and provides a framework for future therapeutic strategies to treat stress-related disorders that capitalise on lifestyle interventions complemented with endocannabinoid pharmacomodulation.

Sleep as a Modulator of Network Activity in Epilepsy: new Insights from Intracranial EEG

Sana Hannan

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Epilepsy and sleep are tightly linked in a complex, bidirectional relationship. Sleep states and structure are known to play an important role in influencing epileptic activity. However, the precise modulatory effects of sleep on different epileptic phenomena are not well understood. In this talk, Dr Sana Hannan will discuss her latest findings on the impact of sleep states and structure on epileptic activity. Using presurgical intracranial EEG recordings from individuals with drug-resistant epilepsy, this work was aimed at exploring how sleep affects the spatiotemporal dynamics of ictal and interictal activity and examining the intricate relationship between sleep stability and epileptic events. The talk will also highlight the potential of sleep as a tool for understanding epilepsy, as well as future directions for utilising neurophysiological methods to understand brain dynamics in health and disease.

Serotoninergic Modulation of Resting-State EEG Microstates

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A growing body of clinical and cognitive neuroscience studies have adapted a broadband EEG microstate approach to evaluate the electrical activity of large-scale cortical networks. The recorded oscillations are defined as the non-overlapping "states" that are characterized by a unique spatial distribution reflecting the functional cortical networks involved in the process and their temporal aspects. Surprisingly, the neurochemical modulation of microstates has received limited attention. Re-using the openly available EEG resting-state data from crossover placebo-controlled studies by Tagliazucchi et al (2021), who investigated effects of inhaled N,N-Dimethyltryptamine (DMT), and Cavana et al (2022) who investigated effects of microdose with psilocybin mushrooms (*Psilocybe cubensis*) we aimed to assess effect of these serotoninergic system modulating compounds on the functional dynamics of EEG.

24-channel EEG data was collected from two groups (n=34 and n=35) of subjects. A classical resting-state microstate (MS) analysis was performed on the broadband (1-30Hz) and narrow-band (delta, theta, alpha and beta) data. Global explained variance (GEV), duration, coverage and occurrence of MS were extracted and subjected to permutation non-parametric test for paired samples (10000 permutations) with FDR correction of P values.

Five prototypical microstates across frequency bands in both samples were extracted. Microdose with psilocybin resulted mostly in affected GEV of delta and theta ranges, where it decreased for MS A and E, and changed GEV of MS D that decreased for delta but increased in theta range. After the administration of DMT, in contrast, parameters were mostly affected in alpha range with decreased GEVs and durations, and increased occurrence of all microstates. Additionally, for MS C in delta range an increase of parameters was observed, while GEV and duration of MS D decreased in both theta and beta ranges.

The results of MS analysis provide in-depth insights on the neuromodulatory effects of psychedelic compounds on the functional dynamics of the brain activity.

Exploring the Role of Hormonal Contraception in Emotion and Cognition

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The introduction of "the pill" in the 1960s paved the way for female sexual self-determination. Today, hormonal contraception is one of the most reliable birth control methods used by millions of adolescents and adults worldwide. However, both animal and human studies have elucidated that synthetic hormones from hormonal contraceptives can impact brain function, cognition, and behavior. This occurs through interactions with sex steroid, mineralocorticoid, and glucocorticoid receptors in the brain, as well as specific modulatory effects on neurotransmitter systems and the expression of neuropeptides. In our psychophysiological studies, we assessed the performance of females using and not using hormonal contraceptives on various tasks while recording their electrical brain activity (EEG) and eye movements. Here, I will present the main findings demonstrating that visuospatial performance and perception of emotional and social stimuli may be affected by the use of hormonal contraceptives. Nevertheless, the results of our research, along with those of other studies, have been inconsistent, suggesting that numerous factors—ranging from genetic, demographic, and social influences to the type of hormonal contraceptives—should be considered when investigating the impact of hormonal contraceptives.

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P1

Oxidative Environment Effect on Alpha-Synuclein Liquid-Liquid Phase Separation and Aggregation

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Protein aggregation and buildup of amyloid aggregates in cells are linked to neurodegenerative diseases. Among these disorders is Parkinson's disease, widely known for causing motor impairment symptoms. This disorder is associated with the degeneration of dopaminergic neurons in the substantia nigra, a part of the midbrain. This process is thought to be caused by the accumulation of alpha-synuclein (αSyn) amyloid aggregates found within Lewy bodies in the cells. It is believed that the accumulation of aggregates occurs during a process known as liquid-liquid phase separation (LLPS). Dopaminergic neurons are particularly vulnerable to oxidative stress, because they contain dopamine (DA) which is prone to oxidation. Products of dopamine oxidation may influence αSyn aggregation and LLPS. One of the enzymes produced in cells for oxidative stress damage prevention is superoxide dismutase 1 (SOD1). It has been found to inhibit dopamine oxidation and prevent αSyn aggregation promoted by it byproducts. In this study we examined αSyn liquid-liquid phase separation and its aggregation process in the presence of dopamine. SOD1 was used in order to counteract the oxidation process of dopamine. The aggregation kinetics of αSyn was followed by monitoring change in ThT dye fluorescence intensity and optical density over time. The results showed that DA oxidation products can promote the formation of αSyn LLPS droplets and change its aggregation pathway. The difference in droplets and aggregate morphology were observed using fluorescence and transmission electron microscopy, although FTIR spectroscopy analysis did not show changes in the secondary structures of the aggregates.

P2

Age-Related Variations in the Mitochondrial Lesions Caused by Hypoxia in Wistar Rats' Brains

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Risk of ischemic stroke increases by aging. One of the mechanisms leading to cell death during ischemia is mitochondrial permeability transition pore (mPTP) opening though its functioning and regulation during development and aging are not well understood. Therefore, in this study we compared hypoxia induced lesions to 7 days, 2-3, 7-10 and 24-26 months-old rats brain mitochondria respiration and mitochondrial permeability transition pore sensitivity to Ca2+ with particular focus on mitochondrial complex I. Data indicate that hypoxia inhibited cortical mitochondrial respiration rate of animals from all age groups and reduced mitochondrial calcium retention capacity (CRC) in 2-3, 8-10- and 24-26-months animals' groups. Hypoxia inhibited cerebellar mitochondrial respiration in 7 days, 2-3 and 24 - 26-month-old groups, but had no effect on 8–10-month-old group. CRC after hypoxia were reduced in 8 - 10 and 24-26 months - old rats' cerebellum. Western blot analysis showed an age-related decrease of complex I protein NDUFS2 levels, while enzymatic activity of mitochondrial complex I was increasing with aging. Additionally, the size of the hypoxia-induced infarct zone was measured; all animals, regardless of age, had similar brain tissue damage after 90 minutes of hypoxia. Altogether, these findings suggest that, despite age-related variation in Ca2+ induced mPTP or hypoxia-induced acute mitochondrial dysfunction; brain necrosis is doubtfully mediated by mPTP opening.

P3

Expression of Circulating Y RNAs in Blood Serum of Patients with Brain Disorders

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Parkinson's disease (PD) and brain cancers like glioblastoma (GBM) and lower-grade gliomas (LGG) are serious neurological disorders that may share underlying molecular mechanisms. Y RNAs (notably RNY1, RNY3, RNY4, and RNY5) play roles in stress response, apoptosis, and immune regulation—mechanisms central to neurodegeneration and cancer. In recent years, Y RNAs have been abundantly detected in extracellular vesicles (EVs) from various liquid biopsies (LB), with evidence suggesting links to immune processes. Thus, EV-associated Y RNAs may serve as biomarkers in cancer and neurodegenerative diseases. This study aimed to evaluate the expression levels of RNY1, RNY3, RNY4, and RNY5 in serum extracellular vesicles (EVs) from PD, GBM, and LGG patients, examining their associations with clinical data. Blood samples from a total of 88 PD patients, 20 healthy controls, 18 GBM, and 10 LGG patients were included in this study. Total RNA, including miRNA, was isolated from EVs, reverse-transcribed into cDNA, and analyzed using qRT-PCR. Statistical analyses were performed using Student's t-test and Pearson's correlation coefficient in GraphPad Prism 8. For PD patients, RNY3 expression was significantly lower than in healthy controls ($p < 0.01$). Notably, RNY3 expression increased with motor symptom severity, especially with bradykinesia severity ($p < 0.01$). Additionally, RNY3 expression showed a negative trend with age at disease onset ($r = -0.21$; $p = 0.056$) and was downregulated after gamma knife surgery ($p = 0.064$). In blood serum from brain cancer patients, RNY4 and RNY5 expression was elevated in GBM compared to LGG ($p < 0,05$). Additionally, lower RNY4 and RNY5 expression was associated with longer overall survival in brain cancer patients, though this was not statistically significant. A slight negative correlation was observed between RNY1 (($r = -0.335$, $p = 0.08$) and RNY3 ($r = -0.326$, $p = 0.09$) levels and patient age; however, no correlation was found with tumor volume. These findings suggest a modest association of RNY with the pathology of PD, GBM and LGG, though larger sample sizes are needed to confirm these observations. While not robust predictors alone, Y RNAs may offer new insights in neurodegeneration and brain cancer with further study.

P4

Plant Extract Impact on Oxidative Status in Mice Brain

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Introduction. In recent years, growing awareness of the role of oxidative stress in brain health has prompted antioxidants, especially dietary antioxidants, to receive growing attention as possible treatments strategies for patients with neurodegenerative diseases. The most widely studied dietary antioxidants include active substances such as vitamins, carotenoids, flavonoids and polyphenols. Dietary antioxidants are found in usually consumed foods such as fresh fruits, vegetables, nuts and oils and are gaining popularity due to recently growing awareness of their potential for preventive and protective agents against NDs, as well as their abundant natural sources, generally non-toxic nature, and ease of long-term consumption.

Methods. Experiments were performed on outbred white laboratory mice by changing drinking water with plant extract solutions of aronia, pomegranate, elderberry, red orange and blackcurrant. Exposure time was 21 dd. Lipid peroxidation level was estimated spectrophotometrically by measuring the concentration of MDA produced by reaction with TBA at 535nm and 520nm. The concentration of GSH was measured spectrophotometrically by reaction with DTNB to give compound TNB, which absorbs light wavelength at 412nm.

Results. Our experiments showed that GSH (an essential non-enzymatic antioxidant, which can act directly as an antioxidant to protect cells against free radicals and pro-oxidants, and as a cofactor for antioxidant and detoxification enzymes) level in mice brain increased by 281% (with aronia extract), 302% (with pomegranate extract), 297% (with elderberry extract), 34% (with blackcurrant extract) and 184% (with red orange extract). In another series of experiments, we determined the content of MDA (determining the level of MDA is usually the most practical and reliable method for detecting and screening oxidative stress) in mice brain. Our results showed that the amount of MDA in mice brain significantly decreased by 54% in blackcurrant extract and 37% in red orange extract groups as compared to control. But after treatment with aronia, pomegranate and elderberry extracts, lipid peroxidation significantly increased by 50%.

Conclusion. Our studies showed that plant extracts of aronia, pomegranate, elderberry, red orange and blackcurrant increased antioxidant GSH level in mice brain. Some of the treated extracts (blackcurrant and red orange) protected lipids from peroxidation, but others (aronia, pomegranate and elderberry) didn't

P5

Immunomodulatory Effect of Extracellular Vesicles Secreted by Amniotic Fluid Stem Cells in the Neuronal Cell Model of SH-SY5Y

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Recent research indicates the importance of the interaction between the immune system and stem cells in cell therapy and translational medicine (Savitz & Cox, 2023; Rust et al., 2024). Our current study aims to determine how extracellular vesicles (EVs) secreted by human amniotic fluid stem cells (hAF-SCs) modulate the inflammatory phenotype of neuronal cells with suppressed activity of anti-neuroinflammatory miR146a-5p. To achieve this, SH-SY5Y neuroblastoma cells were differentiated towards a more mature neural phenotype using neural differentiation media composed of BrainPhys™ neuronal medium supplemented with Penicillin/Streptomycin, serum- and antioxidant-free B-27™ supplement, 50 ng/ml BDNF, and 10 μM retinoic acid. Neuro-differentiated SH-SY5Y cells were then treated with a mirVana inhibitor targeting miR146a-5p. EVs from the hAF-SC secretome were collected using size exclusion chromatography with qEVoriginal columns and characterized by size and molecular markers. The size of isolated EVs ranged from 30 to 230 nm, while Western blot analysis revealed that collected EV preparations were positive for specific EV markers CD9, CD63, CD81, ALIX, and TSG101, and negative for mitochondrial and Golgi apparatus protein markers (cytochrome c and GM130, respectively). These EVs were then used to treat miR146a-5p-inhibited SH-SY5Y cells, followed by mRNA-seq analysis. Sequencing analysis revealed that treatment with hAF-SC-derived EVs significantly reduced the expression of genes involved in cytokine–cytokine receptor interaction and interleukin signaling, particularly those associated with inflammatory interleukin IL-6 signaling. The results of this study demonstrate the immunomodulatory effects of EVs secreted by hAF-SCs in a neural cell model. Our ongoing research will further investigate how different inflammatory conditions influence the composition of hAF-SC-derived EVs and their effects on miR146a-5p-inhibited SH-SY5Y cells.

P6

Visual Estimation of the Size of a Stimulus of Motion-Defined Contour

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In psychophysical experiments on a monitor screen, a subjective contour of a rectangular shape was formed by a random dot pattern drifting against a background of static random dots. Bidirectional drifting: divergence, and convergence were applied within the rectangle area. The aim was to answer whether the direction of movement selectively influences the perceived relative length of the motion-defined shape. Subjects judged the relative extension of the reference stimulus by adjusting the perceptually equal length of the test gap. It was demonstrated that dots moving horizontally toward the stimulus periphery and tangentially approaching the rectangle edges in the case of divergence caused an overestimation of the rectangle length. The positive errors of the subjects indicated that the rectangle edges perceptually shifted outward. The shift values were about the same for shorter and middle rectangles but lower for longer ones. The size expansion effect appeared to reduce at a certain motion distance. When convergence was tested, dots escaping the rectangle edges and drifting toward the stimulus center caused relatively low error values that continuously declined with stimulus length. There were even negative signs of errors for six subjects out of eight for longer rectangles. The effect of expansion was questionable. Consequently, the approaching and escaping dots don't act the same way on the positions of the subjective contour. But was the expansion produced by the divergent motion of the same origin as the expansion of stimuli outlined by a static spatial contrast in luminance, color, or texture, and defined by perceptual grouping and the Kanizsa contours (Bielevicius, et al., 2023)? To compare the two manifestations of expansion, the control stimuli were formed of static lines and exposed on the same background of random dots in the present study. The divergently drifting dots were still presented within the rectangle area. The rectangle sizes were the same as before that. Such stimuli caused overestimation errors exceeding those of the motion-defined contours. In addition, the expansion strengthened, while not decreasing, with an increase in the length of the stimulus. As a result, for long stimuli, the expansion of the static contour became two to three times higher than that of the motion-defined contour. The size expansion effects for static and motion-defined contours may have different neural origins.

P7

Loxoribine, TLR7 Receptor Agonist, Induces Microglia Activation and Neuronal Loss in Neuronal-Glial Co-Cultures

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Virus-induced neuroinflammation refers to the immune response occurring in the central nervous system (CNS) in response to viral infections. While the activation of immune system is necessary for the elimination of the virus and protection of neural tissue, inflammatory response can sometimes become excessive or dysregulated, leading to neural damage contributing to various neurological conditions. When a virus infects cells, immune system recognizes viral RNA initiating pro-inflammatory response. Toll-like receptor (TLR) 7, a member of the TLR receptor family, serves as a key sensor for viral single-stranded RNA, linking viral infections to the activation of neuroinflammatory pathways in CNS. In this study, to investigate the TLR7-meadiated neurotoxicity, we treated rat neuronal-glial co-cultures with Loxoribine, guanosine analogue, acting as TLR7 receptor agonist. Our results show that Loxoribine induces loss of viable neurons, without any sign of apoptosis or necrosis. Moreover, these neurotoxic effects were accompanied by microglial changes such as enhanced proliferation, morphological changes, increased expression of Iba-1, and TNF-α secretion. Furthermore, microglial depletion prevented Loxoribine-induced neuronal loss implying that Loxoribine induces microglia-dependent neuronal loss. Overall, these data suggest that Loxoribine induces microglial activation leading to neuronal loss in neuronal-glial co-cultures. Acknowledgements: This work has received funding from the Research Council of Lithuania (LMTLT), agreement No S-MIP-23-98 (APNEVIR).

P8

Exploring the Associations of Reproductive Hormones and Stress with Menopausal Symptoms

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Women experience menopause at a median age of 51.4 years, living approximately a third of their lives pot-menopause. Over 80% of women suffer from vasomotor, psychosocial, physical, and sexual menopausal symptoms, which negatively impact their quality of life. While endogenous hormones play a significant role in the occurrence of these symptoms, the mechanisms underlaying the risk to perceive menopausal symptoms remain unclear, and the relationship between symptoms and endogenous hormones is not fully established. Moreover, although hormonal fluctuations during perimenopause are similar across individuals, the type, intensity, and duration of menopausal symptoms vary, indicating the involvement of additional factors. Therefore, our study aims to evaluate the relationship between menopausal symptoms, endogenous hormones, and experienced stress. To investigate this relationship, we conducted an anonymous survey and a clinical study. We used the Menopause-Specific Quality of Life Questionnaire (MENQOL) to assess symptom intensity across four domains: vasomotor, psychosocial, physical, and sexual. Chronic stress was assessed using the Perceived Stress Scale (PSS-10). Or survey, which included responses from 875 menopausal woman, revealed that physical activity, sleeping hours, some gastrointestinal symptoms and experienced stress were associated with more severe menopausal symptoms. In a cross-sectional study of 63 women aged 50.2±2.9 years, in parallel to questionnaires, we measured the levels of reproductive hormones in blood serum and the levels of hair glucocorticoids (cortisol, cortisone) to evaluate the chronic stress. The results of the present study showed that not only hormonal changes, but also other factors, such as age, hours of sleep, and experienced stress, are associated with the intensity of menopausal symptoms. Since many women experience and suffer from menopausal symptoms, more detailed studies are needed examining the factors that influence the development and intensity of menopausal symptoms.

P9

Relapsing-Remitting Multiple Sclerosis: Association of *IKBKB* Rs13278372 and *IKBKG* Rs2472395 with Disease Occurrence and Organ Damage

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Introduction: The immune-inflammatory disease known as multiple sclerosis (MS) affects and damages myelinated neurons in the central nervous system (CNS), leading to nontraumatic neurological disability. Eighty percent of individuals with MS experience relapsing-remitting MS (RRMS). MS appears to start as a chronic dysregulation of immune homeostasis resulting from complex interactions between genetic predispositions and environmental factors.

IKK2, encoded by the IKBKB gene, is crucial in initiating the NF-κB signaling pathway. This activation increases NF-κB signaling and functional disturbances in T and B lymphocytes. Additionally, the protein NEMO/IKKγ, encoded by the IKBKG gene, is vital for the NF-κB pathway activation and is involved in numerous physiological and cellular functions, including immunity, inflammation, proliferation, and survival. NF-κB signaling pathway has also been linked to various human diseases, particularly those related to inflammatory conditions.

Aim: To determine IKBKB rs13278372 and IKBKG rs2472395 in RRMS patients and healthy controls and relate the obtained results to RRMS occurrence and organ damage.

Methods: 1. A total of 514 participants were divided into two groups: a control group (n=260) and a group of RRMS patients (n=254). 2. Genotyping of IKBKB rs13278372 and IKBKG rs2472395 was performed using real-time polymerase chain reaction. 3. Statistical Analysis was conducted using SPSS and SNPStats software.

Results: The analysis showed no statistically significant differences in the distribution of IKBKB rs13278372 and IKBKG rs2472395 genotypes and alleles between patients with RRMS and the control group. The binary logistic regression analysis showed no statistically significant results.

We investigated the associations between the occurrence of genotypes and lesions in the brain stem, eyes, pelvic organs, and cerebellum. For many RRMS patients, vision problems are the initial symptom. We found that the IKBKG rs2472395 CA genotype was statistically significantly less frequent than the control group ($p=0.025$). Binary logistic regression analysis revealed that the CA genotype is associated with 2.3-fold decreased odds of visual impairment in RRMS patients (OR: 0.427; CI: 0.200-0.916; $p < 0.029$).

Conclusion: No association was found between IKBKB rs13278372 and IKBKG rs2472395 and the occurrence of RRMS. However, IKBKG rs2472395 decreases the odds of visual impairment in RRMS patients.

P10

The Effect of Maternal High-Fat Diet on the Inflammatory Response in the Offspring's Retina

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Aim: Increased high-fat content in today's society's diet is one of the leading factors contributing to the rising obesity rates. Many studies suggest that maternal high-fat diet (mHFD) can cause systemic inflammation, which may lead to neurodevelopmental disorders in the offspring. The response to inflammation also changes throughout different stages of the female estrous cycle. CD68 and TSPO are proteins that can be reliable biomarkers for detecting inflammation and microglia activation processes in the central nervous system, including the retina. Although some studies that show mHFD effect on the retina, little research has been done to investigate its impact on the retina of the offspring. This study aims to evaluate changes of microglia, CD68 and TSPO levels in the peripheral retina of mHFD offspring and assess how they depend on the stages of the estrous cycle.

Methods: Female C57Bl/6J mice from weaning to lactation were fed with control diet (CD, 10% fat) or high-fat diet (HFD, 60% fat). The offspring were weaned to CD. The eyeballs of the offspring were collected, fixed with 4% PFA, cryoprotected and sliced using cryotome. Microglia, phagosomes and mitochondrial TSPO were labeled immunohistochemically using anti-RFP, anti-CD68 and anti-TSPO antibodies respectively, while cell nuclei were labeled with DAPI. The estrous cycle stages were determined by vaginal cytology in female offspring on the day of tissue collection (22 weeks old).

Results: We evaluated the area of microglia, CD68 and TSPO in the peripheral retina and compared the measurements between the groups of offspring. Our results show that mHFD influenced microglia, CD68 and TSPO levels in the mHFD offspring peripheral retina compared to mCD diet offspring. In addition, during the evaluation of microglial CD68 and TSPO areas, alterations were observed in the estrous cycle stages of female offspring due to mHFD.

Conclusion: Our findings showed that mHFD affected the area of microglia, CD68 and TSPO in peripheral retina of offspring as well as revealed changes in microglial CD68 and TSPO areas in mHFD female offspring during estrous cycle stages.

P11

Mapping Neural Differences in Parkinson's Disease: A Source Reconstruction Approach to EEG Data

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Introduction: Parkinson's disease (PD) affects millions worldwide, yet early and accurate diagnosis remains challenging. Electroencephalography (EEG) based identification of neural signatures may offer new insights for distinguishing PD from healthy individuals. Objective This study aimed to identify brain regions through EEG source reconstruction that could be used to differentiate between PD patients and healthy individuals.

Materials and Methods: Publicly available EEG data, provided by OpenNeuro, from 14 healthy and 14 PD subjects was used for the study. Data underwent Finite Inpulse Response filtering, denoising with Principal Component analysis and Independent Component Analysis, and MinMax thresholding to remove noise. Source reconstruction, a method to trace EEG electrode signal origins to specific brain regions, was performed using OpenMEEG's Boundary Element Method, registered to the Desikan-Killiany-Tourville (DKT) atlas, resulting in EEG signal reconstruction across 62 DKT-defined brain regions. Five power spectral densities (PSD) were calculated for a total of 310 features per recording. The Maximum Relevance Minimum Redundancy (MRMR) algorithm was used to select key brain regions and frequency bands. Machine learning (ML) algorithms Support Vector Machines, Logistic Regression, K-Nearest Neighbor, Naïve Bayes, Random Forest, and Deep Neural Network (DNN), with 10-fold cross-validation were used to discriminate PD patients from the healthy group Wilcoxon analysis was used to assess statistical significance of classification results among ML methods.

Results: All ML methods successfully classified PD with the highest accuracy (96% ± 10%) achieved by DNN using five PSD features - left lateral occipital, right precuneus, and left cuneus in the Delta range, medial orbitofrontal in Theta range, and right lingual in Alpha range. ML methods used did not yield statistically significant differences in classification accuracy. The classification results demonstrate the potential of using EEG source reconstruction to distinguish between Parkinson's disease and healthy individuals. However, due to the limited dataset size, these findings should be interpreted with caution. Future large-scale studies incorporating additional biomarkers and a broader parameter space are essential to validate and extend these preliminary insights.

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P12

The Application of Gene Editing in Neuronal Cells

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The development of various CRISPR-Cas genome editors has rapidly expanded, yet their translational implementation remains hindered. A key obstacle is the scarcity of effective delivery tools for Cas nucleases and their sgRNA. It is especially challenging to access the highly privileged central nervous system and target neuronal cells specifically. The most commonly used adeno-associated viral vectors are constrained by their limited packaging capacity, requiring gene editors to be delivered as dual or triple vectors, which drastically reduces their efficacy. Precise and universal state-of-the-art prime editing tools (PEs) present an even greater challenge due to their complex structure. To address these delivery challenges, we propose using herpes simplex virus (HSV) vectors, which can accommodate larger constructs and are well-suited for central nervous system applications, including in vitro, ex vivo, and in vivo models. We aim to implement HSV delivered Staphylococcus aureus Cas9 prime editors for treating neurodegenerative monogenic disorders. We started by characterizing the cell tropism of HSV in various cell cultures and determining the timeline of expression in mouse organotypic hippocampal slice cultures. We then constructed a single HSV vector capable of delivering all components of the prime editing system, by employing an extensible mammalian modular kit. We tested the PE transforming green fluorescent protein to the blue one on our established reporter neuroblastoma cell line with genome-encoded nuclear green fluorescent protein and red fluorescent protein localized to plasma membrane. In addition, we assessed the efficacy of Staphylococcus aureus Cas9 nuclease to knock-out green fluorescent protein gene. Following successful validation in neuroblastoma cells, we will now focus on applying this technology to repair specific mutations in neurodegenerative lysosomal storage disease cell model. With this study we demonstrated the potential of HSV vectors as robust platform for prime editor delivery to neuroblastoma cells. The successful implementation of HSV delivered prime editing for neurodegenerative diseases could pave the way for further advancements of CRISPR/Cas-based therapies.

P13

The Metabolic Roles of Astrocytes and Neurons in the Diving Brain

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The mammalian brain is highly dependent on oxygen for its metabolism, with significant dysfunction occurring within minutes of insufficient oxygen supply (hypoxia). However, mammals that are regularly exposed to oxygen deprived environments, like pinnipeds, show a remarkable brain hypoxia tolerance. Oxygen is the final electron acceptor in the electron transport chain and is therefore crucial for ATP production in the mitochondria. Studies in mice and primates reveal that mitochondrial distribution differs between neurons and astrocytes; neurons have higher mitochondrial density and rely primarily on aerobic metabolism, whereas astrocytes have lower mitochondrial density and produce energy mainly anaerobically. There is also evidence of a metabolic coupling between astrocytes and neurons, particularly at synapses, via the astrocyte-neuron lactate shuttle (ANLS). However, research on the brain of the deep-diving hooded seal (Cystophora cristata) suggest a metabolic shift between astrocytes and neurons where the ANLS may be reversed. Our project further investigated hooded seal brain metabolism by quantifying the mitochondrial distribution between astrocytes and neurons. Visual cortex from juvenile seals, adult seals and mice were fixed, sectioned and stained with antibodies for neurons, astrocytes and mitochondria. Using fluorescence microscopy and image analysis the mitochondria in each cell type was measured and quantified. Our results show significantly lower mitochondrial density and larger mitochondria in astrocytes compared to neurons in adult hooded seals, while juvenile seals and mice exhibited the opposite trend. The adult seals also had the overall lowest densities of mitochondria. This gives further evidence of a metabolic shift and aligns with previous findings of reduced brain metabolism and suppressed synaptic transmission in the adult hooded seal brain. Further, the differences between juvenile and adult seals indicate that brain metabolism may be influenced by age and the development of diving capabilities. These findings further enhance our understanding of the cellular mechanisms underlying hypoxia tolerance in pinnipeds.

P14

Genetic Predictors of Pituitary Adenoma Activity in Females: Insights from CXCL12 Polymorphisms

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Introduction: Pituitary adenoma (PA) is one of the most common brain tumors, yet its pathogenesis remains unclear. PA varies significantly in activity; some secrete excess hormones, causing symptoms related to hormonal imbalance, while others are non-secreting but may still cause symptoms due to size, exerting pressure on nearby structures. CXCL12, a homeostatic chemokine regulates the tumor microenvironment by promoting angiogenesis and recruiting immune cells, potentially supporting tumor growth. CXCL12 gene polymorphisms, particularly those affecting expression or function, may influence PA risk, size, invasiveness, and treatment response. Understanding the genetic role of CXCL12 could support personalized treatments and improve prognostic tools for PA management.

Materials and Methods: A case-control study enrolled 90 females with PA and 160 healthy females. DNA samples from peripheral blood leukocytes were purified by the DNA salting-out method. Single nucleotide polymorphisms (rs1801157, rs2297630) were determined using real-time polymerase chain reaction (RT-PCR). The results were analyzed using the "IBM SPSS Statistics 29.1" statistical analysis method.

Results: We found that CXCL12 rs2297630 AA genotype and A allele were statistically significantly more frequent in controls compared to the hormonally inactive PAs (8.1 vs. 0, $p = 0.013$, 29.7 vs. 11.7, $p = 0.003$, respectively). In the active PA group, the CXCL12 rs1801157 TT genotype and T allele were statistically significantly more frequent than in the controls (6.7 vs. 2.5, $p = 0.042$, 27.5 vs. 16.9, $p = 0.012$, respectively). However, the rs2297630 A allele was statistically significantly less frequent in the hormonally active PAs than in the controls (19.2 vs. 29.7, $p = 0.026$). CXCL12 rs1801157 T allele was associated with 1.2-fold increased odds of active PA occurrence under the additive model (OR: 1.910, CI: 1.143–3.191, $p = 0.014$). Furthermore, the CXCL12 rs2297630 A allele decreased the odds of inactive and active PA development by 3.3-fold and 1.8-fold under the additive models (OR: 0.301, CI: 0.130–0.700, $p = 0.005$; OR: 0.545, CI: 0.320–0.927, $p = 0.025$, respectively).

Conclusions: The CXCL12 rs2297630 A allele suggests potential protective effect against both inactive and active PA development. In contrast, the CXCL12 rs1801157 T allele may be a risk factor for developing more active forms of PA.

P15

Exploring Resting-State EEG Associations with Lifestyle and Mental Health Factors

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Resting-state EEG (rs-EEG) assesses the brain`s spontaneous electrical activity at rest. The aperiodic slope, which shows how EEG amplitude decreases as frequency rises, is one variable used to describe this. A steeper slope is linked to better cognitive performance, while a flatter slope is associated with anxiety and depression. Lifestyle factors like physical activity, sleep, BMI, and gender relate to anxiety, depression, and alexithymia. However, no studies currently examine the aperiodic slope`s relationship with lifestyle factors or alexithymia, so we aimed to investigate this link. The sample included 30 males, aged 20 to 35 years, with 12-23 years of education. Participants reported engaging in 1-5 hours of physical activity per week and an average of 5.5-8 hours of sleep per day. BMI ranged from 19.6 to 36.6. Data on lifestyle, alexithymia, anxiety, depression, and overall mental health were gathered using questionnaires. Rs-EEG was recorded for 3 minutes with eyes open and 3 minutes with eyes closed, using a 64-channel system. Data preprocessing was done in EEGLAB, with 1/f offset and slope estimated via FOOOF in Python for statistical analyses. Spearman rank correlation showed significant associations between aperiodic slope and age ($r = -.427$, $p = .023$), daily sleep hours ($r = .370$, $p = .048$), and alexithymia ($r = -.389$, $p = .034$). Additionally, alexithymia was associated with physical activity ($r = -.449$, $p = .013$), BMI ($r = .502$, $p = .006$), and anxiety ($r = .407$, $p = .025$). Depression and anxiety negatively correlated with daily sleep hours ($r = -.436$, $p = .018$ and $r = -.454$, $p = .013$, respectively). Mental health, assessed by WHQ5, was positively associated with daily sleep hours ($r = .556$, $p = .002$). Our results indicate that the steepness of the aperiodic slope in young adult males is not directly related to anxiety and depression. Meanwhile, a flatter aperiodic slope correlates with less sleep as a lifestyle factor, which is associated with higher levels of anxiety, depression, and worse overall mental health. This raises the possibility that sleep serves as a mediating factor, which requires further investigation. Additionally, we found that a flatter aperiodic slope is associated with higher levels of alexithymia, which is positively related to increased anxiety, suggesting that alexithymia may also act as a mediating factor. A limitation of our study is the small sample size, which may impact the generalizability of the findings.

P16

The Role of STAT4 in Pituitary Adenoma Development

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Introduction: Pituitary adenomas (PAs) are benign tumors that develop in the pituitary gland, a small but crucial organ located at the base of the brain responsible for regulating hormone production (Lake et al., 2013). Although PAs are generally slow-growing and non-metastatic, they can cause significant issues if they enlarge and exert pressure on nearby brain structures (Møller et al., 2019). In light of the potential influence of genetic factors on PA development, the Signal Transducer and Activator of Transcription 4 (STAT4) gene has gained attention as a key area of research. This study examines the possible associations between STAT4 polymorphisms—rs7574865, rs10181656, rs7601754, rs10168266 and serum levels with PA occurrence. The goal is to investigate the role of STAT4 in the anti-tumor immune response and its potential involvement in the initiation of PA.

Materials and Methods: This study was conducted at the Laboratory of Ophthalmology, Lithuanian University of Health Sciences, using DNA extracted from peripheral venous blood samples. Genotyping for four STAT4 single nucleotide polymorphisms (SNPs) was performed through real-time PCR with TaqMan® assays.

Results: The study found that individuals carrying the STAT4 rs7574865 GT + GG genotypes had a 1.7-fold increased odds of developing PAs under the dominant genetic model ($p = 0.012$). While no significant associations were observed in females; males with the rs10168266 CC + CT genotypes had 2.5-fold higher odds of PA occurrence than those with the TT genotype ($p = 0.005$). Also, serum STAT4 levels were higher in PA patients compared to the reference group ($p < 0.001$).

Conclusion: The STAT4 rs7574865 and rs10168266 show significant associations with increased odds of PA occurrence. Elevated serum STAT4 levels were also observed in PA patients, highlighting its potential role in PA pathogenesis.

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P17

Glioblastoma-Derived Extracellular Vesicles Alter the Metabolic Functions of Vascular Endothelium Cells and Cardiomyocytes

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Advances in cancer treatment have significantly extended patient survival times, making cardiovascular side effects more noticeable. However, the connection between cancer-related and cardiovascular conditions remains insufficiently understood. Extracellular vesicles (EVs) released by cancer cells vary in size and subtype, carrying oncogenic cargo across all physiological barriers and enabling their spread throughout the body. Glioblastoma (GBM) is the most aggressive brain cancer which secretes an abnormal amount of EVs that have close association with local and peripheral thrombosis. So, this study aimed to assess the impact of GBM-derived EVs of varying sizes on vascular endothelial cells and cardiomyocytes, with the goal of uncovering the potential role of cancer-derived EVs in the cardio-oncology axis. GBM-derived EVs were isolated from human HROG36 cell line and fractionated by size into small EVs (sEVs) and large EVs (lEVs) by differential centrifugation and polymer precipitation. The EVs populations were characterized by total protein (Bradford assay), size and amount (nanoparticle tracking method and dynamic light scattering), RNA quantity (TRIzol™ assay). The metabolic activity in human vascular endothelium cells (HUVECs) and primary Wistar rat cardiomyocytes was analysed by PrestoBlue assay and mitochondria function by Seahorse XFp Mito-Stress test. We demonstrate the differences in size, quantity and biologically active material composition between sEVs and lEvs populations. The data reveal that lEVs contain higher RNA levels but are produced in smaller quantities. Cancer-derived EVs exhibit distinct effects on cardiomyocytes and endothelial cells: they enhance metabolic activity and mitochondrial respiration in cardiomyocytes, while reducing these functions in HUVECs. Notably, these effects were consistent regardless of EVs size, with no significant differences observed between large and small EVs. The results indicate that GBM-derived EVs require further investigation to fully understand their role in contributing to vascular dysfunction and heart failure through the hyperactivity of the heart muscle.

P18

Gender-Dependent Effect of Early Paracetamol Exposure on Behavior and CNS Neurotransmission in Rats

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The sex-related effects of paracetamol on neurotransmission in the central nervous system (CNS) and its behavioral consequences in prenatally exposed offspring remain unclear. This study analyzed the impact of prenatal and early life paracetamol administration (10, 30 mg/kg b.w./day) on neurotransmission and behavior in rats offspring of both sexes. Pups were divided into 6 groups (Con, P10, P30 - ♂ & ♀ separately) based on prior prenatal exposure. After weaning, paracetamol was administered for the next 3 months and during behavioral tests: Novel Object Recognition, Hole Board, Staircase, and Water Maze tests. The regional CNS concentrations of neurotransmitters were assessed by High-Performance Liquid Chromatography (HPLC). Both behavioral and biochemical analyses revealed a differentiated, gender-dependent response to paracetamol. Female rats exposed to paracetamol showed less anxiety compared to males exposed to the same doses of the drug in the Hole Board test. HPLC shoved that in the hypothalamus, the highest levels of dopamine (DA) metabolites - MHPH and HVA - as well as the HVA/DA ratio were observed in ♂ rats after the 30 mg dose compared to Control and rats that received 10 mg. No similar trends were found in ♀. In turn, ♀ rats in the P30 group showed enhanced hypothalamic metabolism of DA to DOPAC compared to ♂ rats receiving the same dose. In the medulla oblongata, DA concentrations decreased in ♂ but not in ♀ rats. In the prefrontal cortex, the highest NA levels were found in ♀ receiving the lower paracetamol dose, while ♂ exhibited the highest NA concentrations after the 30 mg dose. Similarly, a significant decrease in hippocampal NA levels was observed only in ♂ rats after the highest dose of paracetamol. This research addresses the gender gap in neuropharmacological studies regarding the consequences of paracetamol use during prenatal and early postnatal life.

P19

Metacognition Fluctuates Across Menstrual Phases in Naturally Cycling Women in an Emotion Recognition Task

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Hormonal fluctuations are known to be linked to emotional functioning and self-perception. However, the relationship between menstrual cycle phases and metacognition (i.e. confidence in one's own judgments) in the context of emotion recognition remains understudied. This study aimed to explore the association between the phases of the menstrual cycle and metacognition using emotion recognition task. Naturally cycling women (N=34) completed a facial emotion recognition task across the early follicular (FOL), ovulatory (OVU), and mid-luteal (LUT) phases, with stimuli varying in emotion expression (anger, fear, joy, sadness, and neutral) and intensity (100%, 50%, 25%). After each trial, participants identified the emotion displayed and rated their confidence in their answer on a scale from 0 (not confident) to 4 (very confident), allowing to evaluate both of their accuracy and confidence levels (metacognition). Analysis revealed a general tendency for women in the OVU phase to score higher in metacognition compared to those in the FOL ($p = 0.062$) and LUT ($p = 0.073$) phases. Specifically, women in the OVU phase were more confident with their answer when evaluating fearful ($p = 0.029$) and angry ($p = 0.048$) faces compared to FOL phase women, and more confident with happy faces compared to the LUT phase ($p = 0.015$). Moreover, women in the FOL phase scored lower in metacognition with fearful ($p = 0.015$) but higher with happy ($p = 0.010$) faces compared to LUT phase. Interestingly, women in the OVU phase rated their confidence higher even when their accuracy was lowest compared to FOL ($p = 0.006$) and LUT phase women ($p = 0.006$). No phase differences were observed for sad and neutral faces (all $p > 0.511$) and other accuracy levels ($p > 0.050$). In conclusion, the findings suggest that metacognition fluctuates across the menstrual cycle, with the ovulatory phase displaying the highest confidence scores, especially when observing angry and fearful faces.

P20

CCL2 Single Nucleotide Polymorphism Associations with Optic Neuritis Clinical Characteristics

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Optic neuritis (ON) is an inflammation of the optic nerve that results in demyelination of the optic nerve and loss of vision in one or both eyes. The incidence rates of ON ranges from 0,6 to 5,1 cases per 100 000/year across different geographical regions of the world. ON usually occurs with reduced visual acuity, patients describe vision as foggy. ON can be caused by a variety of causes, including infections, trauma, toxins, and genetic diseases. Monocyte chemoattractant protein-1 (MCP-1/CCL2) is one of the main chemokines that regulates the migration and infiltration of monocytes and macrophages. Migration of monocytes from the bloodstream across the vascular endothelium is required for normal immunological maintenance of tissues and regulation of inflammation. Single nucleotide polymorphisms (SNPs) of the CCL2 gene are associated with Parkinson's and age-related macular degeneration indicate an increased risk of developing neurodegenerative diseases. For this reason, we decided to determine the associations of CCL2 SNPs with ON visual acuity.

Aim: To determine the association between visual acuity of ON and single nucleotide polymorphisms of the CCL2 gene.

Methods: DNA was isolated by the salting out method from the venous blood of 84 patients with ON and 174 healthy individuals. Genotyping of CCL2 (rs1024611, rs4586, rs2857656) was performed by real-time polymerase chain reaction (RT-PCR). Statistical data analysis was carried out using "The IBM SPSS Statistics 29.0.2.0" program.

Results: We compared the distribution of alleles of CCL2 polymorphisms in patients with ON when assessing the visual acuity of healthy eye after treatment. The distributions of CCL2 rs4586 T and C alleles were statistically significantly different (p=0,043) according to the established visual acuity intervals. The distributions of CCL2 rs1024611 A and G alleles and rs2857656 G and C alleles were identically statistically significantly different (p=0,045) according to the established visual acuity intervals.

Conclusions: We found that CCL2 rs4586, rs1024611, rs2857656 polymorphisms have an impact on visual acuity after ON treatment.

P21

Ketamine Alters Subcortical Brain Areas to Reduce Cortical Synchronisation

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Schizophrenia is associated with the dysfunction of multiple neurotransmitters, particularly with the glutamatergic system. Post-mortem studies of brain tissues from patients with schizophrenia have revealed alterations in glutamatergic pathways (Hu et al., 2015). To model schizophrenia in rodents, N-methyl-D-aspartate (NMDA) antagonists are often employed. The administration of these antagonists has been observed to induce behavioural and brain activity changes that are analogous to the symptoms of schizophrenia in humans. One of the most prominent characteristics is the alteration in auditory steady-state responses (ASSRs), which has been proposed a potential biomarker for schizophrenia (Thune et al., 2016). The administration of ketamine (KET) has been demonstrated to result in a reduction in ASSRs recorded in the auditory cortex (Cizus et al., 2024). However, it remains unclear which part of the auditory pathway is affected by KET. The aim of this study was to investigate the impact of KET on the synchronisation of cortical networks directly. A total of 16 wild-type C57BL/6 mice were used in this study. ChR2 was expressed via the injection of a viral vector (100 µl, pAAV-CaMKIIa-hChR2(H134R)-mCherry (AAV1)) into the primary auditory cortex (A1). An optic fibre (FT400EMT, 400 µm 0.39 NA) and an electrocorticogram (ECoG) electrode were implanted above A1 to activate ChR2 and record brain activity, respectively. ASSRs were induced by presenting 2 ms white noise stimuli (clicks) at 40 Hz for a duration of 1 second, at 70 dB, with 2 second quiescence intervals. Direct steady-state responses (dSSRs) were induced by presenting 2 ms light stimuli at 40 Hz for a duration of 1 second, at intensity of 0.5-5 mW, with 2 second quiescence intervals. ECoGs were recorded before and 5 min after the administration of a sub-anesthetic dose of KET (20 mg/kg). Signal time-frequency analysis was conducted using the Morlet wavelet transformation, with the power and phase-locking index (PLI) calculated. The administration of KET reduced the PLI of 40 Hz ASSRs while the PLI of 40 Hz dSSRs remained unaltered when cortical neurons were activated directly. These results demonstrate that the synchronisation of cortical networks is not affected by KET administration. The changes observed in ASSRs, namely a decreased PLI after KET administration, are most likely due to changes occurring in subcortical brain areas of the auditory pathway, leading to altered synaptic drive to A1.

P22

Impact of VEGFA Gene Haplotypes on Multiple Sclerosis: Analysis of rs1570360, rs699947, rs3025033, rs2146323, rs1413711, and rs833061 Variants

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Introduction: Multiple sclerosis (MS) is a chronic disease of the central nervous system characterized by demyelination and axonal damage [1]. Excessive angiogenesis driven by vascular endothelial growth factor A (VEGF-A) contributes to MS's pathogenesis [2]. Originally identified as an angiogenic factor, VEGF-A also increases vascular permeability and has been linked to inflammatory diseases [3]. Given the potential role of VEGF-A in MS, our study focuses on the haplotypes of VEGFA rs1570360, rs699947, rs3025033, rs2146323, rs1413711 and rs833061. Aim: This study aimed to determine the association between haplotypes of VEGFA rs1570360, rs699947, rs3025033, rs2146323, rs1413711, and rs833061 and MS.

Methods. The study enrolled 270 patients with MS and 270 healthy controls. DNA was extracted from peripheral blood leukocytes using the DNA salting-out method. Genotyping was carried out using the real-time polymerase chain reaction (RT-PCR) method. Statistical analysis was performed with „SPSS version 29.0". Haplotype analysis was performed using the "SNPStats" web application. Linkage disequilibrium (LD) analysis was estimated by D' and r2 measures.

Results: Statistical analysis showed that individuals carrying haplotypes A-A-A-A-T-C and G-A-G-A-T-C of variants rs1570360, rs699947, rs3025033, rs2146323, rs1413711 and rs833061 were associated with 1.6-fold, and 2.7-fold decreased odds of MS occurrence (OR = 0.62, 95% CI: 0.380 - 0.990; p= 0.046 and OR = 0.37, 95% CI: 0.140 - 0.940; p= 0.037, respectively).

Conclusion. Our study revealed an association between the haplotypes of VEGFA rs1570360, rs699947, rs3025033, rs2146323, rs1413711, and rs833061 and MS.

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P23

Calcium-Mediated Amyloid Co-Aggregation of S100A1 and S100A8 Proteins

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The S100 protein family consists of structurally similar calcium-binding proteins that play diverse roles in regulating calcium homeostasis, cell growth, differentiation, cytoskeleton dynamics and response to inflammation [1]. In recent years, several members have been found to play significant roles in neurodegeneration by facilitating neuroinflammatory signaling and forming amyloid fibrils [2]. Among these proteins, S100A9 has been well-characterized, while the roles of S100A1 and S100A8 remain unclear. S100A1 and S100A8 are expressed in the cerebral cortex [3] and share structural similarities [1]. Both proteins have active roles in Alzheimer's disease (AD) and interact with TLR and RAGE receptors [4], which play a crucial role in the AD cascade for transmitting neuroinflammation signals. Given S100A's ability to form heterodimers with other S100 proteins [2], we aimed to elucidate a potential S100A1/A8 complex formation. Aggregation kinetics of S100A1/A8 was explored with the amyloid-specific Thioflavin T fluorescence assay, followed by visualization of the samples using Atomic Force (AFM), Transmission Electron (TEM) and Total Internal Reflection Fluorescence (TIRF) microscopies. A S100A1/A8 heterodimer formation was investigated via Electron Paramagnetic Resonance Spectroscopy (EPR). Our research revealed that S100A1/A8 aggregation into fibrillar structures is a calcium-dependent process, inhibited at higher calcium concentrations. AFM and TEM imaging confirmed that the interaction between these proteins led to the formation of worm-like fibrils. Using TIRF microscopy, we observed co-localization of fluorescently tagged S100A1 and S100A8 within aggregates. However, EPR did not detect a stable complex, suggesting that interactions between these proteins may be transient or occur within larger, higher-order structures. These findings add to understanding S100 protein aggregation dynamics and offer valuable insights into their potential relevance in various diseases.

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P24

Generation of in Vitro Neuronal Model Stably Expressing Dual-fluorescence Reporters Using CRISPR-Mediated HDR

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Genome editing is making its way towards therapeutic applications. However, genome editing tools are usually researched using cancerous, undifferentiated cell lines as experimental models, which do not accurately represent living organisms. Primary neuronal cells are hard to obtain and maintain. In vitro differentiated neural-like cells are easier to maintain and easier to obtain. Fluorescent reporters are a convenient way to evaluate CRISPR-based editing at a glance, without a need of sequencing. Aim: We aimed to create an in vitro neuronal model expressing EGFP and mRuby2 fluorescent reporters, which could be differentiated.

Methods: The dual-reporter EGFP and mRuby2 template was knocked-in to human neuroblastoma SH-SY5Y and mouse neuroblastoma Neuro-2a cells safe harbor loci AAVS1 and ROSA26, respectively. Template was introduced to cells using lipofection. mRuby2 reporter was positioned under the exogenous promoter, which allowed expression after the transfection. Following the integration of the construct to the genome, both EGFP and mRuby2 were expressed simultaneously. Homogenous cultures of modified cells were selected from the mixed cultures of modified and non–modified cells by single-cell dilution. SH-SY5Y and Neuro-2a cells were differentiated using retinoic acid and serum withdrawal.

Results and conclusions: We developed SH-SY5Y_EGFP_mRuby2, SH-SY5Y_EGFP204A>C_mRuby2 and N2a_EGFP204A>C_mRuby2 cell lines stably expressing EGFP and mRuby2 fluorescent reporters in the nuclei and membranes, respectively. We have selected the conditions for SH-SY5Y differentiation allowing for confocal microscopy and Neuro-2a differentiation. During differentiation cells displayed neural-like features such as neurite outgrowth, halt of proliferation and relocalization of neural markers: vesicular glutamate transporter 1 (VGLUT1), post-synaptic density protein 95 (PSD95) and neurofilament marker (SMI312).

P25

Cognitive Impairment and Depression Symptoms in Parkinson's Disease: Magnetoencephalography Data Biomarkers

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Introduction: Parkinson's disease (PD) is a neurodegenerative disorder that affects motor function, causing tremor and impaired coordination. This study explores changes in neural oscillations in magnetoencephalography (MEG) data to identify potential biomarkers linked to depression, apathy, and cognitive impairment in PD patients.

Methods: MEG data from 20 PD patients were preprocessed and source-reconstructed to 116 time-series. Power spectral density (PSD), its ratios, and spectral slopes were calculated in 5 bands: Alpha (8-12 Hz), Beta (12-30 Hz), Gamma (30-100 Hz), Delta (0.5-4 Hz), and Theta (4-8 Hz). Spearman's correlation and odds ratios of binary logistic regression for PSD and slopes were calculated for MEG features and clinical measures: depression assessed by Beck Depression Inventory (BDI), apathy by apathy evaluation scale, and cognitive function by Montreal Cognitive Assessment (MoCA). Using Minimum Redundancy Maximum Relevance method to avoid overfitting, 6 most significant features were selected, and Machine Learning (ML) algorithms were applied to predict cognitive impairment and depression.

Results: The strongest PSD Spearman's correlation for BDI was in Alpha activity channel 3, corresponding to the left frontal superior orbital region ($r=0.74$, $p<0.05$), and in Alpha activity channel 42 on the right side ($r=0.71$, $p<0.05$). For apathy, Alpha and Beta bands in channel 52 (paracentral lobule right side) were most significant (Alpha $r=0.64$, $p<0.05$; Beta $r=0.60$, $p<0.05$). A negative correlation was found between gamma, alpha band slopes and MoCA scores ($r= -0.66$ to -0.45, $p<0.05$), and between PSD of various bands and MoCA scores ($r= -0.63$ to -0.44, $p<0.05$). The best predictive model was the logistic regression model for BDI with a 90%±9.24 accuracy. The most significant features were PSD power in Alpha band (channels 40, 46), Theta (channels 1, 2), Delta (channel 97), Gamma/Beta ratio (channel 3). ML methods showed a lower accuracy in prediction of apathy (50.86%) and MoCA levels (64.29%).

Conclusion: The findings suggest that altered Alpha and Beta activity in the frontal superior orbital region is related to depressive symptoms, while activity in the paracentral lobule is linked to apathy in PD. Steeper gamma spectral slopes and elevated power in Alpha and Theta frequency bands may be markers of cognitive impairment. The ML models showed strong predictive capabilities, revealing the value of MEG data in identifying depressive symptoms in PD.

P26

Heat Map-Based Analysis of miRNA Expression for Biomarker Identification in Inflammatory Polyneuropathy

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Polyneuropathy (PN) is a common nerve disorder that affects the peripheral nerves. PN are characterized by symmetrical and diffuse damage to the peripheral nervous system, potentially affecting motor, sensory, or autonomic nerve fibers. The disease may manifest with muscle weakness, atrophy, paresthesia, pain, decreased and autonomic symptoms. MiRNAs are small, non-coding RNA molecules, about 20-24 nucleotides long, that play a crucial role in the regulation of gene expression. MiR-146a and miR-31 are linked to immune inflammatory diseases and it plays an important role in controlling T and B lymphocytes and dendritic cells. These miRNAs may affect inflammatory mediators that promote or inhibit the immune response. The aim of this study was to perform a heat-map analysis to compare the expression of miR-31-5p and miR-146a-5p between patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and Multifocal Motor Neuropathy (MMN) and controls. RNA was isolated from blood using mirVana™ miRNA Isolation Kit (ThermoFisher (TF), USA). The cDNR synthesis was performed using the TaqMan® Advanced miRNA cDNA Synthesis Kit (TF, USA). MiRNAs expression was detected by using qRT-PCR method. Results were analyzed using the heat-map method. The significance of the results was assessed using the SPSS Statistics 29.0.2.0. A total of 23 patients with CIDP/MMN and 56 controls were analyzed for miRNA expression in blood. The intensity and gradient of the colors in the heat map indicated the miRNA expression levels and revealed potential differences between CIDP/MMN patients and controls. Heat-map analysis can provide an overview of the miRNA expression profile between the CIDP and MMN subjects and the control group and help identify potential miRNA diagnostic markers.

P27

Plant Derived Nanovesicles Protect Cells in Ischemia Model

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Neurological damage remains one of the most common complications after heart surgery under artificial blood circulation conditions. With increasing number of patients with complex surgeries due to aging society, these complications make it important to look for new neuroprotective options. Plant derived extracellular vesicles (PDEVs) contain microRNAs capable of cross-kingdom regulation of gene expression and metabolites with anti-inflammatory, antioxidant activity. PDEVs, can transport both hydrophobic and hydrophilic substances due to their structure and also increases their stability. Unlike mammalian EVs, the use of PDEVs reduces the risk of immunogenicity making them ideal candidates for medical applications.

Aim: investigate neuroprotective effects of PDEVs in ischemic model on primary neuronal-glial cells (from Wistar rats).

Methods: PDEVs were isolated from Rosa Damascena rose buds, cranberry berries, guelder rose berries and blackcurrant berries using Exoplant-Lo kit (Exolitus, Lithuania). Size and concentration of PDEVs were measured using Nanosight NS300 nanotracking analysis (NTA). TRIzol reagent was used to determine total RNA concentration and Bradford method for total protein concentration in PDEVs. Cells were pretreated with PDEVs for 24 hours and then incubated in hypoxic and normoxic conditions for 48h. Cell viability was determined using Hoechst 33258 and propidium iodide stains.

Results: only PDEVs from Rosa Damascena rose buds in concentration range of 1*109–1*106 particles/ml had neuroprotective effects on mixed neuronal-glial cells in hypoxic conditions. Rosa Damascena PDEVs also contained the highest amount of proteins per particle count and were the largest in size. Summary: nanovesicles from Rosa Damascena rose buds prevented neuronal – glial cell death in ischemia model showing a potential in cardiac surgeries to prevent ischemic brain lesions.

P28

Association of TNF rs2229094, EXOC3L1 rs868213, and CTC1 rs3027234 Variants with Visual Acuity in Optic Neuritis Patients

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Introduction: Optic neuritis (ON) is a multifactorial, infectious or demyelinating process affecting the optic nerve. ON is usually divided into two broad groups: typical and atypical ON. Epidemiological data on ON and ON-related diseases are limited. Incidence rates (per 100,000 persons per year) vary more than 5 times: from 0.83 (Singapore, 2009) to 5.36 (Barcelona, Spain, 2008-2012). Risk factors for ON include age (20 to 40 years), gender (female:male = 2:1), and race (Caucasian). Recent findings indicate that TNF rs2229094, EXOC3L1 rs868213 and CTC1 rs3027234 are implicated in inflammatory processes central to disease pathogenesis. This evidence supports the hypothesis that these genetic variants may be associated with susceptibility to ON, potentially influencing disease mechanisms linked to inflammation.

Aim: To determine the associations of TNF rs2229094, EXOC3L1 rs868213, and CTC1 rs3027234 gene polymorphisms with visual acuity in optic neuritis.

Materials and methods: The study involved 82 patients diagnosed with ON and a control group of 160 healthy individuals. DNA was isolated from peripheral blood leukocytes using the salting-out technique, and genotyping was performed using real-time polymerase chain reaction (RT-PCR). Statistical analysis was conducted using IBM SPSS Statistics 29.0.

Results: Comparing the correlations of visual acuity of the affected eye before and after treatment with polymorphisms, we found that the CTCT1 rs3027234 were statistically significantly associated with worse visual acuity after treatment (p= 0,044).

Conclusion: Also comparing the correlations of visual acuity of the affected eye before and after treatment with polymorphisms, we found that the CTCT1 rs3027234 was associated with worse visual acuity after ON treatment.

P29

Effect Of Selenium on Lipid Peroxidation and Catalase Activity in Brain and Liver of Mice

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Selenium (Se) plays an important role sustaining brain motor activity, cognition, coordination, and memory. The liver is a major organ involved in the regulation of Se metabolism. When received in adequate doses, Se, mainly in the form of selenocysteine, is inserted into the structure of antioxidant selenoproteins and exerts its antioxidant activity. At supranutritional doses, organic Se, as well as inorganic Se, is known to exhibit prooxidant activity, causing an increased risk of brain disorders. The aim of this study was to determine the effect of Se on the level of oxidative stress in the brain and liver of 4-6 weeks-old laboratory BALB/c mice, which were given inorganic sodium selenite or organic selenomethionine (0.2 mg Se/kg body weight) solution for 8 weeks (License no. G2-80). The lipid peroxidation product malondialdehyde (MDA) and the activity of the antioxidant enzyme catalase were evaluated by spectrophotometric assays. Results revealed that exposure to organic and inorganic Se did not cause any significant changes in the MDA concentration in the mice brain: it increased by 11% after selenomethionine administration and decreased by 10% after sodium selenite administration, as compared to control (81.13 ± 3.06 nmol/g). Meanwhile, exposure to selenomethionine decreased lipid peroxidation in mice liver by 30% ($p<0.05$), compared to the control (57.59 ± 3.32 nmol/g). The MDA concentration was by 193% higher ($p<0.05$) in the liver of sodium selenite-exposed mice as compared to the control. The activity of antioxidant enzyme catalase in the brain of selenomethionine-exposed mice was 32% lower ($p<0.05$) as compared to control (18.03 ± 2.73 U/mg protein). Meanwhile, the activity of this enzyme in the brain of sodium selenite-exposed mice was statistically insignificantly reduced by 10%. The catalase activity decreased by 1.6 times ($p<0.05$) in the liver of selenomethionine-exposed mice and by 1.8 times ($p<0.05$) in the liver of sodium selenite-exposed mice as compared to the control (45.00 ± 3.014 U/mg protein). In summary, after 8-week-long Se-supplemented water consumption, in the liver of mice sodium selenite acted as a pro-oxidant by statistically significantly increasing the level of MDA. Meanwhile, selenomethionine, on the contrary, decreased the level of lipid peroxidation. The activity of antioxidant enzyme catalase was inhibited in both organs after selenomethionine administration and in the liver after sodium selenite administration.

P30

The Effect of the Anesthetic Propofol on Connexins of Cardiovascular System

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Propofol is a widely used general anesthetic, which causes a rapid induction of anesthesia. The most prominent side effect of propofol is the decrease of systemic vascular resistance that leads to hypotension. Moreover, in some cases, propofol has been shown to inhibit cardiac conduction and cause bradycardia, but its pathophysiological mechanism is still not fully understood. On the other hand, propofol was shown to have a protective effect against ventricular arrhythmias during myocardial ischemia. Several studies have shown that propofol may regulate cell coupling through gap junction (GJ) channels formed of Cx43. However, it is unclear how propofol affects all cardiac connexins. It is known that Cx37, Cx40, Cx43 and Cx45 form gap junction channels in cardiovascular system. These connexins are required for coordination of vascular responses and play a key role in ensuring propagation of action potential in cardiac tissue. The aim of this study was to get a better understanding of the capacity of propofol to affect cardiovascular connexins. First, we compared the effect of various propofol concentrations on GJs formed by cardiovascular connexins which were expressed exogenously in human cervix epithelial adenocarcinoma cells (HeLa). The junctional conductance was measured using double whole-cell patch clamp method. Our data show that Cx40 and Cx43 channels exhibit similar sensitivity to propofol (IC50 Cx40 - 17μM; Cx43 – 15μM), while Cx45 channels are sensitive to much higher propofol concentrations (IC50 60μM). Interestingly, the vascular Cx37, which is an important player in dilation of vascular beds, was the most susceptible to propofol (IC50 5μM). Propofol may affect Cx43 GJ channels through activation of protein kinase C (PKC), which in turn phosphorylates Cx43 and reduces coupling through GJs. In our study, the kinase inhibitor GF109203X was used to assess this putative pathway of propofol action on GJs. It is established that low concentrations (40nM) of GF109203X specifically inhibit PKC while higher concentrations (2 μM) inhibit both PKC and protein kinase A (PKA). Our data showed that low concentration of GF109203X significantly reduced inhibition of Cx43 channels by propofol. In contrast, both concentrations of GF109203X had no effect on inhibition of Cx40 and Cx45 channels by propofol. The findings indicate that both low and high kinase inhibitor concentrations considerably lessened propofol's blocking effect on Cx37.

P31

Examining Asymmetry in the Müller-Lyer Illusion: a Quantitative Study of Wings-In and Wings-Out Variants

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Aim: The aim of the study was to further develop a quantitative model of the filled-space illusion and test it to account for the effects caused by stimuli containing the wings-in and wings-out versions Müller-Lyer illusion distractor.

Methods: The psychophysical experiment involved three-dot stimuli, with a single set of Müller-Lyer wings added to either the left or right ending dot in different trial series. To investigate potential summation of the illusory effects, additional experiments were conducted using two sets of wings forming the Judd figure. To analyze the isolated effect of the filled-space illusion, we included trials with a distracting cross (two sets of overlapping but oppositely oriented wings) centered on the lateral endpoint of the stimulus. Data obtained in different series were fitted with relevant functions of the model.

Results: To analyze the experimental data, we applied computational methods based on previously developed quantitative models of hypothetical visual mechanisms responsible for the Müller-Lyer illusion and the filled-space illusion. The theoretical calculations successfully explained the variations in illusion magnitude across all stimulus modifications, strongly supporting the hypothesis that the concurrent effect of the filled-space illusion is significant enough to be considered a primary factor contributing to the asymmetric properties observed in Müller-Lyer-type extent illusions.

Conclusions: A close approximation of the experimental results by theoretical functions supports the hypothesis that the asymmetric characteristics of Müller-Lyer-type illusions can be explained by the combined effects of neural processes involved in extracting the centroid of the visual target and in perceptually encoding its retinal location.

P32

A Study of Length Comparison of Geometric Objects Using Eye-Tracking

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Aim: This psychophysical study utilizes eye-tracking technology to investigate gaze patterns as participants evaluate the lengths of various geometric shapes.

Methods: Six geometric shapes were used as stimuli: rectangle, ellipse, triangle, line, rectangle with concave lateral edges, and two crossed segments. Each shape measured 8.2 × 2.7 arc minutes and was presented alongside a reference spot with a diameter of 0.27 arc minutes. Stimuli were displayed in two sizes: the larger size had a reference distance of 11.9 arc minutes, and the smaller size had a reference distance of 5.1 arc minutes, both defined by the spot. Each stimulus was displayed for 1.5 seconds, during which participants judged whether the left or right segment of the shape was longer. Participants used a computer mouse to indicate their responses: the left mouse button for "left side longer" and the right mouse button for "right side longer." All tests were conducted monocularly in a darkened room. Eye movements of the 10 participants were recorded throughout the experiment, with data processed and visualized using MS Excel and a proprietary author's software.

Results: The data revealed distinct eye fixation patterns influenced by stimulus size and shape. For larger stimuli such as rectangles and ellipses, participants' fixations occurred approximately 7 arc minutes from the center, directed towards the reference spot. For triangles positioned peripherally, fixations shifted further, averaging 8.3 arc minutes. Smaller stimuli, in contrast, elicited fixations closer to the center: lines prompted a fixation shift of only 1.6 arc minutes, rectangles with concave edges 1 arc minute, and two crossed segments demonstrated the smallest shift at 0.8 arc minutes.

Conclusions: Observers' gaze points were either centered on the midpoint of the comparison distance or near the center of larger stimuli. For smaller stimuli, fixation points tended to cluster close to the center.

P33

Influence of Liquid-Liquid Phase Separation on Amyloid Fibril Structural Variability

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Protein aggregation in the form of amyloid fibrils is associated with the development of various neurodegenerative disorders, including the well-known and widespread Alzheimer's and Parkinson's diseases. Researchers around the world have been trying to find out the causes of such disorders, the mechanisms of pathology, and possible treatments or effective drugs for the diseases for many years, but there still are difficulties. Recent studies show that some amyloid proteins, such as alpha-synuclein (α-syn, associated with Parkinson's disease) or Tau protein (associated with Alzheimer's disease), tend to form protein droplets in the cellular environment during liquid-liquid phase separation (LLPS). It is believed that these structures may be an intermediate state between the native protein and cytotoxic amyloid fibrils. The aim of this study was to determine whether alpha-synuclein fibrils formed during liquid-liquid phase separation differ in structure or morphology from those formed without a crowding agent. To induce LLPS, 20% of polyethylene glycol was added to the reaction mixture as a crowding agent. During LLPS, the formation of alpha-synuclein droplets was monitored by measuring the changes in the optical density and fluorescence of the sample, as well as using fluorescence microscopy. In order to determine the changes in the secondary structure of the formed fibrils, Fourier transform infrared spectroscopy was also used. The amyloid fibrils were further analyzed using atomic force microscopy. The results of the study showed that polyethylene glycol causes LLPS in the reaction mixture and alpha-synuclein droplets are formed from the very beginning of the reaction, and after 6 hours of incubation, the droplets transform into amorphous aggregates. When analyzing the changes in FTIR spectra during incubation, a decrease in the sample unstructured region and increase in parallel and antiparallel beta-sheets was observed. AFM images showed that the fibrils formed under LLPS conditions were characterized by high variability (5 morphologically distinct aggregates), while under non-LLPS conditions only one type of fibril was obtained.

P34

Impact of Data Preprocessing on EEG Signal Classification Using Adjacency Matrices

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Major depressive disorder (MDD) is characterized by unique patterns of resting-state functional brain connectivity (FBC). Electroencephalography (EEG) based computations of FBC can improve MDD diagnostics, particularly when used with machine learning methods. Functional brain connectivity, defined by correlations between EEG electrode signals, is often represented as an adjacency matrix in graph form. Different metrics capture distinct connectivity aspects, making comparative analysis crucial for robust classification. In this study, several FBC metrics are examined, such as Pearson's correlation, phase-locked value (PLV), phase lag index (PLI), and the imaginary part of coherence (iCoherence)—to classify two resting-state conditions. The analysis uses two datasets: the EEG Motor Movement/Imagery Dataset, containing data from 100 subjects with both eyes-closed and eyes-open states recorded via 64 electrodes, and the Republican Vilnius Psychiatric Hospital dataset, which includes recordings from 100 controls and 100 patients diagnosed with depression, using 20 electrodes. Furthermore, classification results were compared based on different preprocessing techniques, including raw data versus filtered data. Combined with LASSO for feature selection, machine learning methods yielded robust classification results on the EEG Motor Movement/Imagery Dataset. Using binarized adjacency matrices, bootstrapped mean accuracies were as follows: 84.15% for support vector machines (SVM), 83.40% for random forests (RF), and 81.70% for XGBoost. For analysis on the Republican Vilnius Psychiatric Hospital dataset, raw data classification accuracies were 67% for SVM, RF, and XGBoost. The results were improved as data was filtered with an FIR filter, as acquired classification accuracies were 74.5% for support vector machines and XGBoost and 74% for random forests. Similar results were acquired when FIR and IIR filters were applied, resulting in 74% accuracies for SVM, RF, and XGBoost.

P35

Associations of TPH2 (rs7305115), BDNF (rs6265), and LINC01180 (rs12526133) Polymorphisms with the Clinical Course of Major Depressive Disorder

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Major depressive disorder (MDD) is one of the leading global health burden.The age of onset, severity of depressive symptoms and duration of the disease differ between patients. The data shows that SNPs may influence the age of onset, the duration of MDD and severity of depressive symptoms. The SNPs of TPH2 gene, which is responsible for serotonin transmission, can be found in those with MDD [1]. Additionally, dysregulation of brain-derived neurotrophic factor (BDNF) is associated with the pathogenesis of mood and anxiety disorders [2]. Moreover, long non-coding RNAs have also been associated with MDD pathogenesis [3]. Specifically, the expression of LINC01108 rs12526133 has been found to be relatively higher in individuals suffering from MDD [3]. The aim of this study was to investigate whether specific SNPs – TPH2 rs7305115, BDNF rs6265, and LINC01108 rs12526133 – are associated with the development and clinical course of MDD. DNA was extracted from blood samples via the salting-out method and genotyped by real-time PCR. Data analysis was performed using „IBM SPSS Statistics“ on 135 samples, comparing 85 MDD patients with 50 controls. The secondary comparisons were performed across MDD patient groups: among different severities of MDD (using the Montgomery–Åsberg Depression Rating Scale total score, age of onset, total duration of the disorder and the duration of current depressive episode). The selected SNPs did not significantly distinguish between patients with MDD and healthy controls, nor were there significant differences in SNP frequency among patients with different severity of depressive episode. However TPH2 rs7305155 SNP was associated with a longer duration of MDD, with the GG genotype ($p = 0.032$) and G allele ($p = 0.073$) being more prevalent in patients with depression lasting

fewer than six years compared to those with a duration of 6–10 years. BDNF rs6265 had a trend with an older age of disease onset ($p = 0.052$) (CC genotype was more prevalent in those, who developed depression >26 years old, than in those, who developed disorder before at the age of ≤25). Also, none of the SNPs had any impact on the duration of current depressive episode. These findings suggest that while the SNPs may have a modest relation with clinical course of MDD, they are not robust predictors on their own. Further research with larger sample sizes is needed to confirm these findings.

[1] PMID: 22693556
[2] PMID: 17632285
[3] PMID: 27940106

P36

The Effect of Xkr8 Scramblase Deficiency on Synaptic Activity and Firing Properties of Mouse Hippocampal Pyramidal Neurons During Early Postnatal Development

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During postnatal development, hippocampal pyramidal neurons experience significant morphological and electrophysiological changes leading to effective neural network formation and functional maturity. At the same time, neurons undergo microglia dependent synaptic pruning, a process crucial for effective signal transmission. Pruning is guided by the "eat me" signal phosphatidylserine, translocated across the cell membrane by the Xkr8 scramblase. Recent findings show that the Xkr8 scramblase is highly expressed in mice immediately after birth, with expression levels decreasing as they age. Mice lacking Xkr8 during postnatal period exhibit an excess of excitatory nerve terminals, a higher density of cortico-cortical and cortico-spinal projections and altered morphology of neuronal boutons. These alterations can lead to electrophysiological changes in firing properties. Moreover, Xkr8 deficiency changes synaptic activity in postnatal day 40 mice, however, it is still unknown when those changes occur and how develop over the age. To investigate the effect of Xkr8 scramblase deficiency on the synaptic activity and firing properties of mouse hippocampal pyramidal neurons during postnatal development, the Xkr8 knockout and wild-type mice, both males and females, were used in this study. Electrophysiological properties were assessed with the whole-cell patch-clamp technique. The firing properties were evaluated as a steepness of frequency-current (f-I) relation, presenting how neurons integrate inputs and encode outputs through action potential frequency. Synaptic activity was measured by evaluating the amplitude and interevent intervals of spontaneous excitatory postsynaptic currents (sEPSCs). Additionally, we examined the rate of spike frequency adaptation. Our findings reveal a significant increase in the steepness of the f-I relation in both male and female Xkr8 knockout mice after spike frequency adaptation, indicating a decreased precision in neurons output control. However, the amplitude and interevent intervals of sEPSCs in Xkr8 knockout mice remained similar to the control group, suggesting comparable levels of synaptic activity. Overall, while we did not observe the effect of scramblase on synaptic activity across the selected age groups, we found that scramblase deficiency does influence the information-processing properties of neurons.

P37

The Effect of Hyperoside on Superoxide Dismutase (SOD) Activity in Mice Brain

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Background: Superoxide dismutase is a key antioxidant enzyme that protect cells by converting harmful superoxide radicals into hydrogen peroxide and oxygen. SOD activity increases in response to higher superoxide levels and certain chemicals. Hyperoside has been studied for its role in reducing oxidative damage in cells. Research indicates that hyperoside exhibits antioxidant effects by scavenging reactive oxygen species (ROS) and enhancing antioxidant enzyme activity. It has been shown to protect against hydrogen peroxide (H2O2)-induced cell damage by inhibiting apoptosis. [2] Hyperoside activates nuclear factor erythroid 2-related factor 2 (Nrf2), a key regulator of antioxidant responses, leading to the upregulation of antioxidant enzymes like superoxide dismutase. [3].

Aim: The aim of this study was to evaluate the effect of hyperoside on the superoxide dismutase activity in mice brain after aluminum consumption.

Results: Although literature data indicate that SOD activity increases during oxidative stress, this study found no effect of aluminum on the SOD in the brain of mice compared to the control group ($p>0.05$). However, hyperoside (21 day of 50 mg/kg) reduced SOD activity in the brain of mice compared to the control group, but this change was not statistically significant ($p>0.05$). Also, no statistically significant difference was found when hyperoside was administered after aluminum-induced oxidative stress, compared to both the aluminum and control groups (Fig. 1). Since there is evidence of a positive effect of hyperoside on oxidative stress markers [1], the results of this study suggest that its effectiveness in combating aluminum-induced oxidative damage in brain cells may depend on the dose of administration.

Conclusions: Despite the antioxidant properties of hyperoside, the results show that its 50 mg/kg dose does not significantly affect superoxide dismutase activity in the mouse brain, and therefore does not provide significant protection of brain antioxidant systems against aluminum-induced oxidative stress.

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P38

Age-Related Alterations in Neuropeptide Expression within Nodose Ganglia of Hypertensive and Normotensive Rats

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Hypertension impacts the autonomic nervous system, particularly through changes in sensory ganglia associated with the vagus nerve. The nodose ganglia (NG), a key hub in cardiovascular regulation, contain neuropeptides such as CGRP, nNOS, and TTN3, essential for neural signaling. This study investigates changes in neuropeptides CGRP, nNOS, and TTN3, and neuronal size within NG of spontaneously hypertensive rats (SHR) compared to normotensive Wistar-Kyoto rats (WKY) across ages (9–64 weeks). Left and right ganglia differences were also examined. Cryosections of NG were immunohistochemically stained with primary antibodies against CGRP, nNOS, TTN3, and PGP9.5 (general neuronal marker). Fluorochromes Cy3, FITC, and A488-conjugated secondary antibodies were used for visualization under fluorescence microscopy. Neuropeptide expression was quantified with ImageJ, and neuronal area calculated with AxioImage. Statistical analyses included T-tests and one-way ANOVA. With SHR rats exhibiting chronic hypertension and WKY rats serving as controls, significant differences in neuropeptide expression were observed between the groups. Young SHR showed higher CGRP and TTN3 expression ($p<0.01$), while older SHR displayed primarily TTN3 differences. Middle-aged SHR presented elevated CGRP and TTN3 expression, and very old SHR demonstrated increased nNOS and TTN3, especially in the left NG. Additionally, older SHR showed significant left-sided CGRP, nNOS, and TTN3 expression differences, with age-related neuronal size differences, notably for nNOS in NG ($p<0.05$). This study reveals age-related neuropeptide expression differences in NG between hypertensive and normotensive rats, with SHR showing higher CGRP, nNOS, and TTN3 levels, especially in the left-sided NG. These findings underscore the role of NG neuropeptide alterations in neurogenic hypertension pathology and highlight aging's impact on these mechanisms.

P39

Protective Effects of Antidiabetic Drug Imeglimin Against Ischemic Brain Damage in Young and Aging Rats

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Imeglimin is a novel oral drug suggested as a safe drug for glycemic management in patients with type 2 diabetes mellitus. Growing evidence shows that it has many purposed mechanisms of action though they are not fully understood. To provide deeper insight into the pharmacological properties of imeglimin we aimed to assess the effect of intraperitoneal injection of this drug (109 μg/kg) on ischemic brain injury in Wistar rats of different age groups - young (2-3 months-old), middle-aged (10 months-old) and aged (24 months-old). The application of imeglimin 24 h before simulated brain ischemia in vitro reduced infarct size only in young and middle-aged rat groups. Elucidating the neuroprotection at the subcellular level we found that imeglimin directly added to isolated mitochondria of 2-3 months-old and 10 months-old rat brains suppressed NADH-linked oxidative phosphorylation and enzymatic activity of Complexes I and IV of the electron transfer system. The opposite, stimulating effect on Complex II activity was observed within the same groups as mentioned above. In the aged rat group (24 months), imeglimin had no effect in reducing cerebral infarct size or directly modulating mitochondrial respiration and enzymatic activities of the complexes. In conclusion, we expanded knowledge on potential effects of imeglimin in the brain by demonstrating a direct stimulating effect on mitochondrial Complex II activity and age-dependent protective effects against brain injury under in vitro simulated ischemia.

P40

Males' Response to the Short Sing-a-Song Stress Test: Assessment of Psychophysiological Parameters

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The short Sing-a-Song Stress Test (sSSST) was developed as a cost-effective alternative to the Trier Social Stress Test for inducing psychosocial stress. In this task participants are suddenly cued to sing in front of a video camera. Although the sSSST reliably elicits subjective and physiological stress, its effect on different physiological parameters remains understudied. This study aimed to establish the sSSST procedure and to evaluate its impact on subjective arousal and parameters of heart rate, heart rate variability (HRV), electrodermal activity (EDA), and salivary cortisol concentrations. Eighteen males participated in the study. Before the procedure, electrocardiography (ECG) electrodes and electrodermal sensor were attached to participants. While seated in front of the computer participants completed three neutral tasks followed by a 60 s countdown. Then males were informed that they have to sing the National Anthem of Lithuania within 90 s, with a camera turned on to make them believe that their performance will be recorded. After 90 s, participants were informed that they do not need to sing and could relax. The 90 s preparation period was regarded as a stress condition. Baseline (before the task) and stress-recovery (after the task) values of ECG and EDA were measured for 90 s. Additionally, both before and after the task males rated their subjective arousal on a Visual Analog Scale (VAS) from "completely calm" to "aroused to the maximum". Furthermore, saliva samples were collected before the sSSST, immediately after, and 20 minutes later to asses cortisol changes. The analysis of study results revealed increased heart rate during stress condition compared to both baseline and stress-recovery. Both low and high frequency components of the HRV demonstrated a significant stress response. Males' EDA was also elevated during stress compared to baseline. Subjective arousal ratings during stress-recovery were higher compared to baseline. However, there were no significant differences in cortisol concentrations across conditions. These results suggest that the sSSST reliably induces mild stress, which is reflected in heart rate, heart rate variability parameters, electrodermal activity, and subjective ratings. However, induced stress was too mild to reliably increase cortisol levels.

P41

TERC Variants: A Genetic Link to Relapsing-Remitting Multiple Sclerosis

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Multiple sclerosis (MS) is a progressive autoimmune neurological disorder of the central nervous system resulting from autoimmune damage to the white matter of the central nervous system. MS is currently classified into four different types, with relapsing-remitting multiple sclerosis (RRMS) being the most common. RRMS is characterized by new or worsening symptoms (relapses) followed by a period of improvement (remission). The pathophysiology and causes of MS are complex, with environmental, infectious, genetic, nutritional, and epigenetic factors potentially affecting the onset and progression of the disease. Recent studies suggest that cellular senescence resulting from telomere shortening may play a role in the development of MS. TERC also plays a role in regulating telomere length and influences chromosome maintenance and stability. Alterations in TERC affect telomere length and can have significant effects on cell aging, disease progression, and susceptibility to various health conditions. In this study, we investigated how TERC SNVs are involved in the development of RRMS.

Aim: To evaluate the link between RRMS occurrence and SNVs of TERC.

Materials and methods: The study included 225 patients with RRMS and 250 healthy individuals. Genotypes of the TERC rs12696304 and rs35073794 variants were determined using real-time polymerase chain reaction. The obtained data were statistically evaluated using IBM SPSS Statistics 29.0.1.0 software.

Results: The TERC rs12696304 G allele is less common in the RRMS patients than in the control group (11.6% vs. 18.6%, $p = 0.013$). Binary logistic regression analysis showed that the TERC rs12696304 GG is associated with 3.4-fold decreased odds of developing RRMS under the codominant model (OR = 0.292, CI: 0.128-0.666, $p = 0.003$). Also, AG + AA genotypes of TERC rs35073794 are associated with 1.5-fold decreased odds of RRMS occurrence.

Conclusion: The genetic variations rs12696304 and rs35073794 in TERC are associated with the development of relapsing-remitting multiple sclerosis.

P42

A Neurochemical Perspective on Gamma-Frequency ASSRs

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Gamma-range (30-80 Hz) auditory steady-state responses (ASSRs) are vital for studying sensory and cognitive processes and have broad applications in neuropsychiatric research. However, the neurochemical nature of ASSRs is not fully understood. We performed a systematic review aiming at generalisation of known involvement of different neurotransmitter systems into ASSR generation. We focused on nine neurochemical systems: glutamatergic, GABAergic, dopaminergic, serotonergic, cholinergic, opioidergic, cannabinoidergic, adrenergic, and mixed systems. The review resulted into inclusion of 77 articles. Of these, 61 focused on distinguishable systems, while 16 examined multiple systems. A major finding across systems was the essential balance of excitatory and inhibitory neurotransmission for stable gamma synchronisation. It was mainly mediated by glutamatergic and GABAergic systems, where NMDA antagonists (e.g., ketamine or MK-801) reduced phase-locking and coherence, underscoring the role of glutamate in excitation. Conversely, GABAergic modulation via GABA-A receptors enhanced coherence and amplitude, highlighting fast-spiking interneurons' importance for oscillatory stability. Distinct receptor effects emerged in other systems. Dopaminergic modulation, especially via D1 receptors, typically increased gamma coherence with agonists, substantiating the links to cognitive functions. Serotonergic modulation via 5-HT2A agonists or reuptake inhibitors generally reduced evoked power and synchronisation, suggesting inhibitory effects on gamma response. The cholinergic system, through muscarinic receptors, enhances gamma synchronization, supporting attentional processes. Opioidergic and cannabinoidergic modulation activity reduces gamma amplitude and coherence, aligning with their sedative effects. Mixed-system studies, such as those involving antipsychotics that target dopamine and serotonin, showed complex interactions that underscore the interdependence of these systems. This review highlights the roles of neurotransmitter systems in gamma modulation, emphasizing the importance of balanced excitatory-inhibitory control, receptor specificity, and multi-system interactions. Enhanced understanding and targeted modulation of these pathways may offer promising strategies to correct gamma oscillation disruptions commonly seen in neuropsychiatric disorders, potentially leading to improved therapeutic outcomes.

P43

Application of Microfluidic Technology to α-Synuclein Liquid-Liquid Phase Separation Study

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α-Synuclein (α-Syn) is an intrinsically disordered protein implicated in the pathogenesis of neurodegenerative diseases such as Parkinson's disease, dementia with Lewy bodies, and multiple system atrophy. α-Syn aggregates into amyloid fibrils, a major component of Lewy bodies, which is a marker for neuronal degeneration [1]. α-Syn aggregation can be initiated through the biophysical process of liquid-liquid phase separation (LLPS) – the phenomenon of membraneless organelles formation [2]. Imitating intracellular environment requires precise control, therefore, our goal is to apply microfluidic technology for an in-depth LLPS study of α-Syn aggregation. For this study α-Syn with four fluorescent protein tags – eGFP, mCherry, mOrange, mCerulean – was constructed and purified. Initially, we observed the aggregation through LLPS of each fluorescently labeled protein with wild type α-Syn using fluorescence microscopy (FP). Then, we applied microfluidic technology that enables the study of rapidly generated subnanoliter volume droplets within microchannel systems [3]. We examined droplet formation of α-Syn suspended in a buffer solution as well as with the molecular crowder polyethylene glycol (PEG), followed by analysis of the droplets through FP. Our findings demonstrate that droplets of α-Syn with PEG, formed through microfluidic technology, create amyloid fibrils on the droplet surface, whereas α-Syn without PEG did not aggregate. Optimizing the application of microfluidic technology for α-Syn aggregation studies remains our future challenge.

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P44

Evaluation of Catalase Enzymatic Activity and Distribution of Some Trace Elements in Blood of Patients with Glioblastoma

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Glioblastoma (GBM) is the most malignant brain tumor, and its resistance to radiation and chemotherapy has been attributed to a variety of mechanisms, including radio resistance, glioma stem cells, enhanced DNA repair mechanisms, and altered antioxidant enzyme expression. This resistance results in poor patient survival. Catalase (CAT) is an enzyme localized predominantly in peroxisomes and protected against oxidative stress by preventing the accumulation of H2O2. Meanwhile, elevated expression levels of CAT have been reported in cancer tissues compared to normal counterparts. In gliomas, catalase appears to be constitutively overexpressed compared with astrocytes. Nevertheless, the molecular mechanism regulating the expression of CAT in GBM has not been fully elucidated. Metal homeostasis is critical for the proper functioning of the brain, which is a target organ for toxic environmental pollutants. The balance of metals within the brain is regulated through the blood-brain barrier (BBB) and blood-cerebrospinal fluid barrier. Based on metals' abilities to pass through the BBB, it was hypothesized that prolonged exposure to metals could increase the risk of brain cancers, although no association between metal exposure and brain cancer was found. Aim of this study was to evaluate the dynamics of changes in catalase activity in erythrocytes, as well as the concentration of trace elements in the blood. The essay material is the blood of patients diagnosed with glioblastoma. Catalase activity was determined based on the formation of an ammonium molybdate complex with non-decomposed hydrogen peroxide. The concentration of the compound was estimated spectrophotometrically at a wavelength of 410 nm. Concentrations of trace elements were determined using inductively coupled plasma mass spectrometry.

P45

The Effects of st. John's Wort and its Main Component Hyperoside on Catalase Activity in Mouse Brain

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St. John's wort, botanically known as Hypericum perforatum L., is a widespread medicinal herb widely used in Lithuania and around the world. The aerial parts of the plant are rich in antioxidants such as flavonoids, carotene, and vitamin C. Although the plant is well known for its anti-inflammatory, antidepressant, antimicrobial, antiviral, and antioxidant effects, research has been conducted on its ability to reduce oxidative stress. are scarce in the brain. Hyperoside is one of the active components commonly found in H. perforatum L. It is associated with many biological activities that affect the physiological processes of the body. Hyperoside is known to have antioxidant, anti-inflammatory and neuroprotective effects. Due to its antioxidant properties, hyperoside is believed to reduce oxidative stress. Catalase (CAT) is a common enzyme found in almost all living organisms exposed to oxygen. It catalyzes the decomposition of hydrogen peroxide into water and oxygen. It is a very important enzyme that protects the cell from oxidative damage caused by reactive oxygen species. This study aimed to elucidate the potential protective effect of Hypericum perforatum L. and its main component hyperoside in reducing aluminum toxicity on CAT activity in mouse brain. Experiments were performed with BALB/c laboratory mice. CAT activity in brain homogenates was determined spectrophotometrically. Results are expressed as mean ± SEM. The results showed that Al reduces CAT activity in the brain of mice by 69% compared to the control. The effects of St. John's wort extract and its main component hyperoside solution on enzyme activity were similar: 75 and 45% reduction were found, respectively, compared to the control. The administration of St. John's wort extract to aluminum-treated mice group did not restore CAT activity to control level. Meanwhile, the administration of chemically pure hyperoside solution to aluminum-treated mice group restored CAT activity to control level. Thus, the extract of Hypericum perforatum L. and the solution of its main component hyperoside can reduce CAT activity in the brain of mice as well as aluminum. However, only the hyperoside solution could restore CAT activity in the brains of aluminum-treated mice to control level.

P46

Genetic Insights into Optic Neuritis: The Role of TAS2R16 Polymorphisms

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Introduction: Optic neuritis (ON) is one of the most common neuro-ophthalmological causes of vision loss worldwide [1]. It is often triggered by inflammation and demyelination of the optic nerve [2]. ON is recognized as a multifactorial condition, influenced by factors such as autoimmune susceptibility, environmental triggers and genetic predisposition [3]. ON mostly affects individuals between 18 – 45 years, with a higher prevalence in young women [4]. The TAS2R family of bitter taste receptors, widely expressed in various tissues, has been linked to immune and inflammatory processes [5]. Given the potential link to the pathological mechanism, we analyzed the impact of TAS2R16 on patients with ON.

Aim: To investigate the associations between TAS2R16 rs860170, rs978739, rs1357949 gene polymorphisms and the occurrence of ON, considering the gender and age of the participants.

Materials and methods: Study included 82 patients with ON and 160 healthy controls subjects. DNA was extracted from peripheral blood leukocytes using DNA salting-out method. Genotyping was carried out using real-time polymerase chain reaction (RT-PCR) method. Statistical data analysis was performed using "IBM SPSS Statistics 29.0".

Results: We found no statistically significant differences in TAS2R16 SNP genotype or allele frequencies related to ON. Binary logistic regression also showed no significant differences between groups, including analyses by gender and age.

Conclusion: This study did not find any associations between TAS2R16 rs860170, rs978739, rs1357949 and optic neuritis development in Lithuanian population.

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P47

Comparative Analysis of Antioxidant Status in Mice Brain and Liver Following Organic and Inorganic Selenium Supplementation

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Introduction: Se, an essential trace element with strong antioxidant properties, is critical for cellular health, primarily as a component of enzymes like glutathione peroxidase that protect against oxidative damage by neutralizing reactive oxygen species. Recent research has increasingly focused on the unique effects of Se compounds - particularly the differences between organic and inorganic forms on antioxidant status and overall health. Organic Se such as selenomethionine (SeMet), typically obtained from diet, and inorganic Se such as sodium selenite (Na_2SeO_3), often used in supplements, vary significantly in bioavailability and metabolic pathways, which may influence their impact on cellular antioxidant status. The aim of this study was to evaluate and compare the effects of Na_2SeO_3 and L-SeMet on the antioxidant status in different tissues of laboratory mice. Oxidative status was assessed by measuring levels of reduced glutathione (GSH), metallothioneins (MT), and malondialdehyde (MDA).

Methods: The mice were randomly assigned to one of three groups: two Se treatment groups and a control group (with 7 mice per group). The treatment groups received water supplemented with either Na_2SeO_3 or L-SeMet, while the control group received plain tap water. The Se treatment lasted 8 weeks. Antioxidant markers – GSH, MT, and lipid peroxidation marker MDA were measured spectrophotometrically.

Results: Our study found that treatment with Na_2SeO_3 significantly decreased blood GSH levels by 23.7% ($p < 0.05$). Both Na_2SeO_3 and SeMet treatments led to significant increases in blood MDA levels, by 35.87% and 22.3%, respectively ($p < 0.05$). In the liver, MDA concentrations were even more elevated, with Na_2SeO_3 and SeMet treatments increasing MDA respectively by 100.89% and 62.67% over the control level ($p < 0.05$). Additionally, MT levels in the liver of SeMet-treated mice were significantly reduced by 54.06% relative to controls ($p < 0.05$). In the brain, MT levels were 27.54% higher in the Na_2SeO_3 group than in the SeMet group, maybe highlighting tissue-specific responses to different Se forms.

Conclusions: Our study shows that Na_2SeO_3 induces higher oxidative stress, particularly in the liver, indicating weakened antioxidant defense. While SeMet also elevated oxidative stress markers, its impact was notably less severe. These findings underscore the importance of Se form selection in minimizing oxidative damage and potential toxicity.

P48

Accumulation of Immunomodulatory Metabolites in Microglia in Response of Pro-Inflammatory Stimuli

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Background: Activation of microglia by pattern recognition receptor (PRR) stimulation leads to neuroinflammation [1,2]. Activated, pro-inflammatory microglia significantly contribute to neuronal death during neurodegenerative disorders, such as Alzheimer's and Parkinson's, and are hypothesized to participate in the development of these diseases. It has been shown that tricarboxylic acid (TCA)-derived intermediates succinate and itaconate accumulate in LPS-stimulated microglial cells [3-5], however little is known about the effect of other TLR ligands on the accumulation of these metabolites. Succinate and itaconate have received attention for their immunomodulatory properties, however recently a compound structurally related to itaconate and succinate - citraconate has been shown to exhibit immunomodulatory properties [5]. Little is known about the production and role of citraconate. Delving into immunomodulatory metabolites in microglia may provide novel therapeutic approaches to mitigate the deleterious effects of abnormal inflammatory microglia and regulate excessive inflammation in brain diseases.

Methods: We investigated the accumulation of succinate, itaconate, and citraconate in murine microglia (BV-2 cell line) stimulated by various TLR ligands. BV-2 cells were incubated with either LPS, Loxoribine (LOX) or poly(I:C) (PIC) for 24 h. In addition, to test the effect of citraconate, we incubated BV-2 cells with LPS and citraconate. Intracellular metabolites were extracted with 80% methanol and quantified by derivatization with 3-nitrophenylhydrazine and analysis by LC-MS (Agilent 1100 HPLC/Agilent 6510 QTOF MS).

Results: LPS and LOX-stimulated microglia showed an increase in the production of itaconate, but PIC had no such effect. Significant accumulation of succinate was not observed in either group. Small amounts of citracone were also detected in the LPS and LOX groups. Exogenously added citraconate suppressed itaconate synthesis.

Conclusion: Stimulation of different TLRs results in different metabolic responses in BV-2 cells.

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MIR-221-3P, MIR-30C-2-3P, MIR-543-3P Expression in Parkinson's Disease

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Parkinson's disease (PD) is the second most common neurodegenerative disease in the world. The main reason that this disease develops is the death of dopaminergic neurons. Parkinson's main symptoms are bradykinesia, tremor, rigidity. Although there is quite a lot of information about this disease, there is still neither cure nor diagnostic tool to manage it. Now, many researchers study miRNA (microRNA) interference in biological processes that also includes their role in neurodegenerative diseases. MiRNA molecules derived from extracellular vesicles (EV) are expected to become biomarkers that could help to identify diseases as early as possible, determine their progression, severity. Also, EV-derived miRNA should help to pick the most effective treatment based on their individual profile. The aim of this study was to measure the expression of EV miR-221-3p, miR-30c-2-3p, and miR-543-3p in the serum of PD patients and to investigate their association with patient data. Extracellular vesicle (EV) miRNAs were isolated from blood serum and transcribed into cDNA, with their expression measured using RT-PCR. Statistical analyses were conducted using GraphPad Software Inc. Prism 8. The miRNA profiles were evaluated based on age, sex, disease onset, duration, symptom severity, and the chosen treatment method for 109 individuals with Parkinson's disease. Among the participants, 20 do not have PD, 37 received medication, 39 underwent deep brain stimulation and 13 were treated with gamma knife surgery. The results indicated that patients exhibited varying levels of miRNA expression when comparing the medication group to the surgical treatment groups, but no significance in results. MiR-221-3p and miR-30C-2-3P expression in patient, that had bradykinesia, or tremor symptoms, was lower than control group. MiR-543-3p expression increased as bradykinesia symptoms were more severe, with other miRNA molecules results were not significant. Age, disease duration, disease onset and gender did not show significant influence in miRNA levels. Furthermore, miR-543-3p expression decreased when patients were treated with gamma knife surgery. The expression of miRNA molecules did not change significantly after deep brain stimulation. In conclusion, miRNA molecules show potential as biomarkers for Parkinson's disease. However, more research is needed to estimate significance of miRNA molecules potential as biomarkers before suggesting them to clinical trials.

P50

Effect of Metformin on Spontaneous Calcium Signaling in Cultured Astrocytes during Normoxic and Hypoxic Conditions

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Astrocyte function is controlled by intracellular Ca2+ signaling. On the other hand, hypoxia influences calcium dynamics and its homeostatic range because of reduction of ATP synthesis, which inhibits ATP dependent processes. By using Ca2+ sensitive fluorescence dye, we studied how metformin changed spontaneous oscillating Ca2+ signals in soma of astrocytes from 5–7-day-old rats grown under normoxic and mild-hypoxic (2% O2) conditions. Mild hypoxic conditions applied for 24 h did not change astrocyte viability; however, it reduced the relative amplitude of Ca2+ signals, slowed the decay of the signals, and increased the period of spontaneous oscillations. Lower concentrations of metformin, 0,25 or 0,5 mM, applied before hypoxia reduced this detrimental influence by partially restoring the amplitude, fastening the decay, and reducing the period of Ca2+ signaling. In contrast, higher concentration, 1mM, of metformin exaggerated the effects of hypoxia by reducing signals, slowing their decay and prolonged the period between signals. Unexpectedly, in astrocytes grown under normoxic conditions all concentrations of metformin after several hours of application had detrimental effects for Ca2+ signaling. Low concentration of metformin under mild hypoxic conditions helps to rescue the functioning of astrocytes by conditioning the cells to prolonged hypoxic influence.

P51

The Influence of a High-Fat Diet on Maternal Olfactory Function and Its Consequences for Offspring Care and Neurodevelopment in Mice Model

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Aims: Modern diet has high-fat content causing increased obesity rates and metabolic status changes in human population worldwide, including women of reproductive age. Evidence suggests that a maternal high-fat diet (mHFD) may increase the risk of neurodevelopmental disorders in offspring. A mHFD causes gut microbial dysbiosis contributing to increased inflammatory milieu during pregnancy and lactation, thus disturbing both prenatal and postnatal neurodevelopment of the offspring. Additionally, high-fat diet may impair maternal olfactory function, potentially affecting maternal behaviors crucial for offspring development. This study aimed to investigate how a high-fat diet affects maternal olfactory sensitivity, leading to decreased offspring survival and altered neurodevelopment.

Methods: Female C57Bl/6J mice were divided into two dietary groups: one group received a control diet (CD) with 10% fat, and the other received a high-fat diet (HFD) with 60% fat, starting from weaning and continuing through lactation. To evaluate the metabolic effects of the HFD on the dams, we measured their body mass and conducted glucose and insulin tolerance tests. Prior to mating, we tested how the HFD affected the dams' olfactory sensitivity to various odor types, including non-social scents, social cues, and chemical compounds emitted by mouse pups. After the birth of offspring, we monitored the survival rate of pups from birth until weaning. Offspring were then weaned onto a normal diet, and we assessed their neurodevelopment through several behavioral tests, including ultrasonic vocalization recording, three-chamber sociability, reciprocal social interaction, open field, marble burying, novel object recognition, and Barnes maze tests.

Results: We determined that dams consuming HFD had metabolic dysfunction and showed reduced olfactory sensitivity to all tested odor types. Offspring of HFD dams had a lower survival rate until weaning. Furthermore, HFD in dams was associated with impaired neurodevelopment in offspring, including reduced sociability, increased repetitive behaviors, and locomotor activity.

Conclusions: Our findings suggest that HFD consumption in dams reduces olfactory sensitivity, which may contribute to impaired maternal care, resulting in lower offspring survival rates and neurodevelopmental abnormalities.

P52

MicroRNA Expression Analysis in the Blood of Multiple Sclerosis Patients Using Heat-Map Analysis

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Background: Multiple sclerosis (MS) is a chronic autoimmune inflammatory disease that affects the central nervous system, primarily characterized by demyelination, which disrupts neuronal function. Remyelination, the process of forming a new myelin sheath around axons, is crucial for MS patients as it helps restore neurological function. MicroRNA (miRNA) molecules, known for their role in regulating gene expression, are believed to play an important role in remyelination. The small, non-coding miR-219 and miR-338 are known to promote oligodendrocyte differentiation by inhibiting negative regulators. These miRNAs have also been shown to work in concert during myelination and myelin sheath repair. The aim of this study was to perform a heat-map analysis to compare the expression of miR-219a-5p and miR-338-5p between MS patients and controls.

Methods: Blood samples were collected into special Tempus blood tubes. RNA was isolated from blood using mirVana™ miRNA Isolation Kit (ThermoFisher Scientific (TFS), USA) and the cDNR synthesis was performed using the TaqMan® Advanced miRNA cDNA Synthesis Kit (TFS, USA). MiRNA expression was detected by using qRT-PCR method and the results were analyzed with ThermoFisher Cloud platform. Data visualization was performed using heat-map method. The significance of the results was assessed using SPSS Statistics 29.0.2.0.

Results: In this study, miRNA expression in blood samples was analyzed for 20 MS patients and 43 controls. The heat-map analysis revealed that miR-338-5p expression was lower in the patient group.

Conclusion: Heat-map analysis offers a comprehensive view of the miRNA expression profiles in MS patients compared to the control group, facilitating the identification of miRNAs as potential diagnostic markers.

P53

Epigenetic Factors Modulate the Effects of Transcranial Magnetic Stimulation: An Investigation at Clinical and Cellular Levels

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Addressing treatment-resistant depression (TRD) presents significant challenges. Although transcranial magnetic stimulation (TMS) is a common therapeutic approach, its effectiveness remains inconsistent, highlighting the importance of better understanding both the underlying mechanisms of depression and the action of TMS. In an earlier study [1], we found that TRD patients had notably elevated levels of the pro-inflammatory interleukins-6 and -8 compared to those responding to medication, with these higher levels associated with more severe symptoms. Additionally, TRD patients showed increased interleukin-18 levels and reduced levels of the anti-inflammatory miR-146a-5p relative to healthy individuals. We also observed that miR-16-5p, miR-93-5p, and especially miR-146a-5p levels were linked to clinical improvements after TMS therapy. These findings indicate a heightened inflammatory state in TRD patients and suggest that miR-146a-5p could serve as a potential biomarker for predicting TMS treatment outcomes. Our study further explored the molecular effects of TMS using the SH-SY5Y neural cell model, with miR-146a-5p activity altered by miRNA mimics and inhibitors. Cells treated with either the miR-146a-5p mimic or inhibitor were subsequently stimulated with two TMS protocols: intermittent (iTBS) or continuous Theta Burst Stimulation (cTBS). Using the Agilent Seahorse Mito Stress assay to assess mitochondrial function, we found that in miR-146a-5p mimic-treated cells, iTBS enhanced mitochondrial function while cTBS reduced it, whereas neither TMS protocol significantly affected cells treated with the inhibitor. mRNA-seq analysis revealed that, with miR-146a-5p upregulation, cTBS increased the expression of genes coding for neuroactive ligands and receptors, while iTBS in either context reduced expression of genes tied to inflammatory pathways, such as IL-6 signaling. In summary, our findings suggest that miR-146a-5p plays a role in shaping inflammatory and mitochondrial responses to TMS, pointing to its potential as both a biomarker and a target for enhancing TMS effectiveness in TRD therapy.

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P54

The Effect of Licorice (Glycyrrhizae glabrae L.) Extract on Glutathione and Malondialdehyde Concentrations in Mice Brain

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Background: Glycyrrhiza glabra L., a plant from the Fabaceae family, is widely used in traditional medicine. This plant is a source of secondary metabolites and various plant compounds including triterpenoids, flavonoids, isoflavonoids and chalcones, which are responsible for many biological activities [1]. The powerful antioxidant activity is probably due to the phenolic content. The compounds mainly responsible for this activity are reported to be isoflavones such as glabridin, hispaglabridin A and 30-hydroxy-4-O-methylglabridin [2].

Aim: The following study was aimed to evaluate the possible antioxidant effect of Glycyrrhizae glabrae L. extract on glutathione (GSH) and malondialdehyde (MDA) concentrations in the BALB/c laboratory mice brains after aluminium exposure.

Results: The results showed that aluminium reduced brain GSH concentrations by 10.48% and increased MDA concentrations by 4.73% compared to the control group of mice. Glycyrrhiza glabra L. extract decreased the brain MDA concentration by 18.16% compared to the control group but increased the GSH concentration by 15.24%. The results showed that Glycyrrhiza glabra L. extract after AlCl3 exposure statistically significant decreased MDA concentration by 42.13% and increased GSH concentration by 55.24% compared to the control group. The Glycyrrhizina glabra L. extract group showed a statistically significant decrease in MDA concentration of 48.95% and increase in GSH concentration of 28.72%. The results also showed that Glycyrrhiza glabra L. extract after AlCl3 exposure statistically significant decrease concentration of MDA by 44.74% and increase concentration of GSH by 73.40% compared to aluminium-treated group.

Conclusion: Administration of Glycyrrhiza glabra L. extract resulted in a statistically significant increase in GSH concentrations and decrease in MDA levels in the brain of mice after aluminium exposure. It can be suggested that Glycyrrhiza glabra L. extract may affect as antioxidant in vivo.

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P55

Multiple Sclerosis: Exploring EXOC3L1 rs868213 Associations Among Older Age Groups in Lithuanian Population

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Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative, inflammatory autoimmune disease of the central nervous system [1], influenced by a combination of genetic and environmental factors, with age as a key contributor [2,3]. It was revealed that EXOC3L1 is correlated with various immune cells, suggesting that genetic variations may affect the expression of EXOC3L1, potentially leading to changes in immune-related pathways involved in the development of multiple sclerosis.

Objectives/aims: The aim of this study was to determine the association between EXOC3L1 rs868213 and MS among patients over 40 years old. Methods: Study enrolled 250 patients with MS, and 250 healthy controls. DNA was extracted from peripheral blood leukocytes using DNA salting-out method. Genotyping was carried out using real-time polymerase chain reaction (RT-PCR) method. Statistical analysis was performed with „SPSS version 29.0".

Results: The study found statistically significant differences in the occurrence of genotypes and alleles for EXOC3L1 rs868213 and MS among patients over 40 years old ($p = 0.004$, and $p = 0.016$, respectively). Also, the binary logistic regression analysis demonstrated that the rs868213 AG genotype is associated with a 3.4-fold (OR = 3.412; CI: 1.571 – 7.413; $p = 0.002$), under the codominant genetic model. Moreover, AG genotype is associated with a 3.5-fold increased odds of MS occurrence (OR = 3.463; CI: 1.595 – 7.517; $p = 0.002$) under the overdominant model. Also, AG+GG genotypes are associated with a 2.7-fold (OR = 2.722; CI: 1.334 – 5.553; $p = 0.006$), under the dominant genetic model. Each G allele is associated with a 2-fold (OR = 1.972; CI: 1.058 – 3.675; $p = 0.032$), under the additive genetic model.

Conclusion: Our study reveals associations between EXOC3L1 rs868213 and the occurrence of MS among older participants.

P56

Study of the Mechanism of Action of Propranolol in Situational Anxiety

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Propranolol (PRO, ATC code: C07AA05) is an extensively studied and widely described substance used in the treatment of cardiovascular disease, and belongs to the group of non-selective β-blockers. Due to its ability to pass the blood-brain barrier and its affinity for a number of macromolecules (not just adrenoreceptors!), PRO has found use in a variety of therapies beyond the cardiovascular field. In 1987, the EMA approved PRO for the treatment of anxiety symptoms, including generalized anxiety disorder and situational anxiety. However, the detailed information on PRO's mechanism of action on the central nervous system (CNS) is inconclusive. Previous studies described in the literature confirm the effect of PRO on the reduction of somatic symptoms associated with an anxiety. However, the evidence for improving cognitive and emotional impairment by blocking monoamine and GABA reuptake in the CNS is lacking. The goal of this project is to analyze the interactions of PRO with selected monoamine and GABA transporters using in silico methods. The in silico analysis of the stability of R/S-PRO complexes with monoamine neurotransporters such as hNET, hDAT, hSER, and GABA-energic hGAT1 was performed. Validation of the in-silico experiments was performed using the Open Field Test and Elevated Plus Maze in-vivo assays. The in silico studies indicate that the stability of PRO complexes with the tested transporters decreases in the series hNET > hDAT > hSERT. A comparison of the stability of R/S-PRO enantiomers indicates that more stable complexes are formed by the R-PRO stereoisomer. These results indicate a reuptake blockade of the corresponding neurotransmitters at the synapse. The biological effect is to reduce not only somatic symptoms but also psychological anxiety symptoms. The in vivo validation tests performed in the study support this hypothesis, confirming that high doses of PRO cause the strongest anxiolytic, sedative effects and reduction of motor anxiety in animals.

P57

Droplet Formation by Pro-Inflammatory S100A9 and Neurodegenerative Disease-Related Alpha-Synuclein During Liquid-Liquid Phase Separation

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Liquid-liquid phase separation (LLPS) of proteins and nucleic acids is a rapidly emerging field of study, aimed at understanding the process of biomolecular condensate formation and its role in cellular functions. LLPS has been shown to be responsible for the generation of promyelocytic leukemia protein bodies (involved in genome stability and programmed cell death), stress granules (modulation of stress response), and intrinsically disordered protein condensates (onset of neurodegenerative disorders). Recently, it has been discovered that different neurodegenerative disease-related proteins, such as alpha-synuclein (related to Parkinson's disease) and amyloid-beta (Alzheimer's disease) are capable of forming heterotypic droplets. Other reports have also shown non-LLPS cross-interactions between various amyloidogenic proteins and the resulting influence on their amyloid fibril formation. This includes the new discovery of pro-inflammatory S100A9 affecting the aggregation of both amyloid-beta, as well as alpha-synuclein. Combined, these observations suggest that protein interactions during LLPS and heterotypic droplet formation may be a critical step in the onset of neurodegenerative diseases. In this study, we explore the formation of heterotypic droplets by S100A9 and alpha-synuclein using a range of different spectroscopic and microscopic techniques. We show that the protein mixture is capable of assembling into both homotypic, as well as heterotypic condensates and that this cross-interaction alters the aggregation mechanism of alpha-synuclein. In addition, it also stabilises a specific fibril conformation, which has a higher propensity for self-replication. These results provide insight into the influence of S100A9 on the process of neurodegenerative disease-related protein LLPS and aggregation, bringing us one step closer to developing a potential cure or treatment modality.

P58

Betanin Can Partly Ameliorate Behavioral Disturbances Caused by the Administration of the Neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine

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Betanin is a natural component of red beet and opuntia fruit, known for its antioxidant, antibacterial, antiviral, and anticancer properties. This experiment aimed to examine the effect of betanin on cognitive functions, motor skills, and neurotransmission in a rodent model of Parkinson's disease induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Intraperitoneal injection of MPTP leads to the formation of the toxic metabolite MPP+ through the action of MAO-B, resulting in striatal dopamine depletion and neurodegeneration, which produces symptoms mimicking Parkinson's disease. In this study, movement and coordination (Footprint test, Rota Rod), exploration and anxiety (Elevated Plus Maze, Open Field), and spatial learning and memory (Water Maze test) were assessed after long-term betanin administration at doses of 50 or 100 mg/kg b.w./day in drinking water. The subjects were male C57BL/10/Clzd mice aged 18 months. Our findings confirm the beneficial effects of betanin on mouse behavior and a reduction in motor deficits induced by the neurotoxin, as demonstrated in the Rota Rod and Footprint tests. The group injected with MPTP exhibited an abnormal shortening of step length and shorter falling times in the Rota Rod test. Betanin reduced motor problems and anxiety in mice; however, it did not fully compensate the behavioral deficits caused by MPTP intoxication. Water Maze results confirm that betanin administration does not affect learning ability but at the lower dose reduces spatial memory disturbances caused by MPTP. The study demonstrated that betanin could improve both motor and cognitive functions in MPTP-intoxicated mice. The presented data expand our understanding of the previously unknown central action of betanin and its effects on cognitive processes, anxiety, and other psychomotor functions.

P59

Can Betanin Reverse the Neurotoxicity of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)?

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The aim of this study was to assess the impact of betanin on neurotransmission in an animal model of Parkinson's disease (PD). Male C57BL/10/Clzd mice received betanin in drinking water for a total of 55 days at doses of 50 or 100 mg/kg b.w./day. On the 26th day of betanin administration, some animals were intraperitoneally injected with MPTP to establish the PD model. To study the properties of betanin, structures of the central nervous system (CNS) were collected and subjected to biochemical analyses via High-Performance Liquid Chromatography to determine neurotransmitter levels in the hippocampus, prefrontal cortex, striatum, hypothalamus, cerebellum, medulla oblongata, and spinal cord. Biochemical data confirmed that betanin has a moderate effect on the dopamine (DA) loss induced by MPTP; however, it significantly alters DA metabolism and serotonin (5-HT) levels in various CNS structures. Betanin at a dose of 50 mg increased 5-HT levels in the striatum, prefrontal cortex, and hippocampus. Meanwhile, betanin at 100 mg/kg b.w. caused an increase in the level of 5-HIAA - the principal product of 5-HT degradation - in the prefrontal cortex, spinal cord, and cerebellum, reflecting the turnover and metabolism of 5-HT. The increase in the striatal 5-HT levels facilitates the release of DA from dopaminergic terminals in the substantia nigra. This effect may represent a compensatory mechanism related to the destruction of dopaminergic neurons and reduced DA release. Assessing the potential neuroprotective effect of betanin is crucial due to the lack of effective pharmacotherapy for neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, and post-stroke conditions. Therefore, the possibility of influencing these conditions with endogenous betaine represents a promising direction for further research.

P60

Decoding Neural Stem Cell Dormancy: the Role of Cellular Projections and Signalling Pathways

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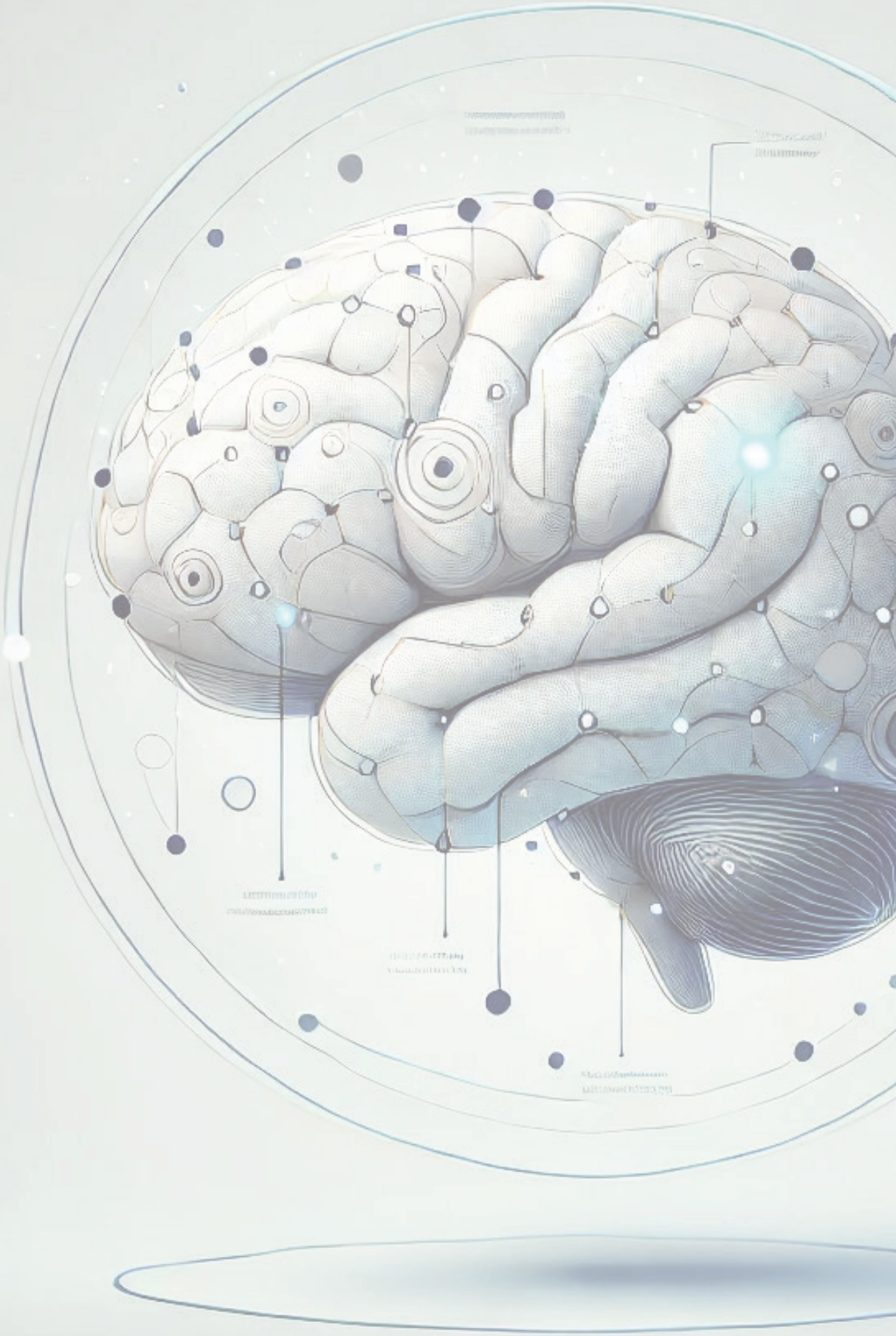
Neural stem cells (NSCs) are essential for their ability to produce new neurons during neurogenesis. These cells undergo dormancy (quiescence), the state when quiescent cells are metabolically active but do not produce new neurons. Understanding and manipulating this critical state is essential due to undiscovered applications in regenerative biology and precision medicine, which lead to better outcomes in neurodegenerative diseases and cancers Our research examined how cellular projections, a distinct feature of quiescence, influence its induction and reactivation, revealing that these projections help guide neuron generation orientation. Additionally, experiments on neuronal signaling demonstrated that manipulating GABAergic and dopaminergic pathways impacts NSC quiescence and reactivation, suggesting a promising strategy for advancing therapies in neurodegenerative and cancer treatment.



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