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Neuronus 2024

NENCKI INSTITUTE OF EXPERIMENTAL BIOLOGY, WARSAW, POLAND

NEURONUS 2024
NEUROSCIENCE FORUM

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PROGRAMME

24TH APRIL 2024
INSTITUTE OF PSYCHOLOGY OF JAGIELLONIAN UNIVERSITY

8:30–12:20 **Workshop I – Room 0.03**
Neuropixels by Cagatay Aydin
KU Leuven, Belgium

12:00–18:00 **Workshop II – Room 1.09**
QuPath by Ewelina Bartoszek
University of Basel, Switzerland

8:30–18:00 **Workshop III – Room 1.02**
DeepLabCut by Konrad Danielewski
Nencki Institute of Experimental Biology, Warsaw, Poland

9:00–13:00 **Workshop IV – Room 1.07**
NeuroImaging Data Analysis by Jakub Szewczyk and Mikołaj Compa
Institute of Psychology at the Jagiellonian University in Krakow, Poland

13:00–16:00 **Workshop V – Room 0.03**
Virtual reality, physiology and biofeedback by Slav Dimov
European Sales Executive bei BIOPAC Systems, Inc.

SCIENCE JAM – PIWNICA POD BARANAMI

19:00–20:00 **Career Development by Ali Jawaid[1] and Michał Ślęzak[2]**
[1] *Nencki Institute of Experimental Biology, Warsaw, Poland*
[2] *Łukasiewicz–PORT, Wroclaw, Poland*

20:15–21:15 **Scientific communication by Joanna Podgórska[1] and Ilona Kotlewska[2]**
[1] *SWPS*
[2] *Institute of Psychology, Jagiellonian University*

25TH APRIL 2024
AUDITORIUM MAXIMUM, JAGIELLONIAN UNIVERSITY

9:00–10:10 **Official Opening and Opening Lecture – Large hall A**
Karolina Warzecha (Head of Neuronus 2024)
Letter of Rector of the Jagiellonian University Prof. dr hab. Jacek Popiel
Translating computational mechanisms to clinical applications
Speaker: Quentin Huys (Max Planck & UCL, UK)

10:10–10:45 **Flashtalks – Large hall A**

10:45–11:15 **Coffee Break**

11:15–12:45 **Symposia Session I – Large hall A**
Towards Precision Psychiatry
Speakers: Juan P. Lopez, Charlotta Henningson, Magdalena Ziemiańska, Anna Guguła

Symposia Session II – Large hall B
Integrating Spiking Neural Networks in Neurobiology and Computer Science
Speakers: Matej Mertik, Maciej Wielgosz, Kinga Przybylska, Szymon Mazurek, Joan Falco-Roget, Jan Argasiński

Symposia Session III – Medium hall B
Visual perception in cognitive psychology
Speakers: Piotr Buczkowicz, Ingrida Zelionkaitė, Katarzyna Jurewicz, Julia Papiernik

12:45–13:15 **Lunch**

13:15–14:30 **Poster Session I – Exhibition room**

14:30–15:30 **Keynote lecture – Large hall A**
Dynamic Algorithmic Networks of Visual Categorizations
Speaker: Philippe Schyns (University of Glasgow, Scotland)

15:30–17:00 **Symposia Session IV – Large hall A**
Visual perception in naturalistic environment
Speakers: Marius Peelen, Natalia Rutkowska, Michał Bola, Marek A. Pedziwiatr, Diana Kollenda

Symposia Session V – Large hall B
Bilateral Brain-Body Interactions
Speakers: Urte Neniskyte, Edyta Bulanda, Weronika Tomaszewska, Magdalena Gomolka, Ivan Arzhanov

Symposia Session VI – Medium hall B
Aging Retina
Speakers: Kai Kaarniranta, Michał Bogocz, Piotr Rodak, Anna Pacwa

17:00–17:30 **Coffee Break**

17:30–18:30 **Keynote lecture – Large hall A**
Non-canonical mechanisms underlying amygdala mediated memory representation
Speaker: Andrew Holmes (NIAAA, NIH, USA)

18:30 **Welcome Reception**

26TH APRIL 2024
AUDITORIUM MAXIMUM, JAGIELLONIAN UNIVERSITY

8:00–9:00 **NeuroFitness**
Speaker: Anna Pałasz

9:00–10:00 **Keynote lecture – Large hall A**
Neural circuits underlying curiosity-driven exploration
Speaker: Sebastian Haesler (NERF, Belgium)

10:00–11:30 **Symposia Session VII – Large hall A**
Inhibitory control: Responses, errors, and their neural and psychophysiological correlates
Speakers: Bob Barry, Krzysztof Bielski, Patrycja Kałamała- Ligęza, Christina Thunberg

Symposia Session VIII – Large hall B
Molecular profiling of neurodegenerative disorders
Speakers: Jörg Hanrieder, Jack Wood, Alicja Szadziewska

Symposia Session IX – Medium hall B
Posttranslational Modifications in the Brain
Speakers: Thomas Klarić, Ugne Kuliesiute, Natalia Pudełko-Malik, Savani Anbalagan

11:30–12:00 **Coffee Break**

12:00–13:30 **Symposia Session X – Large hall A**
Molecular Mechanisms of Synaptic Plasticity
Speakers: Jakub Włodarczyk, Monika Puchalska, Anbarieh Saadat, Bogna Badyra

Symposia Session XI – Large hall B
Computational approaches to understand brain complexity
Speakers: Wiktor Młynarski, Katarzyna Sawicka, Emilia Kaczmarczyk, Magdalena Szponar

Symposia Session XII – Medium hall B
Psychedelics
Speakers: Paweł Orłowski, Anastasia Ruban, Maja Wójcik, Čestmír Vejmola, Adam Wojtas

13:30–14:00 **Lunch**

14:00–15:15 **Poster Session II – Exhibition hall**

15:15–17:00 **Symposia Session XIII – Large hall A**
Untangling neural circuits supporting specific behavior
Speakers: Bianca Silva, Anthony Kischel, Katarzyna Hryniewiecka, Aleksandra Nogaj, Jakub Mlost, Oskar Markkula

Symposia Session XIV – Large hall B
Face Perception and its application in audiovisual integration
Speakers: Maria Ida Gobbini, Ilona Kotlewska, Magdalena Szmytke, Maria Nalberczak-Skóra

Symposia Session XV – Medium hall B
Exploring New Drugs for Brain Therapy
Speakers: Sara Xapelli, Angelika Jagielska, Nicolas Singewald, Judith Schweimer

17:00–17:30 **Coffee Break**

17:30–18:30 **Keynote lecture – Large hall A**
Hyperalignment: modeling shared and individuating information embedded in idiosyncratic fine-scale cortical topographies
Speaker: James Haxby (Dartmouth College, USA)

21:00 **Neuronus Party**

27TH APRIL 2024
AUDITORIUM MAXIMUM, JAGIELLONIAN UNIVERSITY

9:00–10:00 **Keynote lecture – Large hall A**
From Molecular Codes to Behavioral Patterns: Deciphering Autism Spectrum Disorders
Speaker: Gaia Novarino (IST, Austria)

10:00–11:30 **Symposia Session XVI – Large hall A**
Automatization in behavioral studies – a key to objectivity
Speakers: Aleksandra Badura, Veronika Kovarova, Patrycja Ziuzia, Julia Świderska, Anjaly Yadav

Symposia Session XVII – Large hall B
Microglia in Health and Disease
Speakers: João Relvas, Izabela Lepiarz-Raba, Natalia Małek, Natalia Stelmach

Symposia Session XVIII – Medium hall B
EEG correlates of consciousness
Speakers: Marcin Koculak, Klaudia Krystecka, Urszula Górska-Klimowska, Anna Zofia Leśniewska

11:30–12:00 **Coffee Break**

12:00–13:30 **Symposia Session XIX – Large hall A**
Neuroendocrine Brain
Speakers: Michael Greenwood, Svenja Leibnitz, Julian Zacharjasz, Natalia Konopinska, Naveen Nedunchezhian

Symposia Session XX – Large hall B
OpenfUS
Speakers: Marcin Lewandowski, Alan Urban, Michiel Camps, Nora Fitzgerald, Klaudia Csikós, Tianzi Wang

Symposia Session XXI – Medium hall B
How to train the brain
Speakers: Alicja Olszewska, Aurimas Mockevičius, Syanah Wynn, Tomasz Ściepuro, Gabriela Rajtar

13:30–14:00 **Lunch**

14:00–15:15 **Poster Session III – Exhibition hall**

15:15–16:45 **Symposia Session XXII – Large hall A**
Neuroimaging of abnormal brain functions in schizophrenia
Speakers: Todd Woodward, Rafał Skiba, Wiktor Więcławski, Camilo Enrique Sánchez

Symposia Session XXIII – Large hall B
Cellular Mechanisms of Pain and Touch
Speakers: Mateusz Kucharczyk, Felipe Meira de-Faria, Basil Duvernoy

Symposia Session XXIV – Medium hall B
Reading brain in blind individuals
Speakers: Anna-Lena Stroh, Maksymilian Korczyk, Małgorzata Paczyńska, Maciej Gaca, Jacek Matuszewski, Cemal Koba

16:45–17:15 **Coffee Break**

17:15–18:15 **Keynote lecture – Large hall A**
Habitats and human physiology on multiple time scales
Speaker: Kathrina Wulff (Umeå University, Sweden)

18:15 **Awards & Closing Ceremony – Large hall A**

KEYNOTE SPEAKERS

TRANSLATING COMPUTATIONAL MECHANISMS TO CLINICAL APPLICATIONS

Quentin Huys

Max Planck UCL Centre for Computational Psychiatry and Ageing Research, United Kingdom

Emotions promote our well-being in survival-salient situations. They are triggered by biologically relevant signals such as threats and physical harm or rewards including food consumption or social interaction. Yet, also abstract and "simulated" pleasures and threats such as love stories, misfortunes, and tragedies shown in films can trigger powerful emotions in the viewers. In my talk I present an overview on brain mechanisms supporting human emotions and show how we can use cinema for simulating real life for studying the emotional brain. I present data from our laboratory showing how viewing emotions in films makes individuals to "tune in" with each other, and how specific neurotransmitter systems in the brain govern out vicarious experience of the emotions we see in movies. Finally, I discuss the origins of our captivation for strong, sometimes also distressing and unpleasant, emotional movies. I propose that we are drawn to affective cinema because it provides a safe simulation environment for preparing to meet actual emotional challenges in real life.

DYNAMIC ALGORITHMIC NETWORKS OF VISUAL CATEGORIZATIONS

Philippe G. Schyns

University of Glasgow, United Kingdom

In cognitive neuroscience, a pivotal remaining challenge is the translation of brain activity into comprehensible information processing. Though sophisticated tools measure brain activity with exceptional spatial and temporal resolution, across varying scales of observation, how do we interpret this activity as a process that computes information? To address this critical question, I will introduce a framework that leverages generative models of visual categories to enable interpretation of the information that brain networks represent and transmit, and the computations that underlie perception. Using this approach, we can extract meaningful insights into information processing from dynamic brain activity and its Deep Neural Network models, thereby pushing the frontiers of brain imaging and computational neuroscience.

NON-CANONICAL MECHANISMS UNDERLYING AMYGDALA MEDIATED MEMORY REPRESENTATION

Andrew Holmes

Laboratory of Behavioral and Genomic Neuroscience, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health

Brain systems mediating responses to previously encountered threats are critical to animals' survival. While learned threats have been shown to generate neural representations of fear state in the basolateral amygdala (BLA), the contribution of non-neuronal cells to this process remains unclear. Here, employing a combination of *in vivo* calcium (Ca^{2}+) imaging and chemogenetics, we demonstrate that BLA astrocytes track fear state and causally contribute to cued fear memory retrieval. Then, by performing *in vivo* cellular-resolution neuronal Ca^{2}+ imaging and electrophysiological recordings, we show dynamic astrocyte Ca^{2}+ activity enables fear-cue BLA neuronal encoding and supports fear state neural representation by enriching the amount of motivationally-relevant information contained in the neuronal population. Our findings reveal a key role for astrocytes in memory retrieval through amygdala neural representation of fear state, revising current neurocentric models of an essential survival function.

NEURAL CIRCUITS UNDERLYING CURIOSITY-DRIVEN EXPLORATION

Sebastian Haesler
Neuroelectronics Research Flanders, Department of Neuroscience, KU Leuven, Belgium

Curiosity refers to the intrinsic desire of humans and animals to explore the unknown even when there is no apparent reason to do so. The most fundamental form of curiosity may be found among orienting behaviors. Across animal species, novel or surprising stimuli elicit arousal and evoke sensory inspection and exploration. These orienting responses habituate after few exposures, suggesting a very rapid form of non-associative learning. At the level of neural circuits, orienting involves distinct processing steps including the evaluation of sensory stimuli to detect novelty and surprise, the activation of catecholaminergic systems and eventually the initiation of orienting reactions. In my lab, we investigate these processing steps using brain-wide functional ultrasound imaging, large-scale electrophysiology and cell-type specific manipulations in mice in order to understand how neural circuits transform sensory inputs into curious exploration behaviors.

HYPERALIGNMENT: MODELING SHARED AND INDIVIDUATING INFORMATION EMBEDDED IN IDIOSYNCRATIC FINE-SCALE CORTICAL TOPOGRAPHIES

James V. Haxby
Dartmouth College, USA

The neural representation of information that is shared across brains is encoded in fine-scale functional topographies that vary from brain to brain. Hyperalignment models this shared information in a common information space. Hyperalignment transformations project idiosyncratic individual topographies into the common model information space. These transformations contain topographic basis functions, affording estimates of how shared information in the common model space is instantiated in the idiosyncratic functional topographies of individual brains. This new model of the functional organization of cortex – as multiplexed, overlapping basis functions – captures the idiosyncratic conformations of both coarse-scale topographies, such as retinotopy and category-selectivity in the visual cortices, and fine-scale topographies. Hyperalignment also makes it possible to investigate how information that is encoded in fine-scale topographies differs across brains. These individual differences in cortical function were not accessible with previous methods.

FROM MOLECULAR CODES TO BEHAVIORAL PATTERNS: DECIPHERING AUTISM SPECTRUM DISORDERS

Gaia Novarino
Institute of Science and Technology, Austria

Recent advancements in the field of autism spectrum disorder (ASD) research have uncovered an array of genes associated with the risk of developing this complex condition, shedding light on crucial biological pathways. Despite this progress, critical questions remain unanswered, particularly regarding the mechanisms through which genetic mutations translate into ASD and the reasons behind the phenotypic similarity across different genetic forms of the disorder. Addressing these questions is not only pivotal for ASD understanding but can also unravel fundamental principles of brain function and development. In this presentation, I will introduce our integrative strategy that goes from single-cell sequencing to comprehensive functional studies, aiming to dissect a diverse array of ASD models. This approach is designed to reveal both convergences and divergences across various forms of autism, providing insights into the common and unique molecular pathways that underlie this spectrum of disorders.

HABITATS AND HUMAN PHYSIOLOGY ON MULTIPLE TIME SCALES

Katharina Wulff
Umeå University, Sweden

Time is crucial. It is one of those, often very dynamic or very complicated (or both), elements that ranges from action potentials to sleep span to be inherited in a myriad of biological processes, yet temporal relationships are easily missed. Everyone appreciates time being important when confronted with serious disasters or medical errors due to shortened sleep and we lament poor treatment response in which physiological timing was seemingly ignored. It is not unusual to employ unconventional techniques to try to recognize expressions in time patterns, because time demands a high level of precision and endurance to trace sequences such as bodily states. Time manifests at multiple scales in physiology – and at the interface with the environmental time. Environmental time itself differs with your position on Earth. For example daylight length conveys particular information on seasonal changes predictably from the equator to the poles. Physiology of all living organisms is preoccupied with natural light and time, increasingly also with man-made electrical light. When we consider the human habitats, we think of very contrasting places filled with different qualities of natural light, visible and thermal, and man-made illumination. In this illustrated presentation, particular examples of environmental, physiological and behavioral time series will be used for recognizing time expressions in human phenotypes. Data collected from adults and children living under different conditions will enrich our management of foreseeable health problems arising from universally imposed timetables. The interpretability of time patterns and the physiological adjustability makes time expressions a valuable method in the context of human adapted and maladapted behavior, calling attention to human habitats corresponding to biogeographic regions.

SYMPOSIA SESSION I – TOWARDS PRECISION PSYCHIATRY

25th April 2024 (Thursday), 11:15–12:45

Speaker: Juan Pablo Lopez (11:15–12:00)
Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

Chair: Jakub Mlost

Charlotta Henningson (12:00–12:15)
Magdalena Ziemiańska (12:15–12:30)
Anna Guguła (12:30–12:45)

INCREASING RESOLUTION IN STRESS NEUROBIOLOGY: FROM SINGLE CELLS TO COMPLEX SOCIAL BEHAVIORS

Juan Pablo Lopez
Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

Dr. Juan Pablo Lopez is an Assistant Professor in the Department of Neuroscience at Karolinska Institutet. He is interested in understanding the behavioral language, molecular mechanisms, and cellular circuits associated with stress-related psychiatric disorders and their treatments. His research program tackles psychiatrically relevant questions such as: Why, if exposed to the same trauma, does one individual develop psychiatric symptoms, whereas another does not? What are the critical periods of development where adversity becomes neurobiologically embedded? What are the molecular mechanisms underlying clinical improvement? What are the biological correlates of treatment response? To achieve these objectives, his laboratory implements a combination of state-of-the-art molecular, cellular, and computational neuroscience tools, which ultimately aims to bridge pre-clinical research and human psychiatry. During this talk, he will discuss new findings describing cell-type specific molecular mechanisms underlying the response to chronic stress, the sustained antidepressant effects of ketamine, as well as the implementation of automated behavioral tracking and analysis systems of complex behaviors for groups of mice.

THE EFFECT OF SSRIS ON THE SPATIO-MOLECULAR ORGANIZATION OF THE SEROTONIN SYSTEM

Charlotta Henningson*, Jakub Mlost, Iskra Pollak Dorocic
Pollak Dorocic Lab, Department of Biophysics and Biochemistry, Stockholm University, Stockholm, Sweden
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The serotonergic system has been implicated in the pathophysiology of both depression and anxiety and is the target of the most prescribed class of medications for these disorders, the selective serotonin reuptake inhibitors (SSRIs). Serotonergic neurons have historically been defined as a single population, but more recent work uncovered molecular diversity within the system. This opens new questions about the function and organization of these subgroups of serotonergic neurons and how they may be differently modulated by SSRIs. Using spatial transcriptomics, a novel RNA sequencing method that connects the gene expression to a position in the tissue based on location specific barcodes, we investigated the molecular organization of the mouse serotonin system in the major forebrain projecting serotonergic nuclei, the dorsal raphe (DR). We uncovered six molecularly distinct and anatomically segregated serotonergic subpopulations within the DR. Next, we explored gene expression changes within the nucleus after acute and chronic SSRI treatment. We found a large number of differentially expressed genes between the treatment categories, and identified specific and opposite changes in expression of two neuropeptides that are co-expressed in serotonergic neurons, thyrotropin-releasing hormone and prodynorphin. Both have previously been shown to play a role in the depressive state. Our data expands the knowledge on the serotonergic organization within the DR and identifies multiple differentially expressed genes and expression dynamics over the course of SSRI treatment, ultimately providing new insights into the molecular effects of SSRIs.

SPATIAL PROFILING OF TRANSCRIPTIONAL EFFECTS OF RISPERIDONE IN GENETIC MODEL OF SCHIZOPHRENIA

Magdalena Ziemiańska[1]*, Mateusz Zięba[2], Sławomir Gołda[2], Anna Radlicka-Borysewska[1], Łukasz Szumiec[1], Marcin Piechota[2], Michał Korostyński[2], Jan Rodriguez Parkitna[1]

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[2] Department of Molecular Neuropharmacology, Laboratory of Pharmacogenomics, Maj Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

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Despite the well-established use of psychotropic medications in psychiatry, the neurobiological basis underlying their therapeutic effects remains elusive. Drug-induced spatial gene expression profiling in the brain offers insight into the mechanisms of drug action. The transcriptional response patterns may expose the molecular mechanisms of long-term neuronal plasticity affected by the treatment. Here, we examined a spatially resolved transcriptomic profile of risperidone, an antipsychotic medication. This approach sheds new light on the drug-action therapeutic mechanism responsible for alleviating the symptoms of schizophrenia. The spatial transcriptomics signature recapitulates the patterns of gene expression consistent with neuroanatomy of the mouse brain. Subsequently, drug-induced transcriptional alterations were mapped on the brain sections. Region-specific changes in gene expression regulation were found in 95 genes ($p<0.01$, log2 ratio=0.8, minimum expression threshold=0.2). Further enrichment analysis of the risperidone-induced genes identified 18 genes enriched in schizophrenia, 8 of which were previously identified in genome-wide associated studies in humans e.g., Cacna1i, Cldn5. Further investigation is needed to understand how the antipsychotic drug action mechanism is linked to gene expression changes occurring in the course of schizophrenia.

Funding: This work was supported by the National Science Centre, Poland NCN OPUS UMO-2020/39/B/NZ7/01494.

MATERNAL SEPARATION IMPACTS THE MORPHOLOGY, ELECTROPHYSIOLOGY AND STRESS SENSITIVITY OF RAT NUCLEUS INCERTUS NEURONS

Anna Guguła[1]*, Patryk Sambak[1], Aleksandra Trenk[1], Sylwia Drabik[1], Aleksandra Nogaj[1], Zbigniew Sołtys[1], Andrew L. Gundlach[2], Anna Błasiak[1]

[1] Department of Neurophysiology and Chronobiology Institute of Zoology and Biomedical Research, Jagiellonian University, Krakow, Poland

[2] The Florey Institute of Neuroscience and Mental Health, and Florey Department of Neuroscience and Mental Health, The University of Melbourne, Parkville, Victoria, Australia

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Early-life stress (ELS) disrupts brain development, increasing susceptibility to stress-related disorders and compulsive behavior in adulthood. Expanding evidence links these disorders with the activity of the stress-sensitive brainstem nucleus incertus (NI), synthesising the neuropeptides relaxin-3 (RLN3) and cholecystokinin (CCK). Despite the known involvement of NI RLN3 neurons in stress responses and drug-seeking behavior, their vulnerability to developmental stress remains unexplored, and the knowledge about NI CCK neurons is sparse. Thus, this study investigated the impact of an established ELS model, maternal separation (MS), on NI neuronal populations. Control and MS-subjected adult male Sprague-Dawley rats underwent acute restraint stress and subsequent immunostaining of NI neurons, in situ hybridisation, or whole-cell patch-clamp recordings combined with dendritic tracing and morphological assessment of NI neurons. MS triggered multi-level, cell-type specific changes in NI neurons, altering their activation in response to acute stress, active and passive membrane properties, and action potential characteristics. Additionally, MS caused dendritic tree remodelling of NI CCK neurons and altered expression of stress-related CRHR1 and TrkA receptor mRNA in the NI. These MS-induced changes within NI neurons may contribute to the development of ELS-related disorders, including compulsive behaviors, emphasising the need for further exploration, particularly regarding MS stress-sensitive NI CCK neurons.

Funding: The National Science Centre, Poland, UMO-2018/30/E/NZ4/00687, UMO-2023/49/B/NZ4/01885, UMO-2017/27/N/NZ4/01545.

SYMPOSIA SESSION II – INTEGRATING SPIKING NEURAL NETWORKS IN NEUROBIOLOGY AND COMPUTER SCIENCE

25th April 2024 (Thursday), 11:15–12:45

Speaker: Matej Mertik (11:15–11:45)
Alma Mater Europaea ECM, Maribor, Slovenia

Speaker: Maciej Wielgosz (11:15–11:45)
[1] Faculty of Computer Science, Electronics and Telecommunications, Department of Electronics, AGH University of Science and Technology, Krakow, Poland
[2] ACC Cyfronet AGH, Krakow, Poland

Chair: Jan Argasiński

Kinga Przybylska (11:45–12:00)
Szymon Mazurek (12:00–12:15)
Joan Falcó-Roget (12:15–12:30)
Jan Argasiński (12:30–12:45)

INTEGRATIVE APPROACHES IN SPIKING NEURAL NETWORKS: BRIDGING MACHINE LEARNING, COMPUTER SCIENCE, AND NEUROBIOLOGY

Matej Mertik[1] and Maciej Wielgosz[2,3]
[1] Alma Mater Europaea ECM, Maribor, Slovenia
[2] Faculty of Computer Science, Electronics and Telecommunications, Department of Electronics, AGH University of Science and Technology, Krakow, Poland
[3] ACC Cyfronet AGH, Krakow, Poland

Spiking neural networks (SNNs) stand at the intersection of machine learning (ML), computer science (CS), and neurobiology, promising to revolutionize computational paradigms by mimicking the temporal dynamics of biological neural systems. This presentation explores the landscape of SNNs, emphasizing the synthesis of concepts from ML, such as learning algorithms and frameworks like BindsNET and SpikeJelly, with the structural and functional insights from neurobiology. We discuss the role of computer science in developing simulation tools like NEST, which enable the mapping of neural architectures. The contribution of neurobiology is underscored by providing biological fidelity to models, influencing both architecture and function. Moreover, we delve into the emerging field of neuromorphic engineering, which aims to translate the computational efficiency of SNNs into hardware implementations. By converging these fields, SNNs hold the potential for creating more efficient, adaptive, and biologically realistic computing systems. The presentation concludes with a discussion on the current challenges and future directions in SNN research, outlining a collaborative path forward for these intertwined disciplines.

EXPLORING THE VERSATILITY OF MULTIELECTRODE ARRAY SYSTEMS IN *EX VIVO* NEURAL RECORDINGS

Kinga Przybylska*, A. Trenk and A. Blasiak
Department of Neurophysiology and Chronobiology, Institute of Zoology and Biomedical Research, Jagiellonian University, Krakow, Poland
**Email: kinga.przybylska@doctoral.uj.edu.pl*

Multielectrode array (MEA) systems present one of the several methods of data acquisition from the brain, offering a window into neural dynamics. This presentation will provide a comprehensive overview of MEA systems, positioning them as a robust tool in neuroscience research. Focusing on *ex vivo* recordings, the discussion will highlight the diverse applications of MEA technology, particularly in conjunction with other advanced techniques, such as optogenetics and chemogenetics. Furthermore, the intricacies of data analysis and interpretation will be delved into, providing practical insights for researchers. By elucidating the functional aspects of MEA technology, this talk aims to enhance understanding of this technique and empha-

size its potential as a valuable resource for researchers seeking comprehensive neural activity data.

Funding: This research was supported by a research grant from the National Science Centre, Poland (UMO-2023/49/B/NZ4/01885).

ENRICHING SPIKING NEURAL NETWORK MODELS WITH PROPERTIES OF NEUROTRANSMITTERS

Szymon Mazurek[1,2]

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Modern artificial neural networks recently reached stellar performance across various tasks, previously deemed as unsolvable by machine models. Their principle of operation, however, resembles the biological intelligence phenomena poorly. Spiking neural networks show promise in bridging this gap. Yet still, they need to be completed in terms of biological plausibility, operating on simplified neuron models and mostly Hebbian-based learning rules. Recent advances in neuroscience shed more light on the principles of brain operation, showing new ways of modeling intelligent systems *in silico*. Today I would like to show how neuromodulatory mechanisms can be included in these networks, possibly improving their performance in various environments.

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TRAINING BIOLOGICALLY PLAUSIBLE NEURAL NETWORKS: CURRENT CHALLENGES

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The successful deep artificial neural networks barely resemble how networks in the mammal brain operate. Behavioral experiments and computational modeling of those offer the possibility to hinder some of these differences. First, I will discuss the basic properties of cortical networks and how we can incorporate them into biologically plausible mathematical models. Second, I will emphasize how the training of these network models remains an open challenge. Moreover, these challenges increase enormously if we incorporate further biological constraints into the learning process; for example, Hebbian-based and/or dopamine-based learning rules. Finally, and most importantly, I will discuss how we could bypass these constraints to obtain network models to mimic information processing in real brains and how they can be used to understand how behavior and cognition emerge from low-level computations.

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MODELING BRAIN ACTIVITY WITH SPIKING NEURAL NETWORKS

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Spiking neural networks (SNNs) represent a sophisticated approach to modelling brain activity, closely mimicking the dynamics of biological neural networks. By incorporating the fundamental principles of how neurons spike and communicate, SNNs provide a more realistic representation of neural processing compared to traditional artificial neural networks. When it comes to integrating multielectrode array recordings from rat brain areas into computational modeling, SNNs play a crucial role. These recordings offer rich, detailed data about neuronal activity patterns, including the timing of spikes, which is critical for SNNs. By inputting this data into SNNs, researchers can simulate how specific brain areas process information. This approach allows for a deeper understanding of complex neural mechanisms and can lead to advancements in neuroscientific research, offering insights into brain function, neural disorders, and potential therapeutic strategies. The alignment of SNNs with real neural data enhances the accuracy and relevance of computational models in neuroscience.

SYMPOSIA SESSION III – VISUAL PERCEPTION IN COGNITIVE PSYCHOLOGY

25th April 2024 (Thursday), 11:15–12:45

Chair: Michał Kuniecki

Piotr Buczkowicz (11:15–11:40)
Ingrida Zelionkaitė (11:40–12:00)
Katarzyna Jurewicz (12:00–12:20)
Julia Papiernik (12:20–12:40)

EEG AND EYE FIXATION-RELATED POTENTIALS IN ADHD CHILDREN

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Candidate neuromarkers for attention deficit hyperactivity disorder (ADHD) have long been sought because the disorder is common but difficult to diagnose. The use of objective physiological measures, particularly EEG and oculography, may be a promising way to overcome these difficulties. This study aimed to preliminary explore the differences between children with ADHD and control group in bioelectric brain activity, eye movement, and performance of Flanker task. 64-channel BioSemi EEG, EyeLink 1000+ eye-tracker and Flanker task using child-friendly fish instead of arrows were used during the experiment. We analysed behavioral and electrophysiological data from 17 children (13 with ADHD, 4 without ADHD; 6 girls, 11 boys), aged 6-11 (m=8,7). The mean reaction time (rt) in the ADHD group (873 ms) was longer than in the control group (674 ms), but this difference was below the significance threshold. Children's answers were faster (rt) and more often correct (corr) in congruent trials (rt=740 ms, corr=97%) than in incongruent trials (rt=801 ms, $p<0.005$; corr=92%, $p<0.001$). There was a positive association between age and rt ($p=0.014$, t=-2,77). Alpha frequency (8-12 Hz) power in midline channels was significantly ($p<0.05$) higher in control group than in ADHD group. No other differences in resting state EEG were observed. The preliminary results obtained are consistent with previous findings. Further studies should use larger sample sizes, which should allow statistically significant effects. Furthermore, the results suggest that the use of both EEG and oculography may provide new insights into neurocognitive function in ADHD.

LOWER PUPILLARY RESPONSE AND LESS ATTENTION TOWARDS FACES IN ORAL CONTRACEPTIVE USERS: AN EYE TRACKING STUDY

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Women taking oral contraceptives (OC) may exhibit differences in how they perceive and process emotions compared to naturally cycling (NC) women. However, the relationship between the use of OC and emotional perception is complex and not fully understood. The eye-tracking study aimed to evaluate the association between women's hormonal status and emotional perception. Women using OC (n=28) or in the follicular phase of their menstrual cycle (n=36) freely looked at the erotic, negative, and neutral pictures while their eye movements and pupil diameter were recorded. Participants evaluated pleasantness and arousal after each picture. Saliva samples were taken to assess the 17β-estradiol, progesterone, and testosterone concentrations. NC women tended to evaluate erotic pictures as more pleasant than the OC-users ($p=0.050$), but there was no between-group difference in arousal evaluation. However, larger pupil diameter in NC women compared to OC-users ($p=0.039$) in response to affective pictures, suggests differences in physiological arousal. NC women dwelled longer (erotica, $p=0.027$) and had more fixations (neutral, $p=0.025$) to human faces than OC-users.

There were no group differences in gaze parameters when watching negative stimuli (all p>0.05). In conclusion, results revealed changes in emotional perception among OC-users, characterized by lower pupillary response and less attention towards faces.

EYE-MOVEMENTS IN NATURALISTIC SEARCH: EVIDENCE FOR A HIGH PREVALENCE OF INFORMATION TRANSFER ACROSS SACCADES

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When searching for an object in a scene, are saccade targets selected independently at each fixation? The timing between saccades suggests this is not always the case: saccade latencies can sometimes be much shorter than the usual minimum of ~125 ms, indicating that such second saccades are based on visual information obtained prior to the first movement. Here, we examined information transfer in goal-directed visual search in naturalistic context. We used a large open dataset of eye-movements from participants (n=10) performing category-search with 18 target categories (COCO-Search18) on over 4000 unique photographs of complex everyday scenes. When the target was present in the scene, short-latency second saccades occurred frequently (~45%) and foveated the search target more often than saccades executed after longer latencies. These were not small-amplitude "corrective" saccades: they were both more common and more likely to foveate the target when initiated further away from the target and in the opposite direction to the preceding saccade. There were fewer short-latency second saccades in target-absent scenes, highlighting the contribution from the top-down salience of the search-target. Together, these results reveal a "satisficing" strategy used in naturalistic searches and a prominent role of information transfer in naturalistic vision.

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WORKING MEMORY PERFORMANCE VARIES ACROSS THE VISUAL FIELD – FINDINGS FROM BEHAVIOR AND BRAIN STRUCTURE

Julia Papiernik[1,2]*, Simon Hviid del Pin[3], Michał Wierzchoń[1,4], Renate Rutiku[1]

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Visual performance is best at the center of our gaze and worst in the periphery. It is also better along the horizontal than the vertical axis, and at the lower half of the vertical axis. These asymmetries have been well-established for various perception tasks and are linked to differences in brain structure and function. Albeit it remains unclear to what extent these asymmetries extend to cognitive performance, particularly visual working memory, and whether sensory cortices are involved in maintaining working memory content. We replicated a previous study demonstrating visual field asymmetries in a working memory task in a large sample (N=292). The results reiterate the horizontal *vs.* vertical meridian asymmetry in the processing of stimuli. Notably, we observed unexpected results regarding the superior performance in the right compared to the left part of the visual field. Additionally, vertical asymmetries were found to be reversed compared to effects reported in prior research. Quantitative Multi-Parameter Mapping was performed to shed light on how interindividual structural differences in the early visual cortex are linked to behavioral performance patterns. We observed notable outcomes in the gray matter density specific to the R2* maps – a contrast that reflects

variations in accumulated iron levels. This aligns with prior research associating increased iron deposition in the brain with a decline in memory capabilities and the onset of neurodegenerative diseases. Taken together, this work helps to uncover the complex relationship between perception and working memory, and the involvement of sensory cortices in working memory tasks.

Funding: This work was supported by the National Science Centre, Poland (research project No. 2021/42/E/HS6/00425 awarded to Renate Rutiku and research project No. 2017/27/B/HS6/00937 for data collection awarded to Michał Wierzchoń) and by the European Cooperation in Science and Technology (COST, Action CA18106).

SYMPOSIA SESSION IV – VISUAL PERCEPTION IN NATURALISTIC ENVIRONMENTS

25th April 2024 (Thursday), 15:30–17:00

Speaker: Marius Peelen (15:30–16:10)
Donders Institute for Brain, Cognition and Behaviour Radboud University, Nijmegen, The Netherlands

Chair: Michał Bola and Marek Pędziwiatr

Natalia Rutkowska (16:10–16:22)
Michał Bola (16:22–16:34)
Marek Pędziwiatr (16:34–16:46)
Diana Kollenda (16:46–16:58)

PREDICTIVE PROCESSING OF SCENES AND OBJECTS

Marius Peelen
Donders Institute for Brain, Cognition and Behaviour Radboud University, Nijmegen, The Netherlands

Expectations derived from scene context influence perception. For example, objects presented in their typical context (e.g., a car on a road) are more easily recognized than objects presented in an atypical context. Recent behavioral studies have shown that context-based expectations influence not only semantic judgements, but also how sharply we perceive objects. Furthermore, there is now also evidence for the reverse influence, with objects affecting scene perception. Here, I present results from fMRI and MEG studies investigating the neural basis of such bidirectional interactions between object and scene processing. Results provide evidence for scene-based sharpening of object representations in visual cortex from around 280 ms after stimulus onset, reflecting feedback signals after the initial parallel processing of scenes and objects. This expectation-based modulation was observed even when the stimuli were task-irrelevant and attention was temporally and spatially directed away from the scenes. Interestingly, the reverse influence – with objects sharpening scene representations – was found at the same latency, in line with a common predictive processing mechanism for bidirectional object-scene interactions. These results indicate that objects and scenes, while initially processed in parallel pathways, engage in mutual and facilitatory interactions. These interactions then shape the feedback signals propagated within each pathway, modulating activity in hierarchically lower levels of the visual system, thereby resulting in overall reduced uncertainty and sharpened visual perception.

TEMPORAL DYNAMICS OF REAL-WORLD SCENES PERCEPTION INVESTIGATED WITH DRIFT-DIFFUSION MODELS

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The present study aimed to elucidate how perceptual representations of scene elements – specifically, backgrounds and objects – develop and interact over time. In the conducted experiment participants (N=31) were presented with grayscale images of real-world scenes, which depicted a natural or a man-made background and a single natural or man-made foreground object, combined in semantically congruent or incongruent ways. Participants performed a speeded classification of backgrounds or objects (in separate blocks) as natural or man-made. We analysed reaction-times (RTs) of a manual response to target stimuli and two measures derived from the drift-diffusion model (DDM): boundary separation (a) and drift rate (v). Classification was faster for objects as relative to backgrounds and, in case of man-made targets, for congruent as relative incongruent images. In line, the DDM analysis indicated that less perceptual evidence was needed to categorise objects in comparison to backgrounds; and that accumulation of evidence was faster for congruent as rel-

ative to incongruent images, with the effect stronger for man-made targets. Thus, our findings indicate that local objects can be classified before the global background, and provide insights into how semantic incongruence slows down and hampers visual recognition.

Funding: The National Science Center Poland grants (2018/29/B/HS6/02152; 2022/46/E/HS6/00150).

DO SEMANTICALLY INCONGRUENT OBJECTS CAPTURE AND HOLD OUR ATTENTION?

Michał Bola

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In real-world scenes objects do not occur in isolation, but rather in relation to other scene elements. That such relations play a key role in the object recognition process has been shown by studies investigating perception of semantically incongruent objects – defined as objects with a very low probability of occurring in a given context – recognition of which is slower and less accurate in comparison to congruent ones. However, whether semantic relations present in scenes are able to guide spatial attention automatically remains an open research question. To address this question, in the first study (N=25) we investigated whether semantically incongruent objects automatically capture attention (i.e., cause a semantic "pop-out") using a combination of behavioral and ERP indicators of attention shifts. In the second study (N=46), which was conducted and published in the registered report format, we investigated whether semantically incongruent objects automatically hold (or engage) attention for a longer time than congruent ones. Therefore, results of both studies inform us to what extent semantic relations present in natural scenes are able to automatically guide attentional selection and scene exploration.

Funding: The National Science Centre Poland grant (2022/46/E/HS6/00150).

PRIOR KNOWLEDGE ABOUT EVENTS DEPICTED IN SCENES RENDERS EYE MOVEMENTS TO THESE SCENES LESS EXPLORATORY

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The visual input that the eyes usually receive contains temporally continuous information about unfolding events. Therefore, humans can accumulate knowledge about their current environment. Typical studies on scene perception, however, involve presenting multiple images that are unrelated to each other and, thereby, render this accumulation unnecessary. Our study, instead, facilitated it and explored its effects. Specifically, we investigated how recently-accumulated prior knowledge affects gaze behavior. In our preregistered study, participants viewed sequences of static film frames from films directed by Alfred Hitchcock. Each sequence contained several 'context frames' followed by a 'critical frame'. The context frames showed either events from which the situation depicted in the critical frame naturally followed or events unrelated to this situation. Therefore, identical critical frames were viewed by participants possessing prior knowledge that was either relevant or irrelevant to their content. When that knowledge was relevant, participants' gaze behavior was less exploratory, as revealed by two complementary analyses: one based on traditional metrics of oculomotor behavior and one based on modelling individual gaze traces using hidden Markov models. Therefore, our results demonstrate that recently gained prior knowledge impacts oculomotor exploration.

Funding: Funded by a Leverhulme Trust grant (RPG-2020-024).

PERCEPTUAL AND NEURAL CORRELATES OF INDIVIDUAL GAZE IN COMPLEX SCENES

Diana Kollenda[1,2]*, Elaheh Akbarifathkouhi[1,2], Maximilian D. Broda[1,2], Benjamin de Haas[1,2]

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Recent research has demonstrated systematic differences in the gaze patterns of observers when freely viewing complex scenes, with prominent differences in terms of text and social salience as well as the extent of visual exploration. These findings give rise to further questions: Are individual gaze patterns associated with different impressions of identical scenes and what neural correlates underlie individual biases in visual attention and exploration? I will present recent work showing that similarities in observers' gaze patterns serve as predictors of similarities in subsequent scene descriptions. In addition, a direct relationship was found between an observer's systematic visual biases and subsequent references to corresponding object categories, such as text and people. Furthermore, I will present preliminary results of a neuroimaging study investigating the relationship between, individual salience biases, visual exploration, and the functional layout of visual cortices in the individual brain. Taken together, I will present data on the underlying mechanisms of our individual perception of the world.

Funding: This work was supported by European Research Council Starting Grant 852885 INDIVISUAL; BdH was further supported by Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) Project Nos. 222641018-SFB/TRR 135 TP C9 as well as „The Adaptive Mind", funded by the Excellence Program of the Hessian Ministry of Higher Education, Science, Research and Art.

SYMPOSIA SESSION V – BILATERAL BRAIN-BODY INTERACTIONS

25th April 2024 (Thursday), 15:30–17:00

Speaker: Urte Neniskyte (15:30–16:10)
Life Sciences Center, Vilnius University, Lithuania

Chair: Ali Jawaid

Edyta Bulanda (16:10–16:22)
Weronika Tomaszewska (16:22–16:34)
Magdalena Gomółka (16:34–16:46)
Ivan Arzhanov (16:46–16:58)

MATERNAL HIGH-FAT DIET IMPAIRS SOCIAL BEHAVIOR OF THE OFFSPRING: CELLULAR AND MOLECULAR MECHANISMS

Urte Neniskyte
Life Sciences Center, Vilnius University, Lithuania

Western diet today has excessive fat content, causing increased obesity rates in human population worldwide, including women of reproductive age. There is growing evidence that maternal high-fat diet (mHFD) increases the risk of neurodevelopmental disorders in the offspring. To investigate the pathways that mediate the effect of mHFD on offspring neurodevelopment, we set up mHFD model, in which female C57Bl/6J mice were fed a control diet (CD, 10% fat) or high-fat diet (HFD, 60% fat) from weaning to lactation and were mated with males maintained on normal diet. The offspring were weaned to normal diet. We investigated the phenotype of the offspring social interaction, cognitive function, repetitive behavior and in other behavioral tests. The changes of offspring brain structure were determined by high-resolution voxel-based morphometry. Structural analysis was supplemented by immunohistochemistry of brain tissue sections, while gut microbiota was determined by 16S amplicon sequencing. We found specific deficits in offspring social behaviors that were accompanied by the alterations in olfactory areas of the brain and microglial activation in olfactory bulb. The consumption of HFD changed the relative abundance of different gut bacteria genera in the dams and this dysbiosis was transferred to the offspring as well. Interestingly, observed changes were sex-dependent, as structural brain alterations were more prominent in males, while microbiota changes were more notable in female offspring. Overall our findings suggest that social deficits observed in mHFD models may stem from impaired olfactory interactions in parallel or together with the dysbalance of gut microbiota composition.

THE INFLUENCE OF MICROBIAL METABOLITES ON BRAIN IMMUNITY

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Our intestines are inhabited by commensal microbes, which interact with human cells to maintain homeostasis. However, one question remains unanswered: how does the gut microbiota influence immune function in distal body organs, such as the brain? In recent years, we and others have gained important advances towards unravelling the mechanisms that underline the „gut-brain axis", as we pointed to the presence of gut-derived metabolites in this organ. Following up on this, we identified one metabolite which inhibited inflammatory responses in cells from these areas. In glial cells, it ameliorated the production of mediators typically upregulated in multiple sclerosis patients (IL-6, CCL2 or CCL20). Testing the efficacy of metabolite's isomer pointed to the active site of the molecule and allowed us to construct the library of 20 rationally designed chemical derivatives. Some of these modifications exerted a stronger anti-inflammatory effect than the original compound, and some showed a distinct anti-inflammatory profile (i.e., inhibited dif-

ferent mediators). Collectively, these findings constitute the grounds for exploring the efficacy of identified metabolites *in vivo* and explaining their mechanisms of action. Our results may constitute the first step towards developing these compounds as drugs.

INTERPLAY OF SERUM LIPIDS AND MICROGLIA IN THE SUSCEPTIBILITY TO THE LONG-TERM BEHAVIORAL EFFECTS OF ADVERSE CHILDHOOD EXPERIENCES

Weronika Tomaszewska[1]*, Izabela Lepiarz-Raba[1], Taufik Hidayat[1], Magdalena Gomółka[1], Ismail Gbadamosi[1], Aleksandra Cabaj[2], Bartłomiej Gielniewski[2], Jacek Miłek[3], Magdalena Dziembowska[3], Ali Jawaid[1]

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Adverse childhood experiences (ACE) constitute a major risk factor for adult-onset neuropsychiatric disorders. Susceptibility to the long-term behavioral effects of ACE varies across individuals. However, the mechanisms underlying susceptibility *vs.* resilience to the pervasive effects of ACE remain largely unknown. Emerging evidence supports a role for metabolic factors in susceptibility to the long-term effects of ACE. We propose microglia as the central mediators of such susceptibility and hypothesize that changes in serum lipids and their associated non-coding RNAs induced by ACE can alter microglial functions. For this, we employ a unique multidisciplinary approach that synergizes investigations of samples from human cohorts with *in vitro/ex vivo* models of human microglia. Our preliminary investigations demonstrate ACE-induced changes in serum lipids and associated microRNA in children with a recent history of ACE in the form of paternal loss and maternal separation (PLMS). Notably, PLMS children that develop moderate to severe depressive symptoms (PLMS-susceptible) after ACE exhibit decreased high-density lipoproteins (HDLs) and differentially expressed serum microRNAs in comparison to PLMS children with no (or mild) depressive symptoms (PLMS-resilient). Furthermore, treating HMC3 human microglia-like cells with serum from the PLMS-susceptible *vs.* PLMS-resilient children lead to differential expression of genes involved in glycolysis. These results were corroborated by functional differences in microglial glycolysis after treatment with PLMS-susceptible *vs.* resilient sera *via* metabolic flux analysis. Our ongoing research focuses on validating these findings and studying the impact of samples collected from human ACE cohorts on microglia derived from human induced pluripotent stem cells, as well as microglia-containing human brain organoids.

THE ROLE OF LIPID METABOLISM AND CIRCULATING MIRNAS IN THE INTERGENERATIONAL TRANSMISSION OF THE EFFECTS OF PARENTAL ADVERSE CHILDHOOD EXPERIENCES

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Adverse childhood experiences (ACE) are associated with detrimental effects on adult physical and mental health. Emerging evidence suggests that behavioral and metabolic perturbations associated with ACE are transmissible across generations. However, the exact mechanisms underlying the effects of ACE on germline for such intergenerational transmission of symptoms remain elusive. Synergizing parallel investigation in a mouse model of ACE induced *via* unpredictable maternal separation and unpredictable maternal stress (MSUS) and human ACE cohorts, we hypothesize that lipid-associated microRNAs (miRNAs) communicate the effects of ACE to the germline for intergenerational transmission. miRNA sequencing followed by RT-qPCR revealed overlapping miRNA changes in the serum collected from children, as well as the sperm from adult men with history of ACE. Parallel investigations in mice involved intergenerational phenotyping after MSUS, as well as lipid-modifying interventions high-fat diet (HFD) and voluntary exercise (VE). Offspring of MSUS- and HFD-exposed male mice showed impaired glucose tolerance and behavioral deficits. Furthermore, miR-

NA carriers were isolated from each group and injected into male control and MSUS mice, which were then bred with naive females. Cross-injections from MSUS into control mice recapitulated the offspring phenotype associated with MSUS, whereas, cross-injections from VE mice into MSUS mice partially mitigated the metabolic phenotype associated with MSUS. Together, these studies provide proof-of-concept for a role of lipids and circulating miRNAs in communicating the effects of ACE to the germline for intergenerational sequelae.

CIRCULATING MICRORNAS AS BIOMARKERS FOR ASSESSING THE SEVERITY OF ACUTE SPINAL CORD INJURY

Ivan Arzhanov[1,6]*, Ruslan Klassen[2,3], Sarka Benesova[2,4], Eva Rohlova[2,4], Ales Hejcl[4,5], Lukas Valihrach[2], Nataliya Romanyuk[1]

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Spinal cord injury (SCI) poses a significant challenge in clinical settings, leading to permanent disability in over 180,000 individuals annually worldwide. The extent of the initial injury greatly influences the subsequent secondary response and thus guides the selection of appropriate therapeutic interventions. However, existing clinical measures for assessing SCI severity rely on functional tests that are not immediately applicable post-injury due to factors such as shock, concurrent injuries, and substance use. To address this need for a novel diagnostic indicator during the acute phase of SCI, we conducted comprehensive microRNA (miRNA) profiling in the blood plasma of 16 healthy individuals and 16 injured individuals. Blood samples were collected from injured patients at various intervals post-injury: 3, 12, and 24 hours, as well as 3 and 7 days. These patients were evaluated using ASIA scores and IMR assessments. miRNA isolation was carried out for all samples, with quality assessment based on hemolysis markers and the concentration of specific endogenous miRNAs. Through our miRNA profiling, we identified miRNAs whose expression levels correlate with the severity of SCI. These findings will be integrated with the individual medical histories of patients to establish robust diagnostic criteria for assessing SCI severity during the acute phase. Our data not only enhances understanding of SCI pathophysiology but also facilitates the development of innovative diagnostic approaches.

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SYMPOSIA SESSION VI – AGING RETINA

25th April 2024 (Thursday), 15:30–17:00

Speaker: Kai Kaarniranta (15:30–16:10)

Department of Ophthalmology, University of Eastern Finland, Kuopio, Finland
Department of Ophthalmology, Kuopio University Hospital, Kuopio, Finland

Chair: Adrian Smędowski

Michał Bogocz (16:10–16:25)
Piotr Rodak (16:25–16:40)
Anna Pacwa (16:40–16:55)

AGE-RELATED MACULAR DEGENERATION – THE ALZHEIMER'S OF THE RETINA

Kai Kaarniranta

Department of Ophthalmology, University of Eastern Finland, Kuopio, Finland
Department of Ophthalmology, Kuopio University Hospital, Kuopio, Finland

Age-related macular degeneration (AMD) is a late-onset, neurodegenerative retinal disease that shares several clinical and pathological features with Alzheimer's disease (AD), including stress stimuli such as oxidative stress and inflammation. In both diseases, the detrimental intra- and extracellular deposits have many similarities. Aging, hypercholesterolaemia, hypertension, obesity, arteriosclerosis, and smoking are risk factors to develop AMD and AD. Cellular aging processes have similar organelle and signaling association in the retina and brain tissues. However, it seems that these diseases have a different genetic background.

MARKERS OF NEURODEGENERATIVE DISEASES IN RETINAL IMAGING METHODS

Michał Bogocz

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Retinal imaging methods have shown promise as potential tools for identifying markers of neurodegenerative diseases. Some of the key markers and features observed in retinal imaging that may be indicative of neurodegenerative conditions, such as retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thinning, retinal microvascular changes, retinal amyloid beta (Aβ) deposits, vascular changes in the retina, changes in the optic nerve head. All of these have been linked with various neurodegenerative diseases, including Alzheimer's disease, multiple sclerosis and Parkinson's disease. Aβ plaques are characteristic of Alzheimer's disease, and their presence in the retina may provide a non-invasive method for early detection. Its important to note that while these markers show promise, they are not definitive diagnostic tools on their own. Research in this field is ongoing, and further studies are needed to validate the reliability and specificity of these retinal imaging markers for different neurodegenerative diseases.

MENOPAUSE-INDUCED NEURODEGENERATION

Piotr Rodak

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The relationship between menopause and neurodegeneration is an area of ongoing research. Menopause is a natural biological process that marks the end of a woman 39s reproductive years and is associated with hormonal changes, particularly a decline in estrogen levels. Estrogen receptors are found in various tissues throughout the body, including the brain, and estrogen has been shown to have neuroprotective effects. Therefore, the hormonal changes during menopause may influence brain health and potentially contribute to neurodegeneration. Researchers have paid particular attention to age-related neurodegenerative diseases because of the overlap of endocrine and neuronal dysfunction observed during aging. Hormonal decline (especially a lack of estrogens during the perimenopausal period) is an important risk factor for ocular neurodegenerative diseases, such as glaucoma, ischemic optic neuropathy and retinopathy, age-related macular degeneration, and diabetic retinopathy. On the other hand, population-based studies highlighted a substantial difference in the prevalence of dementia between men and women, with Alzheimer-associated dementia being more prevalent in women, indicating that estrogen deficiency might be a risk factor for neurodegenerative diseases.

Funding: The National Science Centre (Poland) grant: NCN PRELUDIUM 2021/41/N/NZ4/01271.

AGE-RELATED NEURODEGENERATION OF RETINAL GANGLION CELLS – THE ROLE OF RNA-BINDING PROTEINS

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The decline of retinal ganglion cells (RGC) is a gradual process that occurs slowly over time and is associated with the aging process. External factors, such as ischemia, elevated intraocular pressure, or inflammation, may expedite this age-related cell deterioration, ultimately resulting in blindness by impairing RGC function. Neuroprotective mechanisms aim to mitigate the adverse chain reactions triggered by such insults, thereby extending the survival of RGC. Remarkably, one of the RNA-binding proteins, the ELAVL1 has been identified as a regulatory factor for many stress response-related proteins, positioning it as a crucial element in the network of neuroprotective pathways. It has been demonstrated that silencing the HuR gene accelerates retinal aging in healthy conditions and leads to significant RGC loss in a glaucoma model. Furthermore, it has been shown that functional level of the ELAVL1 protein is pivotal for efficient activity of neuroprotection therapies. Similarly as in the retina, the ELAVL1 has been studied in the context of Alzheimer's disease due to its role in post-transcriptional regulation of gene expression.

SYMPOSIA SESSION VII – INHIBITORY CONTROL: RESPONSES, ERRORS, AND THEIR NEURAL AND PSYCHOPHYSIOLOGICAL CORRELATES

26th April, 2024 (Friday), 10:00–11:30

Speaker: Robert Barry (10:00–10:45)
School of Psychology, University of Wollongong, Wollongong, Australia

Chair: Krzysztof Bielski

Krzysztof Bielski (10:45–11:00)
Patrycja Kałamała (11:00–11:15)
Christina Thunberg (11:15–11:30)

INHIBITION IN THE EQUIPROBABLE GO/NOGO TASK – AN EEG-ERP STUDY

Robert Barry
School of Psychology, University of Wollongong, Wollongong, Australia

Our brain dynamics studies have focused on the auditory equiprobable Go/NoGo task. This is an easy cognitive/behavioral task that can be used readily with a wide range of participants. Using ERP components, we have developed a processing schema that maps some of the cognitive stages involved, and have used this as a tool to explore developmental and sex differences, as well as some of the EEG/ERP brain-dynamics involved. Today I explore some of the correlates of inhibitory processing in this task, using a data-driven approach to the electrophysiology of cognitive processing. We begin our data collection with an eye-calibration task to establish EEG-EOG regression coefficients for subsequent removal of EOG from the continuous task-related EEG data. We then filter, interpolate bad channels, extract 1 s epochs (-500 to +500 ms relative to stimulus onset) for correctly-responded trials, baseline these across the 100 ms period immediately-prestimulus, and reject trials with artefacts. For the ERP quantification, we form average Go and NoGo ERPs for each participant, then submit the -100 to 500 ms data to separate Go and NoGo temporal PCAs to extract the underlying ERP components. For EEG, we take the immediately-prestimulus 500 ms epochs (-500 to 0 ms), DC-correct these, zero-pad each to 1 s, decompose these with a Discrete Fourier Transform, then the Pink and White noise is computed and removed from each participant's mean Go and NoGo spectra, after which the Go and NoGo noise-free spectra are submitted to separate frequency PCAs. We then relate the prestimulus EEG frequency components, and Pink and White noise amplitudes, to the ERP components and behavioral outcomes.

LEFT MEDIAL FRONTAL AREA MIGHT BE OUR GUARDIAN ANGEL DURING PROCESSING OF MORE OR LESS INEVITABLE INHIBITORY ERRORS

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Errors can vary in their inevitability, rendering them more or less significant. Typically, more significant errors trigger more noticeable adjustments in behavior. However, this prompts the question: which specific brain system is accountable for recognizing the inevitability of errors? To address this issue we analyzed functional magnetic resonance imaging scans from 33 adults acquired during the stop signal task performance. Firstly, we observed heightened activity in the left medial frontal cortex (lMFC) during trials with failed inhibition compared to go trials with correct responses. Secondly, we investigated whether the activity within lMFC correlates with error inevitability. Employing mixed linear modelling on the time series of erroneous trials, we discovered a significant relationship between the magnitude of blood oxygenation

level-dependent response within 4-8 seconds post-stop signal and the measure of error inevitability (value of the stop-response interval). We observed that the longer stop-response interval, the more pronounced the activity of lMFC was. Moreover, we also noticed that the more avoidable error was, the greater the slowing of response in the subsequent trial. These findings highlight the sensitivity of lMFC to error inevitability and their role in adaptive mechanisms during error processing. Thus, lMFC could be likened to the guiding role of a guardian angel, striving to make our actions better-suited.

Funding: This research was supported by the John Templeton Foundation grant "The Limits of Scientific Explanation" and by two grants from the National Science Centre of Poland: 2019/35/B/HS6/01173 (Opus) and 2020/38/E/HS6/00490 (Sonata Bis).

EVENT-INDUCED MODULATION OF APERIODIC BACKGROUND EEG: ATTENTION-DEPENDENT AND AGE-RELATED SHIFTS IN E: I BALANCE

Patrycja Kałamała[1,2]*, Máté Gyurkovics[1,3], Daniel Bowie[1], Grace Clements[1], Kathy Low[1], Florin Dolcos[1], Monica Fabiani[1], Gabriele Gratton[1]

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The broadband shape of the EEG spectrum, summarized using a 1/f^x function, is thought to reflect the Excitation: Inhibition (E: I) balance in cortical regions. This balance is an important feature of neural circuits and could inform aging studies, as older adults show a relative inhibitory deficit. Thus far, no studies have leveraged the event-related temporal dynamics of 1/f^x activity to understand the phases of information processing, especially in the context of aging. Here, for the first time, we examined variations of this activity during the foreperiod of a cued flanker task in younger (YA) and older adults (OA). We report a biphasic change in the spectral exponent (negative slopes in log-log space) after cue presentation, independent of ERPs, with an initial period of increased negativity (indicating cortical inhibition) followed by decreased negativity (indicating cortical excitation, especially in OA). The decrease in the exponent negativity was associated with lower performance and greater congruency costs in the flanker task. Finally, more novel cues reduced the shift towards excitation in OA, partly restoring their E: I balance and diminishing congruency costs. These findings demonstrate that the aperiodic EEG varies dynamically in a manner that is predictive of subsequent behavior. They also expand our understanding of how neural communication shapes cognition and have implications for neuroscientific models of cognitive processing and age-related cognitive decline.

Funding: NIA grant RF1AG062666 to G. Gratton and M. Fabiani.

FLAWED ASSUMPTIONS LIMIT KNOWLEDGE ABOUT BIOLOGICAL SUBSTRATES OF RESPONSE INHIBITION

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Response inhibition is crucial for flexible behavior. Significant efforts are made to characterize its biological underpinnings and identify neural markers of an inhibition process. The stop signal task is argued to be the purest inhibition task, and the associated model-based estimate of response inhibition latency (stop signal reaction time or SSRT) is central to much of this work. However, testing hypotheses about biological signatures require additional assumptions to those strictly derived from theory. For instance, when contrasting successful and failed inhibition to identify neural markers, it is implicitly assumed that this allows for isolating inhibitory differences. Similarly, when using the SSRT to validate neural markers, it is implicitly assumed that its variation is caused solely by inhibition variation. Or when using the SSRT as an endophenotype, one must assume that it measures a stable trait. Through a series of studies using stop signal task performance measures together with measures of central and peripheral nervous system activity, we have investigated these assumptions and found that several of them do not hold. Such flawed assumptions can leave findings uninterpretable and inferences invalid, ultimately limiting our understanding of biological substrates of response inhibition.

Funding: University of Oslo Life Sciences.

SYMPOSIA SESSION VIII – MOLECULAR PROFILING OF NEURODEGENERATIVE DISORDERS

26th April 2024 (Friday), 10:00–11:30

Speaker: Jörg Hanrieder (10:00–10:45)

Department of Psychiatry and Neurochemistry, Sahlgrenska Academy, University of Gothenburg, Sweden
Department of Neurodegenerative Disease, Queen Square Institute of Neurology, University College London, United Kingdom

Chair: Alicja Szadziewska

Jack Wood (10:45–11:00)
Alicja Szadziewska (11:00–11:15)

MASS SPECTROMETRY BASED MOLECULAR IMAGING FOR FOLLOWING ALZHEIMER'S DISEASE PATHOLOGY IN SPACE AND TIME

Jörg Hanrieder

Department of Psychiatry and Neurochemistry, Sahlgrenska Academy, University of Gothenburg, Sweden
Department of Neurodegenerative Disease, Queen Square Institute of Neurology, University College London, United Kingdom

Mass spectrometry has gained increasing prominence in biomedical research providing as new apogee of molecular imaging. The technique combines features of molecular histology with the high dimensionality and specificity warranted by mass spectrometry at low um resolution. Our group has been advancing MS imaging approaches for chemical neuroimaging, specifically to understand neurodegenerative disease pathomechanisms. Here, it is of critical importance to our understanding of Alzheimer's disease (AD) pathology, to determine how key pathological factors including beta-amyloid (Aβ) plaque formation are interconnected and implicated in nerve cell death, clinical symptoms, and disease progression. Exactly how Aβ plaque formation begins and how the ongoing plaque deposition proceeds and initiates subsequent neurotoxic mechanisms is not well understood. The primary aim of our research is to elucidate the biochemical processes underlying early Aβ plaque formation in brain tissue. We developed a chemical imaging pardigm including hyperspectral microscopy and mass spectrometry imaging that allows to delineate *in vivo* Aβ build up and deposition at cellular length scales. Specifically, we advanced the integration of conformation sensitive hyperspectral mass spectrometry with MSI modalities to elucidate plaque morphology associated changes in Aβ signatures. We further pioneered means for amyloid chronology based on imaging stable isotope labelling kinetics (iSILK). Here, novel genetic AD mice are labelled metabolically with stable isotopes to follow the fate of aggregating Aβ species from before and throughout the earliest events of precipitating plaque pathology. This allowed to visualize Aβ aggregation dynamics within single plaques across different brain regions. We show that formation of structurally distinct plaques is associated with differential Aβ peptide deposition. These data, for the first time, describe a detailed picture of the earliest events of precipitating amyloid pathology at scales not previously possible. The results from these studies bring considerable novel information about the deposition mechanism of Aβ and its toxic interactions with the surrounding. This will open up for developing tailored strategies to affect AD pathology prior to any neurodegenerative mechanisms as well as to develop new biomarkers for AD.

A SPATIAL TRANSCRIPTOMICS INVESTIGATION ON THE IMPACT OF AMYLOID PLAQUES ON SURROUNDING TISSUE GENE EXPRESSION

Jack Wood[1,2]*, Katie Stringer[1,2], Junyue Ge[1], Eugenia Wong[2], Srinivas Koutarapu[1], Damian M. Cummings[2], Frances A. Edwards[2] and Jörg Hanrieder[1]

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Spatial transcriptomics overcomes limitations of RNA sequencing techniques to allow transcriptomic data to be collected from set regions of an imaged tissue section. This is particularly important for Alzheimer's disease (AD) research as pathologies of AD are spatial specific and unevenly distributed. I will present two projects that use spatial transcriptomics to investigate transcriptomic changes immediately around amyloid plaques in mouse models of AD. The first explores changes in microglial gene expression with decreasing distance to amyloid plaques. The findings reports that the majority of plaque induced genes, a recently published gene set, depend on direct contact of microglia with plaque. Furthermore, crossing in the AD-risk mutation Trem2R47H inhibited the plaque-induced expression of genes involved in phagocytic and lysosomal degradation. The second study demonstrates the integration of spatial transcriptomics with imaging mass spectrometry and stable isotope feeding paradigms to mark Aβ species from initial plaque formation. This approach allows us to track the age of amyloid plaques and correlate it with transcriptomic changes, identifying which genes react to new plaques how they change as plaques age.

NEUROPATHOLOGICAL FEATURES OF TAU368 DEPOSITION: CORRELATION WITH CSF BIOMARKERS IN ALZHEIMER'S DISEASE

Alicja Szadziewska[1]*, Srinivas Koutarapu[1], Maciej Dulewicz[1], Przemyslaw R. Kac[1], Anne Hiniker[2], Denis Smirnov[3], Henrik Zetterberg[1,4-8], Douglas Galasko[2], Kaj Blennow[1,5], Jörg Hanrieder[1,4]

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Alzheimer's disease (AD), accounting for 60–80% of dementia cases worldwide, characterized by neurofibrillary tangles (NFT) made of tau protein. The study focuses on the tau fragment, tau368, cleaved by asparagine endopeptidase (AEP) and found in cerebrospinal fluid (CSF). A new Simoa assay (Single Molecule Array) has been developed to measure CSF tau368 levels. Previous studies show that the ratio of tau fragments with truncated C-terminus, particularly when compared to total tau, shows a robust correlation with the uptake of tau PET tracers. The primary goal of this project is to use immunofluorescence to understand tau368 morphology in the human brain and its relationship with disease severity. The research involved analyzing post-mortem tissue from the hippocampus and frontal cortex alongside CSF, employing multiplex immunofluorescence to elucidate tangle maturation patterns. Luminescent Conjugated Oligothiophenes (LCOs) serve to identify amyloid plaques and neurofibrillary tangles. Tau pathology was detailed using specific antibodies, including for Tau368 and pTau217, highlighting maturation patterns. Tau368 levels in CSF were measured using an in-house Simoa assay. Findings showed Tau368 accumulation in various tau aggregates (e.g., pretangles, NFTs, ghost tangles). We observed negative correlation between tau368-positive tangles in the hippocampus subiculum and CSF tau368/t-tau levels ($r=-0.99$; $p=0.010$). Hippocampal tau368-positive tangles correlate positively with BRAAK staging ($r=0.72$; $p=0.04$) and THAL staging ($r=0.80$, $p=0.021$). This study advances our understanding of tau pathology in AD, emphasizing the role of tau polymorphs and epitope expression in disease progression.

SYMPOSIA SESSION IX – POSTTRANSLATIONAL MODIFICATIONS IN THE BRAIN

26th April, 2024 (Friday), 10:00–11:30

Speaker: Thomas Klarić (10:00–10:45)
Genos Glycoscience Research Laboratory, Zagreb, Croatia

Chair: Ugne Kuliesiute

Ugne Kuliesiute (10:45–11:00)
Natalia Pudełko-Malik (11:00–11:15)
Savani Anbalagan (11:15–11:30)

INSIGHTS INTO THE EVOLUTION OF THE MAMMALIAN BRAIN *VIA* COMPARATIVE N-GLYCOMICS

Thomas Klarić
Genos Glycoscience Research Laboratory, Zagreb, Croatia

Numerous comparative "omics" studies have revealed unique aspects of human neurobiology, yet an evolutionary perspective of protein glycosylation in the mammalian brain is lacking. Asparagine-linked glycosylation (N-glycosylation) is a post-translational modification that is a common feature of transmembrane, secreted, and extracellular proteins and it is critically involved in many aspects of neurobiology. To gain an insight into the evolutionary trajectory of N-glycosylation in the mammalian brain, we comprehensively characterised rat, macaque, chimpanzee, and human N-glycomes from four brain regions using chromatography combined with mass spectrometry, then integrated these data with complementary glycotranscriptomic data. We found that in primates the brain N-glycome has diverged more rapidly than the underlying transcriptomic framework, providing a means for rapidly generating additional inter species diversity. We uncovered numerous phylogenetic trends in brain protein N-glycosylation as well as several human-specific adaptations. Taken together, our data suggest that brain N-glycome evolution in hominids has been characterized by an overall increase in complexity coupled with a shift in sialic acid linkage.

PATTERN OF SIALYLATION SHAPE NEURONAL NETWORK DURING BRAIN DEVELOPMENT AND IN NEUROPATHOLOGIES

Ugne Kuliesiute[1,2]*, R. Prokopovicius[2], U. Kisieliute[2], S. Kutanovas[1,2], K. Merkevicius[2,3], G. Luksys[4,5], S. Rocka[4,5], U. Neniskyte[1,2]

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Neuronal glycocalyx has been recently recognized as an active agent that contributes to neuronal synapse formation, neuron excitability as well as neuron-autonomous and microglia-dependent brain network remodeling. In particular, the sialic acid, which often dominates the ends of the chains of glycoproteins and glycolipids on neuronal surface, is required for appropriate brain development and function. To characterize sialylation during brain development we used bioorthogonal CLICK chemistry to label de novo synthesized sialic acids in organotypic hippocampal brain slice sections. In line, by enzymatic sialidase activity measurements we demonstrated that sialylation of neurons is tightly regulated during the periods of high plasticity such as hippocampal development. Importantly, aberrant sialylation and/or desialylation are implicated in different neuropathological conditions, such as epilepsy and glioblastoma. We employed surgically resected human brain tissue and revealed that sialylation orchestrates glioblastoma tumor formation and network connectivity. Moreover, we discovered altered turnover of sialic acids and compromised enzymatic activity of sialidases

in epileptic human brain tissue proposing increased sialylation of epileptic human brain. Transcriptomics of isolated epileptic and healthy human synaptosomes revealed unique molecular signatures that are found in aberrant neuronal circuitry. Altogether, our findings indicate that turnover of sialic acid as an important factor for neuronal network remodeling in brain development and circuitry diseases.

EXPLORING POST-TRANSLATIONAL MODIFICATIONS IN THE CONTEXT OF NEURONAL PLASTICITY

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Neuronal plasticity is crucial for brain functions, but age-related changes affect it, leading to memory alterations. Current knowledge emphasizes the significant impact of post-translational modifications (PTMs) like ubiquitination, glycosylation, palmitoylation, and SUMOylation on neuronal plasticity. Evidence, suggests that local changes in protein localization and time-dependent activity modulations are more crucial for proper cell function than overall protein expression profiles. In our research, we concentrated on age-related changes in post-translational modifications, manifested as significant alterations in expression profiles of proteins involved in and directly executing PTMs. Our proteomic analyses identified approximately 8217 proteins for each animal group: young mice (1 month), old mice (20-22 months), and old mice treated with BAY U6751 (an inhibitor of glycogen phosphorylase (Pyg)). Our findings indicated a significant age related decrease of protein involved in common types of PTMs. But interestingly, the glycogen metabolism inhibition results in a 'rejuvenation' of the total proteome profile in old animals. We observed promising trends in PTMs pathways, where e.g., de-palmitoylation and palmitoylation were significantly increased after BAY treatment, compared to old controls ($p<0.05$). Our data reveals significant correlations between PTMs patterns and aging, and allow to better understanding of the molecular landscape.

A LIGAND-RECEPTOR INTERACTOME ATLAS OF THE ZEBRAFISH

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Studies in zebrafish can unravel the functions of cellular communication and thus identify novel bench-to-bedside drugs targeting cellular communication signaling molecules. Due to the incomplete annotation of zebrafish proteome, the knowledge of zebrafish receptors, ligands, and tools to explore their interactome is limited. To address this gap, we de novo predicted the cellular localization of zebrafish reference proteome using deep learning algorithm. We combined the predicted and existing annotations on cellular localization of zebrafish proteins and created repositories of zebrafish ligands, membrane receptome, and interactome as well as associated diseases and targeting drugs. Unlike other tools, our interactome atlas is based on both the physical interaction data of zebrafish proteome and existing human ligand-receptor pair databases. The resources are available as R and Python scripts. DanioTalk provides a novel resource for researchers interested in targeting cellular communication in zebrafish, as we demonstrate in applications studying synapse and axo-glial interactome. DanioTalk methodology can be applied to build and explore the ligand-receptor atlas of other non-mammalian model organisms.

SYMPOSIA SESSION X – MOLECULAR MECHANISMS OF SYNAPTIC PLASTICITY

26th April, 2024 (Friday), 12:00–13:30

Speaker: Jakub Włodarczyk (12:00–12:45)
Laboratory of Cell Biophysics, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

Chair: Dominika Drulis-Fajdasz

Monika Puchalska (12:45–13:00)
Anbarieh Saadat (13:00–13:15)
Bogna Badyra (13:15–13:30)

STRESS RESILIENCE IS AN ACTIVE AND MULTIFACTORIAL PROCESS MANIFESTED BY STRUCTURAL, FUNCTIONAL, AND MOLECULAR CHANGES IN SYNAPSES

Jakub Włodarczyk
Laboratory of Cell Biophysics, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

Stress resilience is the ability of neuronal networks to maintain their function despite the stress exposure. Using a mouse model we investigate stress resilience phenomenon. To assess the resilient and anhedonic behavioral phenotypes developed after the induction of chronic unpredictable stress, we quantitatively characterized the structural and functional plasticity of excitatory synapses in the hippocampus using a combination of proteomic, electrophysiological, and imaging methods. Our results indicate that stress resilience is an active and multifactorial process manifested by structural, functional, and molecular changes in synapses. We reveal that chronic stress influences palmitoylation of synaptic proteins, whose profiles differ between resilient and anhedonic animals. The changes in palmitoylation are predominantly related with the glutamate receptor signaling thus affects synaptic transmission and associated structures of dendritic spines. We show that stress resilience is associated with structural compensatory plasticity of the postsynaptic parts of synapses in CA1 subfield of the hippocampus.

PSD-95-DEPENDENT SYNAPTIC TRANSMISSION IN THE DORSAL CA1 AREA (DCA1) OF THE HIPPOCAMPUS IS REQUIRED FOR UPDATING, BUT NOT FORMATION, OF CONTEXTUAL MEMORIES

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It is widely believed that synaptic transmission in the hippocampus plays a crucial role in formation of contextual memories. Data obtained in our laboratory implies that PSD-95 (postsynaptic density protein 95)-dependent synaptic plasticity in dCA1 area is required for updating of contextual fear memory. To check how inactivation of dCA1 area affects contextual fear memory extinction, we stereotactically injected the adenoviral vectors (AAVs) encoding DREADD receptor hM4 [AAV2.1: hSyn_hM4_mCherry]. Next we trained mice in contextual fear conditioning (CFC). We found that chemogenetic inhibition of dCA1 impaired contextual fear memory extinction and redacted the levels of synaptic protein, PSD-95. To see whether PSD-95 in dCA1 affects the contextual fear memory we stereotactically injected the lentiviral vectors (LVs) encoding short hairpin RNA (shRNA) silencing PSD-95 expression [H1-shRNA_PSD95-Ub_GFP] in the dCA1 area of young adult male and female mice. Next, we trained mice in CFC and performed electrophysiological recordings in the dCA1 area to assess the functionality of synapses with PSD-95 depletion. Moreover, we tested mice in the IntelliCages system to study spatial choice and extinction of appetitive contextual memories in close-to-ecologic conditions. We found that local depletion of PSD-95 in dCA1 decreased synaptic transmission and impaired the contextual fear memory extinction, but not formation or recall. It also impaired ability to find a reward in a complex context at the initial stage of learning, but had no effect on place preference extinction. Together, our data indicates that PSD-95-dependent synaptic transmission in dCA1 is required for updating contextual memories.

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THE EFFECT OF SWIMMING ON THE SYNAPTIC PLASTICITY IN THE SOMATOSENSORY CORTEX OF ALS MICE MODEL

Anbarieh Saadat[1]*, Malgorzata Jasinska[2], Emilia Białobrodzka[3], Ewa Rodziewicz-Flis[3], Damian Flis[3], Wiesław Ziółkowski[3], Elżbieta Pyza[1]

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ALS is an incurable, chronic neurodegenerative disease characterized by a selective death of motoneurons in the motor cortex, brainstem, and spinal cord that control voluntary movements of the muscles. The somatosensory cortex is interconnected with other brain areas including the motor cortex. The positive effect of swimming on the progression of ALS disease and the longevity of mice has already been shown. However, the observed effects were related to training before the appearance of the first symptoms of the disease in mice, while the swimming training after the onset of the disease may have a great practical value for ALS patients. In this project, we examined synaptic plasticity in the brains of ALS mice and the imbalance between excitatory/inhibitory synapses in the somatosensory cortex. Mice were divided into three groups: the early stage of ALS, terminal untrained ALS, and terminal swim trained ALS. The number of excitatory and inhibitory synapses in the somatosensory cortex (barrel cortex) was quantified using transmission electron microscopy. The results showed a significant decrease in the number of excitatory synapses between the early stage of ALS and terminal swim trained mice with ALS, indicating positive effects of swimming on the disease.

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JOURNEY THROUGH DEVELOPMENT TO MATURATION IN BRAIN ORGANOIDS: HOW FAR CAN WE GET?

Bogna Badyra[1]*, Matylda Roszkowska[1], Karolina Protokowicz[1], Dominika Kurpiewska[1], Marcin Barański[1], Ewa Liszewska[2], Jacek Jaworski[2], Leszek Kaczmarek[1]

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Brain organoids provide a great tool to decipher human neurodevelopmental diseases, as they can reflect changes occurring even in the prenatal period. Those diseases are often accompanied by aberrant changes in the formation of dendritic spines harboring excitatory synapses. Yet, none of the studies focused on detailed characterization of dendritic spines in organoids. Herein, we present a novel protocol to visualize these phenomena. Human induced pluripotent stem cells were differentiated into cortical spheroids. On subsequent stages of development, organoids were evaluated for proper differentiation. After day 200 live calcium imaging was performed to analyze their maturation and the spontaneous activity of cells. Next, organoids were evaluated for dendritic spines formation using biolistic delivery of lipophilic dye combined with subsequent immunolabeling of pre- and postsynaptic markers. We show that organoids' maturation can be manifested by the spontaneous activity of neurons with visible synchronization. This maturation is accompanied by changes in the expression of repertoire of synaptic-related proteins. Importantly, we were able to successfully visualize dendritic spines in neurons within organoids. Furthermore, within spines, we observed the colocalization of pre- or postsynaptic proteins. This method enables a more detailed characterization of complex dendritic spine structure and function in both health and disease.

Funding: This work was supported by the Foundation for Polish Science (MAB/2018/10; 'Nencki-EMBL Center of Excellence for Neural Plasticity and Brain Disorders: BRAINCITY').

SYMPOSIA SESSION XI – COMPUTATIONAL APPROACHES TO UNDERSTAND BRAIN COMPLEXITY

26th April, 2024 (Friday), 12:00–13:30

Speaker: Wiktor Młynarski (12:00–12:45)
Ludwig Maximilian University of Munich, Munich, Germany

Chair: Tomasz Pięciak

Katarzyna Sawicka (12:45–13:00)
Emilia Kaczmarczyk (13:00–13:15)
Magdalena Szponar (13:15–13:30)

PROBABILISTIC SIMPLICITY IN THE STUDY OF THE BRAIN

Wiktor Młynarski
Ludwig Maximilian University of Munich, Munich, Germany

The tremendous, almost impenetrable complexity of the nervous system is not just one, but a huge collection of mysteries we are all trying to solve. To develop understanding of neurobiological phenomena we need to seek simplicity. In the talk I will discuss one such way to search for simplicity and understanding – through building normative theories of neural computation. Normative theories attempt to identify goals and principles that may be shared by multiple, seemingly different neural systems. I will specifically focus on sensory systems which need to achieve a delicate balance between external and internal influences in order to accurately represent relevant information. Dynamic adjustments of the sensory code to these influences have been traditionally categorized depending on their origin and studied separately. Sensory adaptation is a response of a neuron to exogenouschanges in stimulus statistics, while internal modulation adjusts sensory representations to changes in the endogenous states of the brain such as behavioral goals, attention or uncertainty. I will present a theoretical framework which provides a unifying perspective on how sensory codes adapt to such changes regardless of their origin. Starting from the same set of basic principles grounded in information theory and Bayesian inference, our framework generates candidate normative explanations of the diversity of adaptive responses in the early visual system as well as the attentional modulation of neural populations in the primary visual cortex. I will conclude by presenting an experimental finding of spatio-temporal patterns of neural activity which dominate sensory responses in a brain region that has been thought to be predominantly a sensory relay – the superficial superior colliculus. These findings emphasize the need for new theories which will be required to understand the computational principles of dynamic sensory processing and to further tame the overwhelming complexity of the brain.

CORTICAL REINSTATEMENT IS A DIRECT METHOD EMPLOYED TO ASSESS THE HIPPOCAMPAL INDEXING THEORY'S VALIDITY

Katarzyna Sawicka*, Urszula Włodkowska, Monika Falińska, Rafał Czajkowski
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Episodic memories are crucial for our identity and heavily depend on the hippocampus. Despite this, understanding how these memories form, are maintained, and retrieved is still developing. The indexing theory suggests that hippocampal neurons are interconnected with sensory and associative cortical regions, yet it's unclear if cortical reinstating occurs neuron-to-neuron. To explore this, we induced cortical activity in the retrosplenial cortex (RSC) and observed increased c-Fos activity in hippocampal cells. We then replicated this hippocampal index and observed GCaMP signal activity in the RSC. Our goal is to compare the initially activated neurons with the reactivated population in the RSC. This research delves into cortical reinstatement's

dynamics and its impact on episodic memory. By optogenetically stimulating cortical neurons, we aim to understand how the hippocampus and cortex interact during memory processes. These findings could enhance our understanding of memory formation and retrieval mechanisms, offering insights into conditions like amnesia and neurodegenerative diseases.

EXPLORING ALPHA RHYTHM PROPAGATION IN EEG SIGNALS: A COMPARATIVE ANALYSIS OF PCMCI+ AND GRANGER CAUSALITY ALGORITHMS

Emilia Kaczmarczyk*, Maciej Kamiński

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The aim of my research is to investigate the propagation of alpha rhythm in EEG signals using the PCMCI+ algorithm and to compare the results obtained with analyses using Granger causality-related algorithms. The alpha rhythm is a rhythmic activity of the brain cortex in the 8-12 Hz range, occurring during relaxation with eyes closed. This rhythm is generated in the visual cortex in the occipital lobe, and then is propagated to the front of the head by stimulating other structures. Previous studies aimed at investigating the propagation of alpha rhythm in terms of causality have been conducted using algorithms based on Granger causality, which are unable to detect causal relationships occurring at a rate faster than the sampling frequency. In this study we used PCMCI+ algorithm which is a derivative of the PC algorithm, based on the identification of a Bayesian network describing the given system. This method may help to better identify certain dependencies by examining contemporaneous causal relationships. Preliminary analyses indicate that the direction of alpha rhythm propagation may be correctly identified using only delay-free dependency analysis.

DEVELOPING PSYCHIATRIC DIAGNOSTIC TOOL USING MACHINE LEARNING CLASSIFICATION OF RESTING-STATE ELECTROENCEPHALOGRAPHY

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Currently, diagnosis of mental disorders is based predominantly on subjective and time-consuming self-report techniques. Recent literature proposes applying machine learning classification on electroencephalography (EEG) data to distinguish psychiatric patients from healthy controls, with promising accuracies of 75-95%. However, these studies have substantial drawbacks, like small sample sizes (often less than 100 participants), training and testing the model with data from the same patients and lack of multi-categorical classification. Using the psychiatric hospital's archival data, we prepared the database containing over 13000 restingstate EEG recordings of patients diagnosed with a wide range of disorders, providing a sufficient sample to train multi-categorical algorithms. We extracted over 20000 EEG measures for the five most common disorders in the database and trained a state-of-the-art shallow neural network on this data, using one-*versus*-rest scheme. We obtained the average accuracy of 67.5%, significantly higher than the chance level, for classification of independent patients. Furthermore, this accuracy increases with the model's activation function value, allowing us to evaluate the model's predictions. These results indicate that creating machine learning algorithms distinguishing several psychiatric disorders is possible. We will work further to increase our method's accuracy and investigate features contributing to the correct classification. Hopefully, the final algorithm could aid psychiatrists as an objective and quick method for clinical diagnosis.

Funding: The research was conducted as part of the BRAINCITY project. The BRAINCITY project is carried out within the International Research Agenda Programme of the Foundation for Polish Science co-financed by the European Union under the European Regional Development Fund.

SYMPOSIA SESSION XII – PSYCHEDELICS

26th April, 2024 (Friday), 12:00–13:30

Chair: Jan Rodriguez-Parkitna

Paweł Orłowski (12:00–12:20)
Anastasia Ruban (12:20–12:35)
Maja Wójcik (12:35–12:50)
Čestmír Vejmola (12:50–13:10)
Adam Wojtas (13:10–13:25)

NATURALISTIC USE OF PSYCHEDELICS DOES NOT MODULATE PROCESSING OF SELF-RELATED STIMULI (BUT IT MIGHT MODULATE ATTENTIONAL MECHANISMS): AN EVENT-RELATED POTENTIALS STUDY COMPARING NON-USERS AND EXPERIENCED USERS OF CLASSIC PSYCHEDELICS

Paweł Orłowski[1,2]*, Justyna Hobot[3], Anastasia Ruban[4], Jan Szczypiński[5], Michał Bola[1]

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Psychedelics lead to acute experience of ego dissolution – the blurring of the distinction between representations of self and the external world. However, whether repeated use of psychedelics is associated with prolonged or permanent modifications to the concept of self remains to be investigated. Therefore, we conducted a preregistered, cross-sectional study in which experienced psychedelics users (15 or more lifetime experiences with psychedelics; N=56) were compared to non-users (N=57) in terms of neural reactivity to a Self-name (i.e., each participant's own name) stimulus. Two control stimuli were additionally used: an Other-name stimulus, as a passive control condition in which no reaction was required; and a Target-name stimulus, to which participants provided a manual response. Analysis of the amplitude of the P300 ERP component evoked by the Self-name revealed no difference between the psychedelics users and non-users. However, in comparison to non-users, psychedelics users exhibited a smaller increase in P300 amplitude when processing the task-relevant Target-name (in relation to both Self- and Other-names). Therefore, our data suggests that regular naturalistic use of psychedelics may not be related to long-term changes in the representation of self, but it might potentially affect allocation of attentional resources to task-relevant stimuli.

Funding: This study was funded by the National Science Center Poland grant (2020/39/O/HS6/01545).

PROCESSING OF SELF-RELATED THOUGHTS IN EXPERIENCED USERS OF CLASSIC PSYCHEDELICS AND NON-USERS: A SOURCE LOCALISATION EEG STUDY

Anastasia Ruban[1,2]*, Mikołaj Magnuski[1], Justyna Hobot[3], Paweł Orłowski[4], Aleksandra Kołodziej[1], Michał Bola[4], Aneta Brzezicka[1]

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Psychedelics have gained increasing interest in scientific research due to their ability to induce profound alterations in perception, emotional processing and self-consciousness. However, the research regarding the short- and long-term impact of using psychedelics in non-controlled, naturalistic contexts remains limited. Here we aim to fill this gap and explore differences between naturalistic psychedelics users and non-users

during processing of self-related thoughts, using behavioral testing combined with electroencephalography (EEG) with source localisation. To ensure robustness of our results, we included two datasets collected at two different laboratories. The results from Dataset I (N=70) suggest that during self-related thoughts psychedelics users exhibit weaker increases in alpha and beta power in comparison to non-users, primarily in brain regions linked to processing of self-related information and memory. However, analysis of Dataset II (N=38) did not replicate between-group effects, possibly due to the smaller sample size and spatial resolution limitations. While non-replicability restricts interpretation of our findings, this study contributes to understanding the relationship between the use of psychedelics, self-related thoughts, and well-being, which is crucial for assessing mental health impact of psychedelic substances.

Funding: This study was funded by the National Science Center Poland PRELUDIUM (grant no. 2020/37/N/HS6/02086) and PRELUDIUM BIS (2020/39/O/HS6/01545) grants.

LINKING ASPECTS OF COGNITIVE FUNCTIONING AND NEUROPROTEIN PLASMA LEVELS IN PSYCHEDELIC USERS

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The need to research the long-term influence of psychedelics on neurobiological and cognitive functioning of their users stems from their increasingly widespread use and significant gaps in knowledge about their effects. Psychedelics act mainly as agonists for the 5-HT2A receptors, affecting serotonergic transmission and therefore – numerous biological processes. The serotonergic system plays a crucial role in various cognitive aspects such as memory, attention, spatial navigation, and decision-making. The influence of psychedelics on various proteins that are of essential importance in neurobiological functions and their links to cognitive functioning remain unclarified, especially in naturalistic users (outside of the laboratory context). Accordingly, the aim of the study was to examine the cognitive functions of psychedelic users and the levels of selected neural proteins, along with analyzing their interrelations. Cognitive functions were measured in 46 psychedelics users using the Cogstate battery of behavioral tests (GML, GMR, IDN, OCL, SETS, TWOB, DET). Protein analyses were performed in blood plasma using xMAP technology with simultaneous quantitative determination of multiple proteins in a single sample. Some cognitive function parameters showed significant correlations with the protein concentration: GMR with BDNF, PDGF-AB, and NRG1B1, SETS corelated with BDNF and PDGF-AB, and OCL with BDNF. This study is the first to demonstrate the links between these proteins and the cognitive tests of the Cogstate battery. No statistically significant differences were found between the users and non-users group in terms of the results of cognitive function tests. The number of lifetime psychedelics uses correlated only with BDNF levels. The results might indicate that psychedelics are relatively safe in terms of long term changes in cognitive functioning, but further research is required to confirm these findings.

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ELECTROPHYSIOLOGICAL STUDY OF VISUAL PROCESSING IN PSILOCIN-INDUCED HALLUCINATIONS: EXPLORING EVOKED POTENTIALS AND 5-HT2A RECEPTOR INVOLVEMENT

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Hallucinations are a distinctive feature of the action of 5-HT2A agonist psilocin. Despite growing interest, the underlying mechanisms remain poorly understood. In this study, we employed a series of various visual stimuli evoking EEG potentials to study the functional processing pathways. Three different visual stimuli, each targeting specific cell types and neural pathways involved, were used: the motion-onset, pattern-reversal and flickers to test magnocellular, parvocellular and general multiple pathways, respectively. To disentangle the contribution of 5-HT2A receptors, subjects were also pretreated with the selective 5-HT2A receptor antagonist MDL 100907. Psilocin dose-dependently decreased P1 peak of motion-onset stimuli as well as decrease the P1 peak of flashes. However, did not affect P1 peak of pattern-reversal stimuli. The response showed to be region-specific, corresponding to the functional areas involved. Surprisingly, effects were not blocked by pretreatment with the MDL 100907 as expected. The findings indicate a pivotal role of 5-HT2A receptors in modulating visual processing during psilocin effects, particularly in the magnocellular pathway, crucial for perceiving motion. These insights may contribute to understanding hallucinatory states in psychiatric disorders like schizophrenia and Parkinson's disease.

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THE EFFECT OF LOW DOSES OF PSILOCYBIN ON CORTICAL NEUROTRANSMISSION AND ITS IMPLICATIONS IN PSYCHOSIS

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Clinical studies provide evidence that psilocybin might be used as a fast-acting antidepressant, however, it's mechanisms and toxicity are still not fully understood. Moreover, *via* the activation of the 5-HT2A receptor, this drug can potentially induce a psychotic episode in treated individuals. The aim of this study was to determine the effects of low doses of psilocybin on rat cortical neurotransmission. Moreover, its effects on psychosis-associated behavior and molecular changes were assessed in comparison to selected reference drugs. The study was conducted on male Wistar-Han rats. The animals were treated with single doses of ketamine (10 mg/kg), psilocybin (0.1, 0.3, or 0.6 mg/kg), 25I-NBOMe (1 mg/kg), or MDMA (10 mg/kg). The cortical levels of dopamine, serotonin, glutamate, GABA, and acetylcholine were measured using microdialysis in freely moving animals. The effect on sensorimotor gating was assessed with the prepulse inhibition test (PPI), while the relative activation of the 5-HT2A receptor was examined with the wet-dog shake (WDS) test. The genotoxic effect in the frontal cortex (FCX) and hippocampus (HP) was assessed with comet assay. Psilocybin dose-dependently increased extracellular levels of examined neurotransmitters (except for the glutamate). Moreover, it dose-dependently shifted the GABA/Glutamate ratio in comparison to both control and group treated with selective 5-HT2A agonist, 25I-NBOMe. It induced a significant, but not numerous number of WDS episodes in rats. The highest dose of psilocybin didn't affect the startle response in the PPI test and didn't induce oxidative damage in the FCX and HP.

Funding: This research was funded by the National Science Centre grant no. 2020/37/B/NZ7/03753.

SYMPOSIA SESSION XIII – UNTANGLING NEURAL CIRCUITS SUPPORTING SPECIFIC BEHAVIOR

26th April, 2024 (Friday), 15:15–17:00

Speaker: Bianca Silva (15:15–16:00)

Institute of Molecular and Cellular Pharmacology, French National Centre for Scientific Research, Université Côte d'Azu, Valbonne, France

Chair: Anthony Kischel

Anthony Kischel (16:00–16:12)
Katarzyna Hryniewiecka (16:12–16:24)
Aleksandra Nogaj (16:24–16:36)
Jakub Mlost (16:36–16:48)
Oskar Markkula (16:48–17:00)

BRAIN CIRCUITS FOR MEMORY UPDATE

Bianca Silva

Institute of Molecular and Cellular Pharmacology, French National Centre for Scientific Research, Université Côte d'Azu, Valbonne, France

How are consolidated memories modified on the basis of experience? In this project we aimed to unravel the neural mechanisms at the basis of memory update. Understanding this biological process allows us to decipher how new information is constantly incorporated into existing memory, how a newly formed memory is integrated into previous knowledge and how the fine balance between memory stability and memory flexibility is maintained. By using fear memory extinction as a model of memory update, we combined neuronal circuit mapping, fiber photometry, chemogenetic and closed-loop optogenetic manipulations in mice, and showed that the extinction of remote (30-day-old) fear memories depends on thalamic nucleus reuniens (NRe) inputs to the basolateral amygdala (BLA). We find that remote, but not recent (1-day-old), fear extinction activates NRe to BLA inputs, which become potentiated upon fear reduction. Both monosynaptic NRe to BLA, and total NRe activity increase shortly before freezing cessation, suggesting that the NRe registers and transmits safety signals to the BLA. Accordingly, pan-NRe and pathway-specific NRe to BLA inhibition impairs, while their activation facilitates fear extinction. These findings identify the NRe as a crucial BLA regulator for extinction, and provide the first functional description of the circuits underlying the experience-based modification of consolidated fear memories.

AMOTL1 KNOCK-OUT MOUSE: A NOVEL MODEL OF MANIA

Anthony Kischel

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The angiomotin family, composed of AMOT, AMOTL1, and AMOTL2, has been discovered to regulate angiogenesis by organizing the tight junctions, thereby establishing the cell polarity. The functions of angiomotins in the brain remain widely unknown. AMOT has been proposed to regulate dendritic spine development and dendritic tree complexity. Our current project is focused on AMOTL1's role in neurons. We have performed a panel of behavioral tests on AMOTL1 KO mice. Mutant mice exhibit locomotor hyperactivity in the open field, increased risk-taking behavior, turning behavior, and hypersensitivity to low doses of amphetamine, a compound that increases synaptic dopamine levels. Interestingly, AMOTL1 KO mice exhibit episodes of backward walking, usually induced in rodents by the administration of hallucinogenic drugs. Altogether, our results show that AMOTL1 KO mice recapitulate many features of Mania models and show a function of AMOTL1 in the brain for the first time.

Funding: NCN grant Opus 2019/33/B/NZ3/02528.

THE ROLE OF TCF7L2 TRANSCRIPTION FACTOR IN THE FUNCTION OF THE THALAMO-CORTICAL CIRCUITS

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TCF7L2 is a high-confidence risk gene for neurodevelopmental disorders (NDs), but its role in their pathogenesis is unknown. It is highly expressed in the thalamus – a candidate structure for NDs pathogenesis – regulating its electrophysiological maturation. To understand the role of thalamus-expressed Tcf7l2 in signal processing in thalamo-cortical circuits, we investigated consequences of its deficiency in the somatosensory circuit: first- and higher-order thalamic nuclei (VPM and POM) and the barrel cortex. Tcf7l2 postnatal thalamic knockout mice were used to assess signal gating mechanism *in vivo* (with prepulse inhibition paradigm and Neuropixels recordings). Moreover, we measured spontaneous miniature postsynaptic currents *in vitro*. Male knockout mice showed gating deficits across all considered areas – VPM ($t_{(11)}$=2.73, $p<0.01$); cortical layer 4 ($t_{(17)}$=2.22, $p<0.05$); 5 ($t_{(22)}$=2.17, $p<0.05$); 6 (U=23, $p<0.0001$), and POM ($t_{(57)}$=2.63, $p<0.01$). In females, minor differences were observed in VPM ($t_{(30)}$=2.13, $p<0.05$) and cortical layer 5 ($t_{(25)}$=2.31, $p<0.05$). Patch-clamp showed that the frequency of mIPSC was greatly decreased in VPM (U=66, $p<0.0001$), while neurons of cortical layers 4 (U=22, $p<0.01$) and 6 ($t_{(13)}$=2.51, $p<0.05$) showed frequency decrease in mEPSC. TCF7L2 deficiency in thalamic neurons leads to signal processing impairments in thalamo-cortical circuits. While the deficit in inhibitory activity in the thalamus is congruent with the impairment of gating, the decrease of excitation in cortical neurons might indicate the presence of compensatory mechanisms.

Funding: NCN OPUS 19 2020/37/B/NZ4/03261.

OXYTOCIN AND RELAXIN-3 SIGNALLING INTERPLAY IN THE VENTRAL CA3 – NEUROPHYSIOLOGICAL AND MOLECULAR STUDIES IN RATS

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Oxytocin (OXT) and relaxin-3 (RLN3) play crucial roles in regulating social behavior, stress responses, and anxiety. Research suggests KCNQ potassium channels involvement in both excitatory OXT and inhibitory RLN3 signaling. Receptors for OXT (OXTR) and RLN3 (RXFP3) are expressed by ventral hippocampal CA3 area (vCA3) neurons, known for the involvement in social behavior and anxiety control. However, the potential interplay between OXT and RLN3 in modulating vCA3 activity remains unexplored. Fluorescence in situ hybridization (ISH) identified the neurochemical profile of OXTR and RXFP3 mRNA-expressing neurons in the vCA3. Our findings revealed that the majority of OXTR-positive neurons also expressed vGAT1 mRNA, and a subset of these co-expressed RXFP3 mRNA. Interestingly, RXFP3 mRNA was found in both inhibitory (vGAT1+) and excitatory (vGlut2+) vCA3 neurons. *Ex vivo* multielectrode array (MEA) and patch-clamp recordings demonstrated that OXTR activation had an excitatory, while RXFP3 activation had an inhibitory effect on vCA3 neurons. Importantly, both effects were attenuated by XE-911, a selective KCNQ blocker. Our findings suggest that OXT/OXTR and RLN3/RXFP3 signaling exert opposing effects on subpopulations of vCA3 neurons through differential modulation of KCNQ channels. Further studies are warranted to elucidate how these interactions contribute to behavioral outcomes.

Funding: The National Science Centre Poland (UMO-2018/30/E/NZ4/00687; UMO-2023/49/B/NZ4/01885).

THE ROLE OF PROJECTION SPECIFIC SEROTONERGIC PATHWAYS FROM DORSAL RAPHE NUCLEUS IN MODULATING BEHAVIOR: INSIGHTS FROM BEHAVIORAL TESTS AND NEURAL ACTIVITY MAPPING

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The intricate interplay between serotonin (5-HT) neurotransmission and specific neural circuits plays a crucial role in regulating various behavioral responses. Here, we investigate the role of distinct serotonergic projection pathways originating from the dorsal raphe nucleus (DRN) in modulating behavior, focusing on projections to the basolateral amygdala (BLA), ventral tegmental area (VTA), and lateral hypothalamic area (LHA). Using a combination of behavioral tests, including the elevated plus maze (EPM) and open field test (OFT), coupled with chemogenetics and *in vivo* calcium imaging in SERT-cre mice, as well as advanced machine-learning techniques, we explore the behavioral outcomes resulting from selective manipulation of these pathways. We have established increased activity of serotonergic neurons projecting to BLA, VTA and LHA by fiber photometry, when the animals spend time in the open arms of EPM. We have also discovered that chemogenetic inhibition of neurons projecting to BLA elicits changes in exploratory behavior and anxiety-like behavior. Unsupervised learning classifier technique allows us to cluster a number of stereotypic behavioral motifs in OFT that can be modulated by a specific chemogenetic modulation of distinct serotonergic projections. Our findings delineate the role of projection-specific serotonin pathways in shaping different behavioral responses and highlight the nuanced functional neuroanatomy of DR.

Funding: Polish National Agency of Academic Exchange BPN/BEK/2021/1/00152 and SciLifeLab RED Postdoctoral Fellowships fund.

NEURAL CORRELATES OF SOUND-LOCALIZATION DEFICITS ASSOCIATED WITH SPINOCEREBELLAR ATAXIA TYPE 13 (SCA13)

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SCA13 patients exhibit an extracerebellar auditory phenotype characterized by sound localization deficits, despite normal audiograms. This phenotype is caused by the R420H point mutation in the KCNC3 gene which encodes for Kv3.3 subunits of high-voltage gated potassium channels. Here, we investigate how this mutation leads to disruption of temporal processing along the auditory pathway. The R420H mouse model was created using CRISPR-Cas9. Whole-cell patch-clamp electrophysiology and afferent synaptic stimulation in acute mouse brain slices were used to characterize neural firing properties of affected auditory neurons. Degrees of neurodegeneration were assessed *via* cell number, cell size, p62/cleaved caspase expression and subcellular distribution of Kv3.3. In contrast to cerebellar Purkinje neurons, auditory brainstem neurons survive in age-matched SCA13 mice. Action potential (AP) half-widths of lateral superior olive (LSO) neurons increased in duration by around 2–3 fold. Recovery from refractory periods between APs were insufficient and this prevented the characteristic high-frequency AP following in response to synaptic train inputs. Co-immunolabelling of Kv3.3 protein with the vesicular glutamate transporter protein (VGluT1) and neuronal glycine transporter protein (GlyT2) indicated expression of Kv3.3 in excitatory and inhibitory synapses, respectively. The largely prolonged AP duration in LSO neurons disrupts high-frequency firing which likely contributes the sound localization deficits observed in the human kindred of SCA13. The survival of LSO neurons in 6-month old homozygote mice are in stark contrast to the loss of Purkinje neurons in the same mice and may provide a target to investigate neuroprotective mechanisms in degenerative disease models.

SYMPOSIA SESSION XIV – FACE PERCEPTION AND ITS APPLICATION IN AUDIOVISUAL INTEGRATION

26th April, 2024 (Friday), 15:15–17:00

Speaker: Maria Ida Gobbini (15:15–16:00)
Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

Chair: Ilona Kotlewska

Ilona Kotlewska (16:00–16:15)
Magdalena Szmytke (16:15–16:30)
Maria Nalberczak-Skóra (16:30–16:45)

ROLE OF NATURALISTIC STIMULI TO INVESTIGATE THE NEURAL MECHANISMS FOR FACE PERCEPTION AND RECOGNITION

Maria Ida Gobbini
Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

For decades the face perception system has been investigated with well-controlled stimuli that are still images of strangers' faces limiting the potentiality of characterizing such system in all its complexity. My talk will focus on two major points: the use of naturalistic stimuli to investigate the neural system for face perception and the use of familiar faces to better depict the individual components of this system. I will present fMRI data collected during movie viewing that were used to estimate multiple category-selective topographies including the face selective topography preserving the idiosyncracies of each individual functional brain architecture. I will highlight also how, through the use of naturalistic stimuli, we have shown that, so far, the human face perception system cannot be fully modelled by the state-of-the-art DCNNs. Recognition of familiar faces is remarkably effortless and robust. Automatic activation of knowledge about familiar individuals and the emotional responses play crucial roles in familiar face recognition. I will present data that show how familiarity affects the earliest stages of face processing to facilitate rapid, even preconscious detection of these highly socially salient stimuli, and present data that support the hypothesis that representation of personally familiar faces develops in a hierarchical fashion through the engagement of multiple levels in the distributed neural system from early visual processes to higher level of social cognition and emotion.

LOOKING AT OURSELVES: SELF-FACE RECOGNITION INVOLVES A THETA-BAND NETWORK OF POSTERIOR AND MIDFRONTAL BRAIN AREAS

Ilona Kotlewska[1]*, Bartłomiej Panek[1], Anna Nowicka[2], Dariusz Asanowicz[1]
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Self-related visual information, especially one's own face and name, are processed in a specific, prioritized way. However, the spatio-temporal brain dynamics of self-prioritization have remained elusive. In an EEG study, 25 married women (who changed their surnames after marriage, so that their past and present surnames could be used as stimuli) performed a detection task with faces and names from five categories: self, self from the past, friend, famous, and unknown person. The aim was to determine the temporal and spatial characteristics of early electrophysiological markers of self-referential processing. Local theta power at the occipito-temporal (visual) areas and inter-regional theta phase coherence between the visual and midfrontal areas showed that self-relevance differentiation of faces began already about 100-300 ms after stimulus onset. Posterior theta activity revealed an early signal of self-face recognition.

Funding: NCN Poland 2022/45/B/HS6/01107.

AUDIOVISUAL SPEECH INTEGRATION IN INFANCY: THE ROLE OF FACE ORIENTATION

Magdalena Szmytke[1,2]*, Ilyka D.[3], Duda-Goławska J.[4], Laudańska Z.[4], Malinowska-Korczak A.[4] and Tomalski P.[4]

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Humans pay special attention to faces and speech from birth, but the interplay of developmental processes leading to their specialization is poorly understood. We investigated the effects of face orientation on audiovisual (AV) speech perception in two age groups of infants (younger: 5- to 6.5-month-olds; older: 9- to 10.5-month-olds) and adults. We recorded ERPs in response to videos of upright and inverted faces producing /ba/ articulation dubbed with auditory syllables that were either matching /ba/ or mismatching /ga/ the mouth movement. In younger infants and adults, but not in older infants, we observed increased amplitude of audiovisual mismatch response (AVMMR) to incongruent visual /ba–auditory /ga/ syllable in comparison to other stimuli. AV mismatch response to inverted visual /ba/–auditory/ga/ stimulus relative to congruent stimuli was also detected but only in the younger group of infants and in adults. We show that face configuration affects the neural response to AV mismatch differently across all age groups. This may imply featural face processing in younger infants and adults when processing inverted faces articulating incongruent speech. The lack of differential responses to upright and inverted incongruent stimuli in older infants suggests a likely functional cortical reorganization of AV speech processing.

Funding: Polish National Science Centre, Grant/ Award Number: 2016/23/B/HS6/03860; Institute of Psychology, Polish Academy of Sciences.

AUDIOVISUAL INTEGRATION IN GENERATION OF AUDITORY HALLUCINATIONS

Maria Nalberczak-Skóra*, Aleksandra Bartnik, Aleksandra Olechowska, Łukasz Gawęda

Experimental Psychopathology Lab, Institute of Psychology, Polish Academy of Sciences

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Audio-visual integration plays a big role in better understanding of the world around us. We tend to hear better when we see it and we better see it when we hear it. Sometimes this phenomenon leads to experiencing illusions like sound-induced flash illusion (SiFi) or McGurk's effect. It is theorized that audio-visual integration is a top-down process involved in the generation of hallucinations, a positive symptom of numerous psychiatric disorders including schizophrenia. The research from our laboratory show that audio-visual integration is strongly associated with false perception of the speaking words in both healthy and clinical population. Here, I will present the results from a study investigating neural correlates of the experience of false perception of speaking word and how it is associated with congruent facial expressions of this word.

Funding: The project is financed by National Science Center as SONATINA-5 2021/40/C/HS6/00226.

SYMPOSIA SESSION XV – EXPLORING NEW DRUGS FOR BRAIN THERAPY

26th April, 2024 (Friday), 15:15–17:00

Speaker: Sara Xapelli (15:15–16:00)
Institute of Pharmacology and Neuroscience, Faculty of Medicine, University of Lisbon, Lisbon, Portugal

Speaker: Nicolas Singewald (16:15–16:45)
Department of Pharmacology and Toxicology, Institute of Pharmacy and CMBI, LFU, Innsbruck, Austria

Chair: Sara Xapelli

Angelika Jagielska (16:00–16:15)
Judith Schweimer (16:45–17:00)

DECODING ANTIDEPRESSANT PATHS: FROM CANNABINOIDS TO PHYSICAL EXERCISE *VIA* POSTNATAL NEUROGENESIS REGULATION

Sara Xapelli
Institute of Pharmacology and Neuroscience, Faculty of Medicine, University of Lisbon, Lisbon, Portugal

Chronic stress poses a significant risk for neuropsychiatric conditions such as depression. Adult hippocampal neurogenesis (AHN) has emerged as a promising target for alleviating stress-related disorders. Recent research highlights the interplay between cannabinoids and neurotrophic factors in regulating AHN, influencing cognitive plasticity and emotional flexibility. This study explores the synergistic effects of modulating cannabinoid type 2 receptors (CB2R), devoid of psychotropic effects, and physical exercise (PE) in chronically stressed animals. Contrary to CB2R activation, CB2R inhibition combined with PE improves stress-induced emotional and cognitive changes. This combined approach enhances AHN dynamics, and induces an overall reduction in neuroinflammation. The findings underscore CB2Rs as critical regulators, revealing a potential therapeutic framework for countering chronic stress effects through lifestyle interventions coupled with endocannabinoid pharmacomodulation.

EPIGENETIC MODIFICATIONS IN MENTAL DISORDERS AND THEIR POTENTIAL AS PHARMACOLOGICAL TARGETS

Nicolas Singewald
Department of Pharmacology and Toxicology, Institute of Pharmacy and CMBI, LFU, Innsbruck, Austria

There is accumulating evidence that epigenetic mechanisms, such as DNA methylation, histone modifications, and non-coding RNAs, play a contributing role in dysregulated gene expression patterns and brain circuitry dysfunction associated with various neuropsychiatric disorders. One idea is therefore to explore novel pharmacological interventions ("Epipsychopharmacology") that can modulate epigenetic modifications to restore normal gene expression and circuitry function in these conditions. This involves drugs that target enzymes regulating epigenetic modifications, such as histone deacetylases (HDACs), DNA methyltransferases or utilizing non-coding RNA molecules. In the talk I will discuss the potential of targeting epigenetic mechanisms in anxiety-and trauma-related disorders and will use therapeutic improvement of impaired fear-inhibitory extinction learning as an example. This phenotype is common in PTSD and specific anxiety disorders and is considered an important contributor to treatment resistance in exposure-based therapies. We show that deficits in the formation of fear extinction memories in mice can indeed be normalized by modifying different epigenetic mechanisms. Enhancing histone acetylation *via* HDAC inhibitors was critical to stabilize the newly built extinction memory in the long-term. Neurons in brain areas known to mediate extinction showed particular increases in histone acetylation and modified activity patterns. Recently, first human exposure ther-

apy trials using repurposed drugs with HDAC inhibitor action have started. Although this research field is still evolving and important challenges including safety, drug specificity and efficacy remain to be further investigated, these findings indicate new ways for the development of improved treatment strategies to overcome treatment-resistance in extinction-driven therapies.

EVALUATING NLX-101, A 5-HT1A RECEPTOR BIASED AGONIST, IN MITIGATING IMPAIRMENTS OF COGNITIVE FLEXIBILITY IN MICE

Angelika Jagielska[1,2]*, Aleksandra Koszałka[1,2], Klaudia Lustyk[1], Marcin Kołaczkowski[3], Adrian Newman-Tancredi[4], Karolina Pytka[1]

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Cognitive flexibility, a key executive function, is compromised in individuals with depression, hindering therapeutic goals. This study aimed to investigate the potential of NLX-101, cortical 5-HT1A receptor biased agonist known for antidepressant-like and procognitive effects, in mitigating the impairment of cognitive flexibility induced by the administration of MK-801, an NMDA receptor antagonist. Using a two-choice pairwise visual discrimination and reversal task in male BALB/c mice, we demonstrated that NLX-101 did not affect the percentage of correct responses. However, at a lower dose, the compound decreased the number of correction trials on the fifth day of the reversal phase compared to the group receiving MK-801. The study suggests while the activation of the ERK 1/2-related signal transduction pathway following 5-HT1A receptor stimulation may be beneficial, it might be insufficient to completely reverse cognitive flexibility impairments caused by NMDA receptor blockade.

FROM CIRCUIT BIOLOGY TO PRECISION PSYCHIATRY: FINDING NOVEL TREATMENT OPTIONS AT BOEHRINGER INGELHEIM

Judith Schweimer

Boehringer Ingelheim Pharma GmbH & Co. KG, CNS DR, Biberach, Germany

At Boehringer Ingelheim, we are embracing a patient-centric approach which includes improved patient stratification, identifying innovative targets within the brain and advancing novel chemical, biological and digital approaches in order to find new treatment options for neuropsychiatric conditions. We are offering several possibilities to collaborate and accelerate drug discovery through our Open Science programmes. This includes sponsoring research groups through initiatives like BioMed X, but also our opnMe platform. Via this platform, we offer free Molecules to Order (M2O), as well as Molecules for Collaborations (M4C), these are research grants related to specific compounds and broader grants for scientific questions that we are interested in (opn2EXPERTS). In CNS DR, our research focuses on the patient aiming to better understand and target the maladaptive brain circuitry that underlies the major untreated symptom domains. This is aiming to bring increasing precision to the treatment of psychiatric disorders both pharmacologically and digitally. Precision psychiatry is a novel approach to identify the right patient for the right treatment by connecting symptoms to specific brain-circuit dysfunctions, therefore enabling treatment to target the underlying neurobiological processes.

SYMPOSIA SESSION XVI – AUTOMATIZATION IN BEHAVIORAL STUDIES – A KEY TO OBJECTIVITY

27th April 2024 (Saturday), 10:00–11:30

Speaker: Aleksandra Badura (10:00–10:40)

Department of Neuroscience, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands

Chair: Patrycja Ziuzia

Veronika Kovarova (10:40–10:52)
Patrycja Ziuzia (10:52–11:04)
Julia Świderska (11:04–11:16)
Anjaly Yadav (11:16–11:28)

USE OF MULTI-PARAMETRIC ASSAYS TO CAPTURE SEX- AND ENVIRONMENT-DEPENDENT MODIFIERS OF BEHAVIORAL PHENOTYPES IN AUTISM MOUSE MODELS

Aleksandra Badura

Department of Neuroscience, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands

Current phenotyping approaches for murine autism models often focus on one selected behavioral feature, making the translation onto a spectrum of autistic characteristics in humans challenging. Furthermore, sex and environmental factors are rarely considered. I will discuss our latest work in which we aimed to capture the full spectrum of behavioral manifestations in three autism mouse models to develop a "behavioral fingerprint" that takes environmental and sex influences under consideration. To this end, we employed a wide range of classical standardized behavioral tests and two multi-parametric behavioral assays: the Live Mouse Tracker and Motion Sequencing (MoSeq), on male and female Shank2, Tsc1 and Pcp2-Tsc1 mutant mice raised in standard or enriched environments. We found that most behavioral phenotypes were dependent on sex- and environment. Furthermore, multi-parametric behavioral assays enabled far more accurate classification of experimental groups compared to classical tests. Together, our results provide a complete phenotypic description of all tested groups, suggesting multi-parametic assays can capturing the entire spectrum of the heterogenous phenotype in autism mouse models.

HOME CAGE MONITORING OF INDIVIDUAL AND SOCIAL BEHAVIOR IN MODELS OF STRESS-INDUCED PSYCHIATRIC PATHOLOGIES

Veronika Kovarova[1,2]*, J. Bordes[1], J. van Bergen[1], L.M. Brix[1,2], M. Springer[1], H. Yang[1], S. Narayan[1], S. Mitra[1], L. van Doeselaar[1,2], M.V. Schmidt[1]

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Stress-related psychiatric pathologies impose a substantial societal burden, characterized by a high prevalence and an ongoing challenge in finding effective treatments, particularly for depression. The complexity of these disorders is often also compounded by co-morbidities with metabolic disturbances. Investigating animal behavior in this context has historically been intricate, particularly in translating findings to human studies. However, with the advent of machine learning methods and the introduction of advanced algorithms, unprecedented possibilities have emerged for phenotyping animals. My research focuses on leveraging supervised and unsupervised deep learning methods, employing tools such as DeepLabCut and DeepOF. Through these techniques, I aim to demonstrate an elevated proficiency in characterizing animal behavior

at the level of both individual and social interactions. Additionally, by conducting long-term observations of experimental animals, I demonstrate how these methods can discern nuanced variations in social behaviors that might go by conventional tests.

Funding: This project is funded by: die Deutsche Forschungsgemeinschaft (DFG).

DEPRESSIVE-LIKE BEHAVIOR IN MICE: CLASSICAL *VS.* MODERN APPROACHES IN BEHAVIORAL STUDIES AND THE ROLE OF ASTROCYTE-SPECIFIC GLUCOCORTICOID RECEPTOR KNOCK-OUT

Patrycja Ziuzia[1,2]*, Bartosz Zglinicki[1], Laura Bergauer[3], Michał Ślęzak[1]

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General approach in investigating major depressive disorders (MDDs) is to find the relationship between selected genes and the phenotype, both in the biological and behavioral context. Disruptions in social interactions represent a characteristic feature across various psychiatric diseases, including depression. In MDD, one of the key features is disturbed hypothamalus-pituitary-adrenal (HPA) axis functioning, leading to increased concentration of secreted glucocorticoids (GCs) in the bloodstream and hyperactivation of glucocorticoid receptors (GRs) and affecting the stress response regulation mechanism. In the previously done classical behavioral tests, we noticed that CSDS caused expected alterations in the anxiety and social interaction of CTRL mice, but expected changes were not seen in mice with GR astroKO. Current project involved long-term observations of unknown conspecifics of male mice: wild type (C57Bl/6J background) and mutant (Aldh1l1-CreERT2 x GRflox/flox, C57Bl/6J background) with induced by chronic social defeat stress paradigm (CSDS) depressive-like behavior. Experiment, that was conducted in specially designed arenas indicating semi-naturalistic environment, shown a similar tendency in mice stress-response behavior, what may indicate that astrocytes are an important site of GR-dependent response in the central nervous system.

Funding: NCN OPUS grant 2021/41/B/NZ3/04099 'AstroSyCo' and HE Twinning 'SAME-NeuroID' grant No: 101079181.

MAKING DECISIONS: NOVEL METHOD FOR EXPLORING SPATIAL CHOICES

Julia Świderska[1]*, Lali Kruashvili[1], Błażej Ruszczycki[2], Filip Polański[1], Katarzyna Radwańska[1]

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Most aspects of animal behavior are based on decisions. One of the most extensively researched type of decisions is spatial choice – that uses spatial information to suppress inappropriate behaviors. The population activity of place cells in the dCA1 area underlies spatial choice and memory. Place cell activity can be recorded when an animal is freely moving throughout the space. However, in the majority of studies on spatial choices, behavior is investigated with protocols that require direct involvement of the researcher. Additionally, traditional tools used for assessment of spatial choice do not have required dimensions to monitor changes within place cells' activity using genetically encoded, and relatively slow, calcium indicators. Here, we present a new system for monitoring mice activity and navigation with our recent findings on behavioral protocol that can be employed within it. This apparatus is built of integrated modules including camera system, cue display system, liquid reward dispensers and door control system. Animals are tested within 3 connected corridors, parted with automatic doors, where they can roam undisturbed and consume reward (sweet milk) at the end of reward arms from automatic dispensers. The automation of our task enables evaluation of spatial choices without the researcher's direct involvement. Additionally, an open construction of the maze allows for recording of the brain cell activity of a freely moving mouse with the use of a miniature microscopy and optogenetic tools along with recording of the animal's behavior within the entire space.

Funding: This work is supported by the National Science Centre Grant 2020/38/A/NZ4/00483 to K. Radwańska.

EXPLORING THE ROLE OF PRELIMBIC CORTEX ON SHIFTING FROM OUT-GROUP TO IN-GROUP INTERACTIONS

Anjaly Yadav[1]*, F. Haque[2], M. Kalinowska[1], M. Rycerz[1], A. Bryksa[1], Alicja Puścian[1]

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Identifying individuals from one's social group as in-groups members happens quickly and automatically, without conscious effort. Studying the neural mechanisms behind this phenomenon can be enhanced by conducting behavioral experiments that simulate naturalistic social interactions. We present a novel method to investigate social bond formation between two groups of mice, who are genetically identical, however, unfamiliar. Mice were housed in Eco-HAB, an automated naturalistic environment, for 21 days. Initially, the habitat was divided into two sections, allocating each group its own territory for 7 days. Subsequently, the groups were combined, enabling unrestricted interaction. Our results reveal an initial preference for familiar group members after merging, followed by a shift towards interacting more with unfamiliar animals. Social dynamics then evolved, with some mice maintaining original preference for familiar mice and others forming new bonds. Notably, activating PV cells chemogenetically in the prelimbic cortex reduced voluntary interactions with both, familiar and unfamiliar mice. In summary, our study offers insights into the behavioral and neural processes of merging two separate groups into a cohesive social entity. These discoveries pave the way for deeper exploration of the neuronal mechanisms involved in forging new social bonds.

SYMPOSIA SESSION XVII – MICROGLIA IN HEALTH AND DISEASE

27th April, 2024 (Saturday), 10:00–11:30

Speaker: João Relvas (10:00–10:45)
Institute for Research and Innovation in Health (i3S) – University of Porto, Portugal

Chair: Izabela Lepiarz-Raba

Izabela Lepiarz-Raba (10:45–11:00)
Natalia Małek (11:00–11:15)
Natalia Stelmach (11:15–11:30)

MICROGLIA FUNCTION: INSIGHTS FROM THE CYTOSKELETON

João Relvas
Institute for Research and Innovation in Health (i3S) – University of Porto, Portugal

The actin cytoskeleton dynamically controls many different aspects of cell biology. Its reorganization likely underlies critical microglial function(s), including phagocytosis, process extension required for surveillance and synaptic interactions, and whole-cell migration notably towards pathological foci. The ubiquitously expressed GTPases of the Rho family, including the most well-characterized members RhoA, Rac1, and Cdc42, are critical orchestrators of cytoskeleton reorganization, making them essential players to govern microglial function. Recent studies from our lab highlighted essential and distinct roles for RhoGTPases RhoA and Rac1 in controlling the microglial cytoskeleton and function. While RhoA balances microglial reactivity during neuroinflammation, and its ablation in adult microglia results in microglia dysfunction leading to neurodegeneration, Rac1 is required for crucial microglia-synapse crosstalk driving experience-dependent plasticity. During my talk, I will present and discuss these and other recent unpublished data related to regulation of microglia function by the actin cytoskeleton.

IMPACT OF LIPID METABOLISM ON MICROGLIAL PHAGOCYTOSIS OF AMYLOID-BETA

Izabela Lepiarz-Raba[1]*, Taufik Hidayat[1], Weronika Tomaszewska[1], Sandra Binias[2], Bartłmiej Gielniewski[2], Jacek Miłek[3], Magdalena Dziembowska[3], Ali Jawaid[1]

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Alzheimer's disease (AD), the leading cause of dementia, is characterized by abnormal accumulation of amyloid-β (Aβ) in the brain. Aβ clearance is primarily the function of microglia, the brain-resident immune cells that are highly sensitive to environmental stimuli and respond to homeostatic changes *via* altering the release of inflammatory cytokines and phagocytosis. These functional adaptations in microglia are intricately linked to their metabolism, which provides a unique opportunity to harnessing microglial phagocytosis for selective Aβ clearance in AD without substantially harming healthy neurons. To investigate this further, we tested Aβ phagocytosis in HMC3 human microglia after various metabolic manipulations. Starving HMC3 microglia of lipids *via* delipidation of the medium, as well as, overall nutrients through serum starvation increased the uptake of Aβ. However, efficient degradation of the internalized Aβ was only observed upon lipid starvation, whereas only a minor fraction of the Aβ internalized upon serum starvation degraded over 24 hours. Furthermore, both lipid and serum starvation induced transcriptomic changes in HMC3 microglia in molecular cascades relevant to cholesterol biosynthesis, sterol response element binding factors (SREBF) signalling and steroid metabolism. Notably, knock down of SREBF2 abolished the effect of lipid starvation on Aβ phagocytosis by HMC3 microglia without impacting their phagocytosis of healthy neurosynaptosomes. These results represent microglial SREBF signalling as a novel therapeutic target in AD that can be targeted

for preferential microglial clearance of Aβ. *In vivo* validation of these findings, as well as, clinical correlations based on serum samples from AD patients are subjects of our ongoing investigations.

THE INFLUENCE OF CB2 ACTIVATION ON THE REGULATION OF THE CALCIUM-DEPENDENT PYROPTOTIC PATHWAY IN MICROGLIA

Natalia Małek

Department of Chemical Biology and Bioimaging, Wroclaw University of Science and Technology, Wroclaw, Poland
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Microglia, as integral immune cells within the central nervous system (CNS), play a pivotal role in maintaining immune balance in response to infections or injuries. However, prolonged activation of microglia can lead to neuroinflammation, with microglial pyroptosis emerging as a potential contributor to neuronal inflammation. Despite this, research on microglial pyroptosis remains limited, prompting our investigation into the activation of NLRP3 pathways in these cells. Therapies for microglia-derived neuroinflammation are lacking, yet modulation of cannabinoid receptor type 2 (CB2) shows promise. While the exact mechanism of CB2 agonists in exerting anti-inflammatory effects is unclear, recent research highlights the involvement of inflammasomes, particularly the NLRP3 inflammasome. Our study aimed to elucidate the downstream targets of CB2 stimulation within the canonical and non-canonical components of the NLRP3 inflammasome pathway. Using a murine cell line lacking CB2 receptor expression, we observed that CB2 agonist treatment reduced microglial pyroptosis and neuroinflammation induced by inflammatory stimuli. Specifically, we observed decreased expression of Caspase 4, indicative of involvement of the non-canonical pyroptosis pathway in the absence of CB2 signaling. Furthermore, we detected increased and prolonged calcium influx in the absence of CB2 receptor, leading to activation of the calpain-dependent pyroptotic pathway. Additionally, CB2 activation resulted in reduced release of IL-1β and IL-18, characteristic of pyroptosis, suggesting a neuroprotective role for CB2 receptor stimulation in mitigating NLRP3 inflammasome-mediated pyroptosis in microglia.

Funding: Supported by the National Science Center, Poland grant OPUS 2020/37/B/NZ7/03411.

INFLAMMATION'S IMPACT ON 20S PROTEASOME IN MICROGLIAL CELLS: IMPLICATIONS FOR NEURODEGENERATION

Natalia Stelmach*, Wioletta Rut, Marcin Drąg, Natalia Małek-Chudzik

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Proteostasis is crucial for maintaining the proper synthesis, folding, and degradation of proteins within cells. Disruption of this balance can contribute to the development of neurological conditions characterized by the formation of inclusion bodies, such as Alzheimer's and Parkinson's disease. The dysregulation of proteostasis can be influenced by a decrease in the catalytic activity of the 20S proteasome, leading to the accumulation of various proteins and the promotion of chronic inflammation, particularly involving microglial cells. In this study, we examined how inflammation induced by lipopolysaccharide (LPS) activation affects the expression of the β1, β2, and β5 subunits of the 20S proteasome in a human microglial cell line (HMC3). Our investigation involved analyzing the transcriptome using RT-qPCR, the proteome *via* Western Blotting, and the activome using Activity Based Probes (ABP) staining. Transcriptomic analysis revealed upregulation of β1 and β5 subunits in the presence of LPS, while protein-level analysis showed elevated levels of β1 and β2 subunits along with a decrease in β5 subunit levels. Activome studies indicated higher activity of β1 and β2 subunits and lower activity of β5 in the presence of LPS, consistent with the protein-level findings. Our comprehensive investigation sheds light on the dynamic changes occurring during inflammation in microglial cell proteostasis, suggesting that targeting the activity of β subunits of the 20S proteasome could be a viable approach for therapeutic intervention in neurodegenerative diseases.

Funding: Supported by the National Science Center, Poland grant OPUS 2020/37/B/NZ7/03411.

SYMPOSIA SESSION XVIII – EEG CORRELATES OF CONSCIOUSNESS

27th April, 2024 (Saturday), 10:00–11:30

Chair: Marek Binder

Marcin Koculak (10:00–10:20)
Klaudia Krystecka (10:20–10:40)
Urszula Górska-Klimowska (10:40–11:00)
Anna Zofia Leśniewska (11:00–11:30)

TRACKING NEURAL CORRELATES OF CONSCIOUS CONTENT WITH COMPLEXITY

Marcin Koculak[1,2]*, Michał Wierzchoń[1,2]

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Identifying the brain mechanisms that support consciousness is one of the most challenging tasks that science faces today. In this project, we investigated whether currently available state of the art measures of consciousness can be used to study the variability of consciousness in healthy awake humans at rest. To achieve this goal, we created a suite of resting state conditions, from classical version where participants were not exposed to any stimulation and had either opened or closed eyes, up to watching short fictional stories that included a plot. We designed them to vary both sensory as well as non-sensory informational content. Collected data created a unique database of more than six hundred participants and total number of individual recording sessions exceeding 1600. Taken together, it formed a extensive database of high-quality EEG resting state data that to our knowledge does not have a precedence in publicly available datasets. We analysed the data with most popular complexity measures (Lempel-Ziv complexity, multiscale entropy, and detrended fluctuation analysis) to verify their claimed potential in tracking conscious activity in brain signals. We found that Lempel-Ziv complexity was the best at separating experimental conditions as well as scoring higher in those that were designed as containing more content. This was true for both increased sensory and conceptual information.

Funding: Financed from grants 2016/23/N/HS6/00844 and 2019/33/B/HS6/02233 awarded by the Polish National Science Centre.

NON-OSCILLATORY BRAIN ACTIVITY AS A POTENTIAL INDICATOR OF INFORMATION PROCESSING EFFICIENCY

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Temporal information processing (TIP) constitutes a base of our cognitive functioning. Little is known about the neuronal underpinnings of TIP, however it has been associated with gamma oscillations so far. Recently, researches have focused not only on the oscillatory, but also in non-oscillatory brain activity which reflects the quality of neural communications. Our study aimed to verify whether TIP efficiency is associated with specific EEG resting state cortical activity patterns. 84 young healthy subjects participated in this study. They underwent two tasks: temporal order judgement (TOJ) task to measure TIP efficiency and EEG resting-state to assess oscillatory and non-oscillatory brain activity. Based on the TOJ task, participants were classified into two groups with high and low TIP efficiency. The results revealed group differences in non-oscillatory component across the 30–80 Hz range in fronto-central topography. Participants with low TIP efficiency display higher levels of non-oscillatory component, which may reflect poorer quality and speed of neural processing.

Funding: Supported by National Science Centre, Poland, grant no. 2018/29/B/HS6/02038.

LOW GAMMA AUDITORY STEADY-STATE RESPONSE IS SENSITIVE TO LEVEL OF AROUSAL AND CONSCIOUSNESS DURING NATURAL SLEEP

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During sleep, the level of consciousness varies, but most of the time, we remain disconnected from auditory inputs. Auditory steady-state responses (ASSRs) have been shown to be sensitive to the level of arousal, but it remains unclear whether this effect is related to disconnection and/ or unconsciousness. In this study, we analyzed EEG responses to 25-55 Hz range chirp modulated stimulation in the group of 22 healthy volunteers, 18 of whom were participating in serial awakenings study (54 reports). We evaluated ASSRs with intertrial phase clustering (ITPC) from frontocentral channels. We found significant effects ($p<0.05$) of reduced ITPC values in the low gamma band range (37-43 Hz) from wakefulness to both N2 and N3 NREM sleep, but not to REM sleep, and from REM sleep to both N2 and N3 NREM sleep. Moreover, we found significant effects ($p<0.05$) of reduced ITPC values in 37-43 Hz band between no-dreaming *vs.* dreaming reports in which auditory experience was present, but not when it was absent (although the latter was not significantly differed from wakefulness). Overall, these results suggest that low gamma (about 40 Hz) ASSR is both sensitive to changes in the level of arousal (dropping in NREM sleep), and in the level of consciousness (decreasing during no-dreaming unconsciousness). The latter effect might be related to the functionality of the auditory pathway (disconnection). I will interpret these results in comparison to current literature and preliminary findings from a serial awakening intracranial EEG study, where we observed decreased delta and increased high gamma during dreams *vs.* no-dreams. The current findings strengthen the notion of low gamma ASSRs as a tool for reliable discrimination between levels of consciousness, suitable for clinical applications.

Funding: Opus grant, the National Science Center in Poland, 2018/31/B/HS6/03920.

EFFECTIVE CONNECTIVITY ANALYSIS DURING BRAIN ASSR RESPONSES IN DIFFERENT AROUSAL STATES

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As we transition to sleep, auditory perception weakens, with 40 Hz auditory steady-state responses (ASSRs) notably decreasing during reduced arousal states. However, the precise changes in network connectivity in cortical brain structures with diminished ASSRs remain unclear. To evoke 40 Hz ASSRs, we utilized series of rapid and periodical stimuli, click sounds series, each representing a slice of noise at 40 Hz and duration of 500 ms. These stimuli were presented to 22 healthy volunteers. Our project aimed to to investigate brain connectivity responses during wakefulness and sleep stages (N2, N3 NREM, and REM). EEG source-based effective connectivity analysis employed the direct transfer function (DTF) method, focusing on causal relations between signals. Isolating specific brain areas was essential for DTF analysis, including cortical networks crucial for consciousness maintenance, such as the ‚central area' and frontal-parietal connections. Analysis encompassed activity in resting-state networks (RSNs), including the default-mode network (DMN), salience network (SAL), central executive network (CEN), and the primary auditory cortex (AC). We hypothesize diminished information exchange regarding periodic auditory stimulation among RSNs during deep sleep, particularly in the anterior ROI during SWS. Additionally, we expect to observe heightened DMN activity during N1/REM phases and decreased activity when periodic auditory stimulation is present compared to SAL and CEN. SAL exhibited increased activity during N1/REM under ASSR, potentially facilitating DMN-CEN coordination. However, the precise role of the CEN in these dynamics remains uncertain. Our research sheds light on how the brain's connectivity responds to variations in periodical auditory stimuli processing across different arousal states. It aims to discern neuronal networks and investigate whether information propagation within them favors long-distance connections or local circuits.

Funding: Project funded by the NCN n. 2018/31/B/HS6/03920; Principal investigator: dr hab. Marek Binder and NCN n. 2018/31/G/HS6/02490; Principal investigator: dr hab. Mirosław Wyczesany.

SYMPOSIA SESSION XIX – NEUROENDOCRINE BRAIN

27th April, 2024 (Saturday), 12:00–13:30

Speaker: Michael Greenwood (12:00–12:40)

Molecular Neuroendocrinology Research Group, Bristol Medical School: Translational Health Sciences, University of Bristol, Bristol, United Kingdom

Chair: Savani Anbalagan

Svenja Leibnitz (12:40–12:52)
Julian Zacharjasz (12:52–13:04)
Natalia Konopinska (13:04–13:16)
Naveen Nedunchezhian (13:16–13:30)

DYNAMIC INTEGRATION OF INGESTIVE BEHAVIORS AND HOMEOSTASIS BY MAGNOCELLULAR NEURON GUT PEPTIDE RECEPTORS

Michael Greenwood

Molecular Neuroendocrinology Research Group, Bristol Medical School: Translational Health Sciences, University of Bristol, Bristol, United Kingdom

The magnocellular neurones (MCNs) in the hypothalamus make the peptide hormones arginine vasopressin (AVP) and oxytocin (OXT) and release them peripherally into the blood circulation from nerve terminals in the posterior lobe of the pituitary gland (PP), and centrally from dendrites and axon collaterals. Once secreted, these peptides modulate physiological parameters such as blood osmolality, blood pressure and blood glucose by acting on specific receptors to maintain homeostasis. There is a resurgence in interest in mechanisms regulating AVP and OXT release, which stems from clinical associations with body mass index, and consequently diabetes, obesity, and metabolic syndrome. When we eat a meal the gut releases hormones, aptly grouped as gut peptides, to control the amount of food and fluid we ingest by acting on specific receptors to promote a feeling of fullness. Interestingly, MCNs express receptors for gut peptides GLP-1, GIP and CCK at nerve terminals in the PP, and I will present our data on how those receptors integrate signals from circulating gut peptides.

OXYTOCIN DEFICIENCY – A NEW PITUITARY DISORDER IN PATIENTS WITH VASOPRESSIN DEFICIENCY?

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Oxytocin deficiency is emerging as a potential pituitary disorder in patients with vasopressin deficiency, currently known as central diabetes insipidus. Vasopressin is vital for renal water reabsorption, and its inadequate secretion leads to polyuria and polydipsia. However, despite adequate treatment, patients often experience residual psychological symptoms, such as heightened anxiety and alexithymia, reduced empathy, and impaired social interaction. Both vasopressin (AVP) and oxytocin, nine-amino acid neuropeptides, are released from axon terminals projecting to the posterior pituitary. Disruption of the hypothalamic-pituitary axis leading to AVP deficiency can also impact the oxytocin system, which is crucial for regulating socio-emotional functions such as attachment, fear extinction, emotion recognition, and empathy. Given this evidence, psychopathological manifestations in AVP-deficient patients could be due to a concomitant oxytocin deficiency. Since measuring oxytocin at baseline and during standard pituitary provocation tests is not useful, we recently investigated MDMA as a stimulation test and found a significantly lower increase in oxytocin and the absence of oxytocin-induced effects compared to healthy controls. Our ongoing randomized, placebo-controlled, double-blind study is investigating the potential benefits of intranasal oxytocin in AVP deficiency. Our results could lead to a new therapeutic approach improving psychological symptoms and socio-emotional functioning of patients with vasopressin deficiency.

DYNAMICS OF NON-CODING RNAS EXPRESSION IN THE POSTANTAL MOUSE PITUITARY

Julian Zacharjasz*, Ewelina Kałużna, Marta Sztachera and Monika Piwecka

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Non-coding RNAs (ncRNAs) are RNA molecules that are not translated into proteins, however they play vital role in the regulation of gene expression driving cell fate and stimuli response. How non-coding RNAs such as long non-coding RNAs (lncRNAs), circular RNAs (circRNAs) or microRNAs (miRNAs) are involved in regulation of gene expression programs in different cell types within the pituitary gland still lack comprehensive understanding. We hypothesize that cell-type specific ncRNA are essential contributors to gene expression regulation in the pituitary in different stages of development. We investigated ncRNA expression patterns in mouse pituitary and identified >4000 lncRNAs and >400 circular RNAs in adult pituitary. Additionally, we identified miRNAs that are dynamically regulated over postnatal pituitary development (neonatal, around puberty and adult) and created a resource of stage-specific miRNAs. We evaluate the spatial expression pattern of selected ncRNAs using RNA in situ hybridization methods and spatial transcriptomics.

Funding: NCN, Opus (2021-2024) – project „Non-coding RNAs at single-cell resolution in the pituitary gland and their role in the regulation of gene expression".

FUNCTIONAL HOMOLOGY OF TACHYKININ SIGNALING: IMMUNOMODULATORY PROPERTIES OF INSECT TACHYKININ-RELATED PEPTIDES AND MAMMALIAN SUBSTANCE P

Natalia Konopińska*, Słocińska M., Urbański A.

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Invertebrates and vertebrates have a significant number of physiological similarities. Neuropeptides, which are synthesized and secreted by the neuroendocrine system, are known to play a crucial role for both. One of the largest families of neuropeptides found throughout the animal kingdom are tachykinins (TKs). In insects, neuropeptides showing structural similarity to TKs are tachykinin-related peptides (TRPs). They are involved in neuronal depolarization, processing of chemosensory information and nociception. Interestingly, there is strong functional and structural homology between substance P (SP, one the of mammalian TKs) and insect TRPs, e.g., both neuropeptides have anti-apoptotic properties. Also, our latest results revealed many similarities between immunomodulatory action of these neuropeptides. Moreover, SP can activate insect TRP receptor. Our comparative research can be successfully used in the search for new models to study hormonal regulation of many processes occurring in humans. They will also enrich knowledge about neuroendocrinology, immunology, and entomology.

Funding: OPUS 2021/41/B/NZ9/01054.

ROLE OF GLIAL PITUICYTES IN NEUROHYPOPHYSEAL SYNAPTIC MORPHOGENESIS

Naveen Nedunchezhian[1]*, Savani Anbalagan[1,2]

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Neurohypophysis (posterior pituitary) is a major neuroendocrine interface in the brain through which water homeostasis is maintained. Neurohypophysis majorly consists of glial pituicytes, neuropeptides oxytocin- and vasopressin-loaded synapses and permeable capillaries. We recently identified that pituicyte-derived secreted factors can regulate neurohypophyseal neurovascular morphogenesis. However, the role of other secreted factors expressed in the neurohypophysis in the neurovascular morphogenesis is unknown. Towards this goal, we have been employing pharmacological and genetic perturbations to explore the roles of candidate molecules that could regulate neurohypophyseal synapse morphogenesis. Our studies of the glial pituicytes are expected to reveal novel players in the development of a key neuroendocrine interface conserved in vertebrates.

Funding: NCN SONATA BIS (2020/38/E/NZ3/00090).

SYMPOSIA SESSION XX – OPENFUS

27th April, 2024 (Saturday), 12:00–13:30

Speakers: Marcin Lewandowski[1], Alan Urban[2] (12:00–12:40)

[1] *Company US4US, Instytut Podstawowych Problemów Techniki PAN, Warsaw, Poland*
[2] *VIB, KU Leuven, Belgium*

Chair: Alan Urban

Michiel Camps (12:40–12:52)
Nora Fitzgerald (12:52–13:04)
Klaudia Csikós (13:04–13:16)
Tianzi Wang (13:16–13:30)

OPENFUS: THE GATEWAY TO CUTTING-EDGE BRAIN ACTIVITY MAPPING WITH FUNCTIONAL ULTRASOUND IMAGING

Marcin Lewandowski[1], Alan Urban[2]

[1] *Company US4US, Instytut Podstawowych Problemów Techniki PAN, Warsaw, Poland*
[2] *VIB, KU Leuven, Belgium*

Ultrasound imaging is broadly utilized in medical diagnostics and has recently been extended to specific applications in pre-clinical research on small animals – e.g., functional US (fUS) for real-time monitoring of brain activity, focused US for neuromodulation and opening of the blood-brain barrier, and more. Instrumentation for these techniques is complex and requires programmable ultrasound hardware, dedicated probes, and advanced signal processing software. We have developed a family of research ultrasound platforms with open-source software providing support for the most popular languages: PYTHON, MATLAB, C++. Our systems can work with various probes (linear, annular, matrix) in the frequency range of 1-30 MHz. Real-time access to raw RF or I/Q data, support for ultrafast acquisition, and powerful GPU processing on raw data make the platforms a versatile tool for almost any application. Partnering with the community, we would like to develop software tools for selected pre- clinical applications. I will present a few application use-cases to prove how our platforms' features and functions can bring value to the open-science paradigm.

BRAIN-WIDE RESPONSES TO STIMULUS NOVELTY

Michiel Camps*, Clément Brunner, Micheline Grillet, Gabriel Montaldo, Alan Urban, Sebastian Haesler

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Novel sensory stimuli reliably evoke behavioral reactions in most animals, called orienting responses. While the process of habituation to these stimuli with repeated encounters is well studied, it is unclear how the novelty of a stimulus alone evokes an orienting response. Using volumetric functional ultrasound imaging (vfUSI), we study differences in neural responses to novel *vs.* familiar stimuli at a nearly whole-brain level in a spontaneous novelty detection paradigm. This allows us to identify regions modulated by stimulus novelty as well as characterizing how responses in those regions change during habituation.

FUNCTIONAL ULTRASOUND IMAGING IN DORSAL STREAM AREAS OF THE AWAKE BEHAVING MACAQUE

Nora Fitzgerald

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Functional ultrasound imaging (fUSI) is a promising neuroimaging method offering an exquisite spatio-temporal resolution. In this preliminary investigation, we performed a series of visual, passive fixation experiments in a rhesus macaque while acquiring fUSI images, achieving an in-plane voxel resolution of 100 µm and covering a 15 mm long sagittal plane over dorsal stream areas in the macaque. I will present preliminary data of a phase-encoding retinotopic mapping experiment, a category-localizer (including faces, bodies, objects, etc.), and an optic flow experiment, whereby cortical responses to different types of visual motion were compared. Our results revealed very localized and highly reproducible cerebral blood volume responses across days for the retinotopic stimuli and for some of the visual categories and optic flow stimuli. Our data suggest that fUSI will be highly instrumental to uncover the mesoscale functional architecture of cortical areas in the monkey, *via* a resolution not available through fMRI and by reaching regions not accessible by microscope-based neuroimaging methods.

ARE CORTICAL COLUMNS UBIQUITOUS? HIGH-RESOLUTION IDENTIFICATION OF FUNCTIONAL DOMAINS IN CAT CORTEX USING 3D FUNCTIONAL ULTRASOUND IMAGING

Klaudia Csikós[1,2]*, Ábel Petik[1,3], Domonkos Horváth[1,3], Fanni Somogyi[1,2], Attila Dobos[1], Gabriel Montaldo[4], Botond Roska[5], Alan Urban[4], Daniel Hillier[1,2,3]

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In the cortex of carnivore and primate model species, specific sensory features are encoded into functional maps. It remains unclear how the layout and interrelations of functional maps observed from surface layer activity generalize to deeper cortical layers. Cortical functional maps can be identified using electrophysiology with high temporal but spatially sparse sampling, impeding a holistic understanding of functional organization. Optical imaging can provide spatially extended sampling of cortical activity, but optical access is limited to about 1 mm depth, i.e., cortical layer 2/3 in large brains. FMRI provides information without tissue disruption albeit at limited resolution in space and time. To bridge the gap between established options for sampling brain activity, we applied functional ultrasound imaging to resolve the 3D structure of cortical functional maps. We performed longitudinal recordings from a large part of the cat visual cortex. We analyzed stability and spatial clustering of 3D architecture of functional domains across the visual cortex and seek to identify rules of interrelation between distinct functional maps. Comprehensive identification of the functional architecture in the visual cortex at balanced coverage and resolution provides a new perspective on the functional architecture in the visual cortex of large-brained species, extending the classical columnar view.

Funding: This work was supported by ELKH-POC-2021-026 grant, the Lendület ("Momentum") Programme of the Hungarian Academy of Sciences to DH as well as by project no.129120 that has been implemented with the support provided by the Ministry of Innovation and Technology of Hungary from the National Research, Development and Innovation Fund, financed under the FK18 funding scheme from the Ministry for Culture and Innovation from the source of the National Research, Development and Innovation fund.

ADVANCED FUNCTIONAL ULTRASOUND IMAGING AND BEHAVIORAL ANALYSIS SYSTEM FOR AUTISM SPECTRUM DISORDERS

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In light of the rising prevalence of neurodegenerative and neurodevelopmental disorders, this study endeavours to pioneer a comprehensive platform for characterizing multifactorial pathologies. With autism spectrum disorders (ASD) as a focal example, our approach aims to bridge the gap between animal models and human research by identifying potential functional biomarkers. We propose an integration of brain-wide functional ultrasound imaging (fUS) alongside sensory behavioral tests, coupled with advanced behavioral and functional connectivity analyses. Through this multi-dimensional framework, our goal is to pinpoint behavioral and brain-wide signatures of pathology, offering valuable insights into disease mechanisms. To reach this goal, I will explore differences in innate sensory behaviors and evoked sensory responses in brain-wide neural circuits and long-range correlated activity patterns (using volumetric functional ultrasound imaging, fUS) in Shank3B-/- and wt mice. Finally, I will utilise this integrated platform in assessing the efficacy of a pharmacological treatment on rescuing deviations in behavior and neural activity patterns.

SYMPOSIA SESSION XXI – HOW TO TRAIN THE BRAIN

27th April, 2024 (Saturday), 12:00–13:30

Chair: Tomasz Ligęza

Alicja Olszewska (12:00–12:18)
Aurimas Mockevičius (12:18–12:36)
Syanah Wynn (12:36–12:54)
Tomasz Ściepuro (12:54–13:12)
Gabriela Rajtar (13:12–13:30)

WHAT LEARNING TO PLAY THE PIANO TEACHES US ABOUT THE DYNAMICS OF TRAINING-RELATED NEUROPLASTICITY

Alicja M. Olszewska*, Maciej Gaca, Dawid Droździel, Artur Marchewka, Aleksandra M. Herman
Laboratory of Brain Imaging, Nencki Institute of Experimental Biology, Warsaw, Poland
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Musical training was frequently employed as a tool to study musical-training-related neuroplasticity for the past two decades. However, the dynamic nature of the neuroplastic processes remains less explored. Our research uniquely integrated longitudinal and cross-sectional designs to investigate the changes in brain activation of novice pianists. During the study, participants underwent up to seven functional magnetic resonance imaging (fMRI) sessions, allowing us to track brain activation changes at various time intervals. Novice pianists undertook twenty-six weeks of piano training and participated in a diverse range of in-scanner and behavioral musical tasks, such as music listening and playing with varying bimanual coordination demands, or performing a tonal working memory task. They were compared to a group of passive controls and a group of trained musicians. The results indicate that brain reorganisation occurs mainly in the motor system and is highly dependent on the task and its demands. The adaptations in auditory processing are subtler on the neural level and have no effects on tonal working memory. Noticeably, the observed time-courses are highly region-, timeframe- and task-specific. Thus, no single model of brain plasticity can fully explain the observed changes. These findings highlight the importance of ecological designs in studies on skill acquisition and the complexities of neuroplastic processes which underlie learning.

Funding: This study was supported by the National Science Centre (Narodowe Centrum Nauki) grant number 2018/30/E/HS6/00206.

INDIVIDUALIZED EEG-BASED NEUROFEEDBACK TARGETING AUDITORY STEADY-STATE RESPONSES: A PILOT STUDY

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Gamma-band (> 30 Hz) brain oscillatory activity is linked with sensory and cognitive processes and exhibits abnormalities in neuropsychiatric disorders. Therefore, neuromodulation techniques targeting gamma activity are being developed. One promising approach is neurofeedback (NFB) which is based on the alteration of brain responses *via* online feedback. However, the existing gamma-based NFB systems lack individualized approach. In the present work, we aimed to test an individualized EEG-NFB system. 46 healthy volunteers participated in three sessions on separate days. Before NFB training, individual gamma frequency (IGF) was estimated using periodic chirp-modulated auditory stimulation (30-60 Hz). Gamma-band responses were then targeted during NFB training, in which participants received auditory stimulation at IGF±2 Hz and were instructed to try to increase their response while receiving visual feedback. After training, IGF was reassessed. Experimental group participants were divided into equal groups based on the median success rate during NFB training. The results showed that high-responders had a significantly higher IGF modulation

compared to control group, while low-responders did not differ from controls. No differences in IGF modulation were found between sessions in all participant groups. The initial evaluation of the proposed EEG-NFB system showed potential to modulate IGF. Future studies could test short-term and long-term effects of the IGF-based NFB system in clinical populations.

Funding: Research Council of Lithuania (LMTLT agreement no. S-LJB-20-1).

PREDICTING INDIVIDUAL DIFFERENCES IN THE EFFICACY OF NON-INVASIVE BRAIN STIMULATION IN ALTERING MEMORY PROCESSES

Syanah C. Wynn[1,2,3]*, Christopher D. Townsend[3], Erika Nyhus[2]

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For successful memory, we need to retrieve information and evaluate its validity. The importance of theta oscillations (3-7 Hz) in memory is well established through electroencephalography (EEG) studies. For instance, there is an increase in theta power when items and their context are successfully remembered, and when people make confident memory decisions. While hippocampal gamma oscillations (>30 Hz) have also been linked to memory, the role of neocortical gamma remains largely unknown. The direct functions of oscillations can be investigated with non-invasive brain stimulation (NIBS) methods, like transcranial alternating current stimulation (tACS). In the current study, we used tACS to entrain frontal and parietal oscillations to theta (4 Hz) and gamma (50 Hz) frequencies, aimed to alter memory processes. Participants performed a verbal source memory task, while we recorded their brain activity with EEG (session 1) or manipulated this with tACS (sessions 2-4). With this memory task we measured: memory for words (item memory), memory for the encoding context (source memory), and memory confidence. Our EEG findings confirm and add to the proposed roles of endogenous theta and gamma oscillations in memory processes. In addition, we show how EEG correlates can predict individual differences in tACS effects on memory processes.

Funding: This work was supported by the National Institutes of Health (NIH) grant R15MH114190.

12-WEEK AEROBIC INTERVAL TRAINING IMPROVES DLPFC FUNCTION IN PATIENTS WITH PARKINSON'S DISEASE – RESTING STATE EEG STUDY

Tomasz Ściepuro[1]*, Karolina Lorek[1], Małgorzata Chalimoniuk[2], Sławomir Budrewicz[3], Magdalena Koszewicz[3], Zbigniew Wroński[4], Jarosław Marusiak[1]

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Individuals with Parkinson's disease (PD) experience motor and cognitive deficits, possibly due to impaired dopaminergic meso-cortical projections to key brain regions such as the primary motor cortex (M1) and the dorsolateral prefrontal cortex (DLPFC). While aerobic interval training (AIT) has demonstrated efficacy in alleviating both motor and cognitive symptoms of PD, the underlying neurophysiological mechanisms remain insufficiently explored. This study aimed to evaluate the impact of a 12-week AIT program on resting electroencephalographic (EEG) brain activity parameters in the frequency domain. Mild to moderate PD patients participated, with the trained group (PD-TR, n=14) undergoing a 12-week AIT program on a cycle ergometer in addition to usual care, and the non-trained group (PD-NTR, n=16) receiving only usual care. The AIT program comprised three 1-hour sessions weekly. Both groups were assessed in their medication OFF-phase before and after the AIT period. EEG recordings, employing a 128-electrode system during eyes-open resting states, were analyzed for electroencephalogram power spectral density (PSD-EEG) parameters. Comparisons between post- and pre-AIT testing sessions revealed a significant decrease in the power of the lower-alpha band in the left DLPFC for the PD-TR group. In contrast, the PD-NTR group exhibited

an increase in the mean power of the DLPFC's lower-alpha band. The AIT-induced reduction in lower-alpha band power among trained PD patients suggests a potential neurophysiological mechanism contributing to psychomotor improvements. Conversely, the slowing of EEG signals in the DLPFC of the non-trained group indicates a mechanism associated with further psychomotor impairment.

Funding: The work was supported by the National Science Centre, Poland, under research project no. 2017/25/B/NZ7/02795, entitled 'Effect of high intensity interval training on mechanisms of neuroplasticity and psychomotor behaviors in Parkinson's disease patients: a randomized study with 1-year follow up', awarded to Jaroslaw Marusiak.

THE EFFECT OF REGULAR AEROBIC EXERCISE ON COGNITIVE CONTROL: A LONGITUDINAL RANDOMIZED TRIAL

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Several studies indicate a promising interaction between regular exercise and cognitive benefits, particularly concerning inhibition – a crucial ability to suppress irrelevant thoughts and behaviors. This study explored the effects of regular exercise on both behavioral and neuronal aspects of inhibition using a Flanker task. Fifty-three sedentary young adults were randomly assigned to either an experimental group (EG, N=23) or a control group (CG, N=30). The EG participated in a six-week controlled cycling training program, with three workout sessions per week, while the CG maintained their usual habits. Before and after the intervention, participants completed the Flanker task concurrently with EEG recordings. The task required identifying the central arrow's direction while ignoring surrounding distractor arrows, in both congruent (e.g., <<<<<) and incongruent (e.g., <<><<) conditions. Findings revealed decreased standard deviations of reaction time for incongruent stimuli for AG relative to CG, indicating improved inhibition stability. Furthermore, EEG measures revealed that CG relative to AG exhibited greater conflict between congruent and incongruent stimuli as indicated by neural marker of inhibition N2 component, and suggesting heightened processing demands or greater difficulty in resolving conflict in the CG. Collectively, the results support the hypothesis that regular exercise might improve cognitive performance, particularly in tasks requiring inhibition.

Funding: The National Science Centre in Poland (project number 2021/43/D/HS6/02959).

SYMPOSIA SESSION XXII – NEUROIMAGING OF ABNORMAL BRAIN FUNCTIONS IN SCHIZOPHRENIA

27th April, 2024 (Saturday), 15:15–16:45

Speaker: Todd Woodward (15:15–16:00)
Department of Psychiatry, University of British Columbia, Vancouver, Canada

Chair: Przemysław Adamczyk

Rafał Skiba (16:00–16:15)
Wiktor Więcławski (16:15–16:30)
Camilo Enrique Sánchez (16:30–16:45)

A MACRO-SCALE TASK-BASED BOLD-SIGNAL NETWORK IMPORTANT FOR RE-EVALUATION AND DELUSIONS

Todd Woodward
Department of Psychiatry, University of British Columbia, Vancouver, Canada

Functional magnetic resonance imaging (fMRI) provides information about the flow of blood-oxygen-level-dependent (BOLD) signal in the brain. The fact that BOLD signal flow forms into reliable configurations is well established, referred to as macro-scale BOLD brain networks. Timing information from cognitive tasks can be used to constrained variance in BOLD signal, and when submitted to a dimensional analysis, this produces macro-scale BOLD brain networks which span many tasks, and their function can be determined be observing their activation patterns over a range of task conditions. In this way, task-based fMRI can be used to determine which brain networks are involved in the symptoms of schizophrenia. For example, a brain network involved in re-evaluation of evidence showed reduced activation in patients experiencing delusions, as did another involved in inspection of evidence. This combination of glossing over evidence and neglecting re-evaluation may underlie the jumping to conclusions and fixedness that characterize delusions. For patients experiencing hallucinations, we see hyperactivation of a superior temporal gyrus (STG) network involved in external auditory perception, and hypoactivation in a linguistic processing network (LPN) for internal processing. This combination may underlie the impaired balance between internal and external linguistic processes (underactivity in networks involved in internal auditory imagery and overactivity in networks involved in speech perception) leading to externalizations in hallucinations. However, this must be integrated with the evidence that the on-line experience of a hallucination does not produce the same BOLD brain activity as true auditory perception. This approach to understanding the function of the brain networks underlying the symptoms of schizophrenia can lead to insights regarding optimal treatment through therapy or neuromodulation.

EXPLORING THE INTERPLAY: NEGATIVE SYMPTOMS, COGNITION, AND METACOGNITION IN SCHIZOPHRENIA SPECTRUM DISORDERS

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In this presentation, I will delve into the nuanced dynamics between negative symptoms and cognitive functions in schizophrenia spectrum disorders (SSD). This segment dissects how distinct negative symptoms, such as alogia and flat affect, contribute to cognitive deficits, particularly verbal memory impairment. I will then discuss the linkage between working memory impairments and motor impoverishment, exposing the specific brain networks implicated in this interplay. Drawing on data from two extensive studies involving over 500 SSD patients, I will provide a detailed account of these symptom-cognition relationships. In the sec-

ond part of my talk, I will examine the interface between apathy, asociality and metacognition, offering a novel perspective on how SSD patients' metacognitive capacities are influenced by their emotional detachment and how they are represented in images of the working brain. Concluding the session, the talk will pivot to the implications of these findings for treatment, discussing potential interventions to mitigate cognitive impairments and their underlying symptoms.

Funding: Rafal M. Skiba received a Research Trainee Grant (RT-2021-1899) from the Michael Smith Health Research BC / BC Schizophrenia Society Foundation, which supported his work on this project.

DYSCONNECTIVITY OF THE CEREBELLUM AND SOMATOMOTOR NETWORK CORRELATES WITH THE SEVERITY OF ALOGIA IN CHRONIC SCHIZOPHRENIA

Wiktor Więcławski*, Krzysztof Bielski, Marek Binder, Przemysław Adamczyk

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Disturbances in the motor system are commonly present in schizophrenia. Recent fMRI resting-state findings show aberrant functional connectivity within somatomotor network (SMN) in schizophrenia. Currently, it is important to validate those findings and establish their relationship with psychopathology. Therefore, we decided to take an entirely data-driven approach in our fMRI resting-state study of 30 chronic schizophrenia outpatients and 30 matched control subjects. Utilizing independent component analysis (ICA), dual regression, and seed-based connectivity, we show hypoconnectivity within SMN in schizophrenia and SMN dysconnectivity with the cerebellum. The latter is strongly correlated with the intensity of alogia, i.e., poverty of speech. Our results are consistent with the theoretical approach to the role of the cerebellum in psychiatric disorders. The presented findings suggest that the cerebellum might play an important role in the persistence and severity of alogia in schizophrenia.

Funding: The study was supported by the National Science Centre Poland under grant no. 2016/23/B/HS6/00286 and 2021/41/B/HS6/02967.

THE TRIPLE NETWORK HYPOTHESES, TEMPORAL EXPERIENCE AND DISTURBED SENSE OF SUBJECTIVITY IN SCHIZOPHRENIA

Camilo Sanchez

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Recent functional connectivity studies showed that the increased synchrony between the right anterior insula and the default mode network are associated with psychosis. This association is proposed in the paper to be correlated with the disrupted dynamics between the implicit and explicit temporal experience in psychotic patients. The aim of the paper is to assess the relation between the functional connectivity findings, regarding the dynamics between relevant large–scale brain networks, and the phenomenological psychopathology findings, regarding the dynamics between the relevant temporal and bodily–movement experiences, in schizophrenia patients. The research question is: How is the relation between the functional dynamic activity of the right anterior insula, the Default Mode, Central Executive and Salience Networks, and the dynamic between the implicit and explicit temporal experience, in schizophrenia patients? To answer the question 7 schizophrenia patients (PANSS score≥ 40) and 7 healthy controls were scanned (resting-state fMRI) and interviewed. The scan conveyed two trials, in the first the participants were asked to keep their eyes closed without falling asleep (for 6 min 34 sec) and no stimulus was presented, in the second the participants were asked to keep their eyes open while a digital clock was presented in the screen (for 6 min 34 sec). Then, each participant had a semi-structured interview. The hypothesis is, there is a constitutive relation between the functional dynamics of these large–scale brain networks and these temporal, bodily experiences, which is out of synchrony in schizophrenia patients. Although the results are not conclusive probably due to the small sample and the linguistic limitations faced, nonetheless two main points of contrast involving the function of the insula and the patterns of synchrony of the triple network were elaborated. A phenomenological hypothesis is proposed to account for psychosis as a disturbance of the latter relation resulting in a disturbed subjectivity and sense of the body. A framework is proposed in terms of homeostasis and allostasis, integrat-

ing the functional connectivity dynamics, to account for the psychopathological manifestations.

Funding: Poznan University of Medical Sciences Doctoral School; STER Internationalisation of Doctoral Schools Programme from NAWA Polish National Agency for Academic Exchange No. PPI/STE/2020/1/00014/DEC/02.

SYMPOSIA SESSION XXIII – CELLULAR MECHANISMS OF PAIN AND TOUCH

27th April, 2024 (Saturday), 15:15–16:45

Speaker: Mateusz Kucharczyk (15:15–16:00)

Łukasiewicz Research Network–PORT Polish Centre for Technology Development, Wroclaw, Poland
Wolfson Sensory, Pain, and Regeneration Centre, King's College London, London, United Kingdom

Chair: Marek Brodzki

Felipe Meira de-Faria (16:00–16:15)
Basil Duvernoy (16:15–16:30)

SOMATOSENSATION AND CANCER NEUROSCIENCE

Mateusz Kucharczyk

Łukasiewicz Research Network–PORT Polish Centre for Technology Development, Wroclaw, Poland
Wolfson Sensory, Pain, and Regeneration Centre, King's College London, London, United Kingdom

Neuronal pathways travel from the brain to the spinal cord to influence somatosensation. They regulate spinal and primary sensory neuron activity, enabling the brain to finely tune signal levels transmitted through the spinal cord and govern the periphery *via* neurogenic mechanisms. Our laboratory's dual focus on the somatosensory system and cancer neuroscience seeks to uncover the system's involvement in neurogenic mechanisms governing tumorigenesis and related pain. Employing a combination of *in vivo* electrophysiology and calcium imaging with selective opto- and chemogenetic modulation of genetically and anatomically defined neuronal circuits, we sample the activity in the spinal and peripheral neurons and correlate this activity with behavioral responses using machine learning-supported analysis. We aim to link network-wide brain activity with top-down ability to influence both nociception and tumorigenesis. In this pursuit, we aspire to forge innovative therapies for cancer and associated pain, rooted in a deep understanding of neuronal systems.

BEYOND LABELS: UNDERSTANDING SENSORY NEURON SUBTYPES THROUGH LIVE IMAGING AND SINGLE-CELL SEQUENCING

Felipe Meira de-Faria

Laboratory of Sensory Perception Mechanisms, Center for Social and Affective Neuroscience, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden
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Peripheral sensory neurons (PSN) exhibit considerable diversity and specialization. These neurons are organized in pairs within the dorsal root ganglia (DRG) alongside the spinal cord, projecting their terminals to end organs. The anatomical distribution of PSN can be assessed through retrograde labelling, while DRG live imaging enables the investigation of bodily sensations' organization with real-time exploration of functional properties and dynamics across various PSN types. Concurrently, single-cell sequencing has transformed our understanding of cellular heterogeneity by capturing the transcriptomic landscape of each individual neuron. The integration of cell labelling and *in vivo* monitoring of PSN activities with their molecular profiles represents a powerful paradigm for comprehensively characterizing PSN populations. In my presentation, I will guide you through the intricacies of live imaging of PSN in mice and discuss how its integration with labelling and single-cell sequencing can help unravel the intricate details of sensory neuron subtypes.

EXPLORING THE RELATIONSHIP BETWEEN SKIN MECHANICS AND MECHANORECEPTORS' END-ORGAN IN HUMANS

Basil Duvernoy*, Ewa Jarocka, Emma Kinström, Anders Fridberger, Sarah McIntyre

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Tactile mechanoreceptors consist of neurons whose afferents innervate end-organs embedded in the skin. The characteristics of human mechanoreceptors are usually inferred from the properties of stimuli acting on the skin surface in human studies. Alternatively, insights are gained from animal studies where end organs can be isolated from the skin for direct stimulation and observation. However, these approaches fall short in capturing how the stimulus is altered as it traverses the various layers of the skin, essential information to understand the role of the skin, the end-organs structures, and their locations in the skin. In this presentation, we will introduce an imaging technique that enables the tracking of skin deformations in-depth *in vivo*. By combining this method with microneurography, we aim to demonstrate the neuronal responses of tactile mechanoreceptors in relation to skin deformations at the locations of end organs in humans, highlighting the relationship between skin mechanics, the end-organs structure, and their preferred locations in the skin.

Funding: Research supported by the Swedish Research Council, project grant to SM (2020-01085).

SYMPOSIA SESSION XXIV – READING BRAIN IN BLIND INDIVIDUALS

27th April, 2024 (Saturday), 15:15–16:45

Chair: Artur Marchewka

Anna-Lena Stroh (15:15–15:30)
Maksymilian Korczyk (15:30–15:45)
Małgorzata Paczyńska (15:45–16:00)
Maciej Gaca (16:00–16:15)
Jacek Matuszewski (16:15–16:30)
Cemal Koba (16:30–16:45)

BLIND INDIVIDUALS' ENHANCED ABILITY TO SENSE THEIR OWN HEARTBEAT IS RELATED TO THE THICKNESS OF THEIR OCCIPITAL CORTEX

Anna-Lena Stroh[1]*, Dominika Radziun[2,3], Maksymilian Korczyk[1], Laura Crucianelli[2,4], H. Henrik Ehrsson[2], Marcin Szwed[1]

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Blindness is associated with heightened sensory abilities, such as improved hearing and tactile acuity. Moreover, recent evidence suggests that blind individuals are better than sighted individuals at perceiving their own heartbeat, suggesting enhanced interoceptive accuracy. Structural changes in the occipital cortex have been hypothesized as the basis of these behavioral enhancements. Indeed, several studies have shown that congenitally blind individuals have increased cortical thickness within occipital areas compared to sighted individuals, but how these structural differences relate to behavioral enhancements is unclear. This study investigated the relationship between cardiac interoceptive accuracy and cortical thickness in 23 congenitally blind individuals and 23 matched sighted controls. Consistent with previous studies, we observed thicker occipital cortices in blind individuals. Moreover, we observed a significant positive correlation between performance in a heartbeat counting task and cortical thickness only in the blind group, indicating a connection between structural changes in occipital areas and blind individuals' heightened ability to perceive heartbeats.

Funding: This work was supported by the Polish National Science Centre (NCN; grant no: 2018/30/A/HS6/00595), the Swedish Research Council (VR; grant no: 2017-03135), and Göran Gustafsson Stiftelse. Laura Crucianelli was supported by the Marie Skłodowska-Curie Intra-European Individual Fellowship (grant no: 891175). The funding sources were not involved in the study design, collection, analyses, and interpretation of the data or in the writing of this paper. The authors declare no competing interests.

MIRROR INVARIANCE FOR OBJECTS AND MIRROR DISCRIMINATION FOR BRAILLE CHARACTERS IN PARIETO-OCCIPITAL CORTEX IN THE CONGENITALLY BLIND INDIVIDUALS

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Mirror-invariant phenomenon refers to the visual and tactile process of recognizing objects presented in mirror orientation as identical. In sighted individuals, the fusiform cortex is engaged in visual mirror invariance and mirror discrimination for letters. However, learning to read „breaks" mirror invariance for letters because mirror letters are recognized as different objects („d" *vs.* "b"). Only the parietal cortex is activated during tactile mirror invariance process. In congenitally blind individuals, abstract mirror shapes engage

the lateral occipital cortex. In this study, we aimed to investigate the neural underpinnings of mirror-invariant processing of tactile objects in congenitally blind individuals. Eighteen congenitally blind adults participated in the study. In the behavioral same-different comparison tasks and in the fMRI priming paradigm, we used pairs of Braille characters and everyday objects presented in identical („p"&"p"), mirror („p"&"q"), and different („p"&"z") orientation. Behavioral results showed no interference of orientation on the shape-judgment, either for Braille characters or everyday objects. FMRI results demonstrated a repetition suppression for identical and mirror pairs of everyday objects in parietal and lateral occipital cortex, with the latter region exhibiting repetition suppression only for identical Braille characters pairs. These findings together suggest that Braille characters are primarily processed as shapes in blind individuals.

REPRESENTATION OF PHYSICAL PROPERTIES OF WORD REFERENTS IN THE VISUAL CORTEX OF SIGHTED AND BLIND INDIVIDUALS

Małgorzata Paczyńska[1]*, Marta Urbaniak[2,3], Marta Dębecka[2], Łukasz Bola[2]

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Language processing involves similar brain regions across languages and cultures. Intriguingly, one population escapes this universal pattern: in blind individuals, linguistic stimuli activate not only the canonical language networks, but also the "visual" cortex. What is represented in the visual areas when blind individuals process language? To address this question, we performed an fMRI study in which we presented congenitally blind and sighted participants with spoken and written words. Using the representational similarity analysis, we showed that, in both participant groups, the visual cortex represents physical similarity between word referents, but not more abstract, conceptual similarity. This suggests that activations for language in the blind visual cortex might be driven by representational mechanisms that are present also in the sighted, adult brain. In sighted individuals, the physical properties of word referents might be backprojected to the visual system to predict incoming visual information, initiate visual imagery, and support visuospatial thinking. In blind individuals, this mechanism might be preserved and, when combined with weaker inhibition of activity in the visual cortex, drive strong responses to language in this region.

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TACTILE BRAILLE READING: INSIGHTS FROM BLIND AND SIGHTED INDIVIDUALS

Maciej Gaca[1]*, Alicja M. Olszewska[1], Dawid Droździel[1], Małgorzata Paplińska[2], Agnieszka Kulesza[1], Katarzyna Jednoróg[3], Jacek Matuszewski[1], Aleksandra M. Herman[1], Artur Marchewka[1]

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The human brain possesses an extraordinary capacity to reorganize itself in response to experience. In blind individuals, the occipital cortex undergoes substantial sensory tuning changes to process auditory or tactile inputs. Furthermore, recent neuroimaging studies show that tactile reading can engage the visual cortex of sighted subjects, providing an opportunity to investigate the limits of experience-dependent neuroplasticity. Here, we investigate tactile reading in blind and sighted individuals during a Lexical Decision Task to see differences and similarities in cross-modal plasticity between the groups. The fMRI analysis revealed high activity in both groups in the visual word form area (VWFA), underscoring its modality-independent role. There was a significant increase in activity in the reading network and sensory perception areas in blind participants compared to sighted. On the other hand, sighted individuals showed higher activity than blind individuals in regions associated with motor control and spatial navigation. The findings illustrate cross-modal plasticity, with visual processing areas repurposed for tactile input, enabling linguistic com-

prehension through tactile modality. This research contributes to our understanding of neuroplasticity, revealing converging adaptations in both the blind and the sighted. It highlights the flexibility of the human brain, advancing our knowledge of how sensory experiences shape cognitive processes.

Funding: The National Science Centre (Poland) – Sonata BIS (2018/30/E/HS6/00206).

SHARED REPRESENTATIONS FOR READING AND SPEECH IN THE OCCIPITAL CORTEX OF CONGENITALLY BLIND AND SIGHTED PEOPLE

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People born with sensory deprivation provide a fascinating "natural" model to study the brain's functional architecture. Previous studies showed that Braille and spoken words can activate portions of the blind occipital cortex typically responding to written words in vision. Whether written and spoken material co-activates similar regions and whether such activations are unique to blind people remains debated. Here, we used fMRI to probe brain responses to words, pseudowords and sensory control stimuli during reading and speech in 20 congenitally blind and sighted controls. Our results showed that while the blind early visual cortex (EVC) responded to simple sensory stimuli and linguistic information, activity in the left ventral occipitotemporal cortex (vOTC) was specific to Braille or spoken linguistic material. Similar patterns were observed in sighted subjects, with stronger activation for reading. Multivoxel pattern analyses showed that linguistic information in the EVC and vOTC can be decoded from the control conditions both in reading and speech in both groups. Crossmodal decoding analyses showed that reading and speech representations in vOTC might be partially shared in both sighted and blind. These results suggest that the crossmodal occipital reorganization for linguistic processing observed in blindness might be more quantitative, than qualitative.

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THE EFFECT OF BLINDNESS ON THE MACROSCALE ORGANIZATION OF THE BRAIN

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The cortex is organized along macroscale functional gradients that extend from unimodal (somatosensory/motor and visual) to transmodal association areas, and from somatosensory to visual areas. Whether this core organizing axis is an intrinsic organizational neuro-architecture immune to experience or, instead, depends on sensory input during development has not been tested. To this end, we conducted connectome gradient analyses based on resting-state functional magnetic resonance imaging (rs-fMRI) in congenitally blind (n=14) and late blind (n=11) individuals, comparing them to two groups of sighted controls (n=14, n=11, respectively) who were matched for age and gender. Compared to sighted individuals, congenitally blind individuals showed more extreme gradient values in both axes of the second gradient, which is formed on the visual-somatosensory plane. Our results suggest that blindness leads to dispersion in the sensorimotor-visual organization of the brain. Taken together, our findings provide important insights into the critical role of sensory input during development in shaping the macroscale cortical functional organization.

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POSTER SESSION I – BASIC NEUROSCIENCE

25th April, 2024 (Thursday), 13:15–14:30

TOWARDS OBJECTIVE CHARACTERIZATION OF THE CEREBRAL CORTEX CYTOARCHITECTURE: A DEEP-LEARNING WORKFLOW FOR IDENTIFYING AND SEGMENTING CORTICAL AREAS

Adam Datta[1]*, Agata Kulesza[1], Sylwia Bednarek[1], Marcello G. P. Rosa[2], Piotr Majka[1,2]

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Understanding how the cerebral cortex processes information requires identifying and characterizing its areal and laminar cytoarchitecture. Deep learning offers a promising avenue to address these challenges by streamlining manual segmentation and offering observer-independent insights into cortical structure. We propose a computational workflow for the segmentation of the cerebral cortex into layers and areas. The solution combines estimation of the neuronal density and size, extraction of one-dimensional cortical profiles starting from the pial surface and ending at the white matter, a convolutional deep-learning model that segments the profiles into layers and assigns them to the respective cortical area. We evaluated our solution on a dataset derived from a non-human primate – common marmoset monkey (*Callithrix jacchus*) brain. The model was trained to recognize the layers in cortical areas of a diverse cytoarchitecture. The evaluation revealed that the model's performance increases when the neuronal density and size estimates contribute to the training process, compared to only using the image intensity. Furthermore, the model performs noticeably better when the classification of the profiles to cortical areas is enabled. Beyond automating cortex segmentation into layers, our workflow offers possibilities for valuable insights into the cytoarchitectonic properties of the primate cerebral cortex.

Funding: NCN SONATA 2019/35/D/NZ4/03031.

DISTRIBUTION OF CALBINDIN-POSITIVE NEURONS ACROSS AREAS AND LAYERS OF THE MARMOSET CEREBRAL CORTEX

Piotr Majka[1]*, Nafiseh Atapour[2], Marcello G.P. Rosa[2], Shi Bai[2], Sylwia Bednarek[1], Agata Kulesza[1], Gabriela Saworska[1], Katrina H. Worthy[2]

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The calcium-binding protein calbindin is selectively expressed in specific neuronal populations of the cerebral cortex, including major classes of inhibitory interneurons. We have charted the distribution of calbindin-positive (CB+) neurons across areas and layers of the entire marmoset cortex using a combination of immunohistochemistry, deep-learning-based cell identification, 3-dimensional reconstruction, and cytoarchitecture-aware registration. CB+ neurons formed 10-20% of the cortical neuronal population, occurring in higher proportions in areas corresponding to low hierarchical levels of processing, such as sensory cortices. Although CB+ neurons concentrated in the supragranular layers, there were clear trends in laminar distribution: the relative density in infragranular layers increased with hierarchical level, and the density in layer 4 was lowest in areas involved in sensorimotor integration and action planning. These results reveal new aspects of the cytoarchitectural organization of the primate cortex and demonstrate an efficient approach to mapping the full distribution of neurochemically distinct cell types throughout the brain, readily applicable to most mammalian species and parts of the nervous system.

Funding: Funding was provided by the National Science Centre (2019/35/D/NZ4/03031 to Piotr Majka).

OBSERVER-INDEPENDENT WORKFLOW FOR CYTOARCHITECTURAL CHARACTERIZATION OF NEURAL TISSUE USING VARIATIONAL AUTOENCODER ARCHITECTURE

Julia Jakubowska[1]*, Sylwia Bednarek[1], Gabriela Saworska[1], Marcello G.P. Rosa[2] and Piotr Majka[1,2]

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Deciphering complex rules and patterns behind high-level mammalian brain functions requires understanding their structural underpinnings, including the cytoarchitectural characterization of the cerebral cortex. Traditional manual approaches for addressing these tasks are time-consuming and subject to researcher bias. Consequently, there is a growing demand for automated, observer-independent tools and workflows capable of objectively describing voluminous microscopic brain imaging datasets. We propose a general method based on a variational autoencoder, a generative model ensuring the continuity of its latent space, to explore and characterize the cytoarchitecture and generate synthetic images of neuronal cell somata following the identified properties. We demonstrate the feasibility of this approach using a dataset of images of neuronal cell bodies of the common marmoset monkey (*Callithrix jacchus*) brain. Applying explainability methods, we explored the encoder's latent space in the context of unsupervised clustering, where we observed cell segmentation according to their complex morphological features. We accessed the decoder part of the model, which generates neuron cells representatively reflecting their properties, such as shapes and intensities. We conclude that the proposed method may be suitable for characterizing the cytoarchitectural properties of large neuronal ensembles in various experimental contexts.

Funding: Funding was provided by the National Science Centre (2019/35/D/NZ4/03031 to Piotr Majka).

BEYOND EVENT-RELATED POTENTIALS: SEGMENTATION OF THE EEG SIGNAL TO ASSESS CORTICAL RESPONSE TO STIMULI

Marta Lotka[1,2]*, Jeremi K. Ochab[2]

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The event-related potential technique is commonly used to assess the time course of cortical response to stimuli in studies utilizing electroencephalography. Yet it has inherent limitations, including sensitivity to specific pre-processing choices and reliance on averaging the signal over trials. We propose an alternative to the ERP technique, utilizing an algorithm introduced by Camargo et al. (2011), which recursively divides the EEG time series into quasi-stationary segments. To argue for the utility of this new method, it will be compared with the ERP technique. Method validation will be presented, including both theoretical results and application to the ERP Core dataset.

SPECTRAL ANALYSIS AND PERIODICITY

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Periodicity is one of the commonly estimated features of time series, recorded in a variety of fields, as potentially reflecting the feedback loops present in the signal. Exploratory assessment of the relative contributions of these oscillations is the goal of the spectral analysis. The most popular approach, based upon the Discrete Fourier Transform (DFT), assumes the presence of a fixed number of equally spaced frequencies, and estimates their relative weights. If the signal contains a frequency outside of the set probed by DFT, its power will be spread between adjacent frequency bins. Alternative approaches are based upon the least squares spectral analysis, including "Gauss-Vanicek method" or "Lomb-Scargle periodogram". In some cases, the assumed model may suggest a special role of particular frequencies. For example, in the actigraphic data (recordings of human activity from an accelerometer) we are often looking for the oscillations represent-

ing the circadian rhythms, with a period equal or close to 24 hours. For such cases there are specialized estimators, one of which is the method called "cosinor". We will discuss the mathematical properties of these methods; in particular, we will show that in some cases the cosinor can be treated as a special case of the DFT.

Funding: This research was supported by the Polish National Science Centre, grant number UMO-2018/31/B/ST7/01888.

REAL-TIME IMAGING OF DOPAMINE RELEASE AND NEURONAL POPULATIONS DYNAMICS IN THE MOTOR CORTEX OF AWAKE MICE – DECODING OF REWARD-RELATED SIGNALS AND MOVEMENT PARAMETERS

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The motor cortex (MCtx) comprises circuits for voluntary movement control and motor skill learning. The proposed mechanism for motor learning and updating is dopaminergic modulation of local neuronal activity. Our study focused on D1 and D2 receptor-expressing cells in the MCtx, revealing segregated populations. We then investigated if there is a causal relationship between dopamine (DA) release and neuronal activity in these circuits during the development of skilled forelimb movements. We trained head-fixed mice to make self-initiated joystick movements to collect water rewards while simultaneously monitoring DA release and calcium dynamics in MCtx forelimb area using fiber photometry. We found that both DA fluorescence and neuronal calcium signals increased significantly after initiating joystick movement and receiving water rewards. Furthermore, animals' performance adapted to changes in task parameters (e.g., reward threshold), which were followed by changes in calcium fluctuations and DA concentration recorded in MCtx dopaminoceptive circuits. Finally, we demonstrated that systemic injection of selective DA receptor antagonists or cell-type specific optogenetic perturbations of D1+ and D2+ neurons in MCtx impairs task performance. Overall, our findings revealed a link between DA release and neuronal activity in dopaminoceptive circuits within MCtx in the development of skilled forelimb movements and evaluating their outcomes.

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AMOTL1 DEFICIENCY LEADS TO PERTURBATIONS OF DOPAMINERGIC SYSTEM IN MICE

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AMOTL1, a member of the Angiomotin family of scaffolding proteins renowned for their pivotal roles in cytoskeletal organization, cancer progression, and angiogenesis, presents an intriguing yet enigmatic facet in neurobiology. Despite its expression in the brain and synaptic localization, its precise functions remain largely unknown. To study a potential function for AMOTL1 in the brain we engineered a systemic AMOTL1 knockout (KO) mice, revealing a spectrum of aberrations reminiscent of schizophrenia and mania models. Subsequently, we developed several conditional AMOTL1 mutants with deletions confined solely to neurons, specific neuronal subsets, or discrete brain regions. Detailed behavioral profiling of these strains, complemented by brain anatomical studies and analysis of cultured primary neurons, unveiled the indispensable functions of AMOTL1 in the central nervous system.

Funding: The research was supported by NCN grant OPUS 2019/33/B/NZ3/02528.

EXPLORING AMOTL2'S ROLE IN BRAIN DEVELOPMENT

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Angiomotins, which include AMOT, AMOTL1, and AMOTL2, are scaffolding proteins mainly studied for their role in regulating the Hippo signaling pathway and cancer. However, the function of Angiomotins in the CNS is widely unknown. AMOT has been reported to regulate dendritic outgrowth and spine formation. Our unpublished project shows that AMOTL1 KO mice are a new model of psychiatric disorders involving impaired dopaminergic transmission. However, AMOTL2 functions within the brain remain unexplored. Our initial findings showed that AMOTL2 is expressed in both progenitors and differentiated neurons, which suggests that it might have different roles at different stages in the development. To study AMOTL2 functions, we perform conditional deletion at the early stage of development using the Nestin-CRE mouse line (deletions in progenitors that give rise to astrocytes and neurons) and observed increases in cortical thickness in newborns and adult mice. In parallel, our mass spectrometry analysis of the AMOTL2 protein complex from neurons uncovered interactions with several synaptic proteins, suggesting a possible role in synaptic organization. Moreover, AMOTL2 deletion in cultured hippocampal neurons decreased spine density and impaired spine maturation. We now use molecular, cellular, and behavioral tools to better understand AMOTL2's functions in the brain.

Funding: This research was supported by NCN grant Opus 2022/45/B/NZ3/03688.

CATECHOLAMINERGIC RELEASE IN THE FOREBRAIN AFTER VENTRAL TEGMENTAL AREA AND LOCUS COERULEUS ELECTRICAL STIMULATION

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Ventral tegmental area (VTA) and locus coeruleus (LC) activity leads to dopamine (DA) and noradrenaline (NA) release in the forebrain, regulating similar physiological and behavioral functions. Interestingly, dopaminergic and noradrenergic systems display significant interplay at the level of both brain stem (LC-VTA) and forebrain. We aimed to identify the effects of VTA and LC activation on catecholamine release in the forebrain. We used fiber photometry to detect catecholamine release in the nucleus accumbens (NAc) and basolateral amygdala (BLA) in anesthetized male rats. To selectively detect DA and NA we used virally-induced expression of red fluorescent DA (rDA) and GPCR-activation-based NA (GRABNE) sensors in the NAc and BLA. To drive dopaminergic and noradrenergic activity we used electrical stimulation of the VTA and LC. Stimulation of the VTA induced robust phasic DA release in the NAc and BLA. Stimulation of the LC induced phasic NA signal in the BLA, with less significant NA release in the NAc. Surprisingly, activation of the VTA also evoked NA release, whereas LC activation led to robust phasic DA release in these structures. Here, we demonstrate that activation of the VTA or LC leads to both NA and DA release, suggesting complex LC-VTA-forebrain interplay.

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ORGANIZATION OF THE MITRAL LAYER OF THE MAIN OLFACTORY BULBS MAMMALS DIFFERENT ECOLOGICAL GROUPS

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The olfactory bulbs, among the brain's most ancient structures, are located rostrally and providing primary processing of olfactory information. They have a complex cytoarchitectonic organization. The olfactory bulbs of mammals different ecological groups were studied: the European mole (Talpa europaea), noctule bats (Nyctalus noctula), house mouse (Mus musculus), and treeshrew (Tupaia glis). The histological sections

(7-10 μ) were stained using the Nissl method (creosil violet or thionine). The mitral layer (ML) is functionally important. It includes the largest neurons and is separated from the glomerular layer by the external plexiform layer. Axons and dendrites extend from the mitral cell (MC) perikaryon with a complex synaptic organization. Primary dendrites, in contact with axons of olfactory receptor cells, form glomeruli. Secondary dendrites branch laterally from the perikaryon. The ML is well-defined in all species studied. Noctule MC are arranged in 2-3 rows and cause the greatest thickness of the ML. Mole and mouse mitral cells are mostly in one or rarely two rows, resulting in a layer thickness less than that of the noctule. The ML treeshrew has the largest neurons, which are arranged exclusively in a monolayer with the smallest thickness among the other species studied.

INVOLVEMENT OF D1 AND D2 RECEPTORS IN THE OLFACTORY BULB IN THE MODULATION OF MK801-INDUCED LOCOMOTION AND HIGH-FREQUENCY OSCILLATIONS

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NMDA receptor antagonists, such as MK801, produce hyperlocomotion and enhance the power of high-frequency oscillations (HFO) in many regions, including the olfactory bulb (OB). The OB contains dopamine (DA) receptors (D1R/D2R) and DA neurons which can modulate sensory processing. This study explores the influence of DA in the OB on locomotion and HFO after systemic MK801 administration in rats. Male Wistar rats received 0.15 mg/kg MK801 i.p. followed by local infusions of DA receptor agonists (SKF38393, quinpirole) or antagonists (SCH23390, eticlopride) into the OB. Effects on locomotion and HFO were recorded and analysed. Both DA agonists and antagonists elicited dose-dependent changes in MK801-induced locomotion. Although modulation of D1R/D2R did not significantly affect HFO power, a notable reduction in HFO frequency was observed after local infusion with a D2R agonist. Our findings reveal that DA receptors in the OB can modulate MK801-induced hyperactivation, with D2 receptor activation specifically reducing the frequency of HFO.

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EFFECTS OF THE M OPIOID RECEPTORS ACTIVATION IN THE VENTRAL TEGMENTAL AREA ON DOPAMINE RELEASE IN DIFFERENT SUBREGIONS OF THE NUCLEUS ACCUMBENS

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Reinforcing effects of opioids are associated with dopamine (DA) release in the forebrain resulting from disinhibition of the DA neurons in the ventral tegmental area (VTA) due to μ opioid receptors (MOR) activation on VTA-projecting and local GABA-ergic neurons. Indeed, systemic opioid administration increases dopaminergic activity, but this response is not uniform. In fact, MOR in the VTA are also expressed on some DA neurons as well as other cells. Such heterogeneity of VTA MOR expression is not well understood in context of DA release in the forebrain, as different DA neurons innervate different forebrain structures including nucleus accumbens (NAc) core and shell. We aimed to demonstrate the role of the MOR in the VTA in modulating phasic DA release in different subregions of the NAc. We used fast-scan cyclic voltammetry (FSCV) in anesthetized male Sprague-Dawley rats to study electrically evoked DA release after intra-VTA micro-infusions of selective MOR agonist (DAMGO). Different sites of FSCV recordings were used to discriminate MOR effects on phasic DA release in NAc subregions. Intra-VTA DAMGO had limited effect on phasic DA release in the NAc. Several analysis were performed to demonstrate potential DAMGO effects depending on the recording site within the NAc.

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BRIGHTEN UP DOPAMINE: ASYMMETRICAL STRIATAL DOPAMINE RELEASE IN RESPONSE TO LATERALIZED VISUAL STIMULATION – *IN VIVO* STUDY

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The midbrain dopaminergic system is involved in control of animals' orienting movements and reactions to relevant environmental stimuli. The activity of midbrain dopaminergic neurons (DA) is influenced by retinorecipient superior colliculus (SC), a structure engaged in visual processing and sensory integration. Previous studies neglected impact of SC on dopaminergic neuron activity and DA release on the contralateral side of the brain, focusing primarily on the ipsilateral side. To address this research gap, our group first sought to characterize how dopaminergic neurons in the VTA/SNc respond to asymmetric retinal stimulation during SC disinhibition. As a further step, we aimed to explore the resultant changes in dopamine release within the striatum, which are presented in the current study. Our approach combined *in vivo* fiber photometry recording of striatal dopamine release with SC pharmacological disinhibition and asymmetrical light stimulation of the animal's eyes. Interestingly, we observed differences in both the level and dynamics of striatal dopamine release evoked by monocular stimulation between the hemispheres contralateral and ipsilateral to the stimulated eye. Our findings significantly broaden our understanding of sensory input lateralisation, and how it can modulate the activity of DA system, providing further information on learning, motivation, and decision-making processes.

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HOW LATERALIZED ILLUMINATION OF THE EYES INFLUENCES THE RESPONSES OF MIDBRAIN DOPAMINERGIC NEURONS IN RATS

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Light affects animals' circadian cycles, mood, perception and reactions to their environment. Retinal light information directly influences subcortical relay structures, which further distribute it within the brain. One example of such relay structures are the superior colliculi (SC), where information from various modalities is integrated and transmitted, among others, to the midbrain dopaminergic (DA) neurons within the ventral tegmental area (VTA) and substantia nigra pars compacta (SNc). Interestingly, in species like mice and rats – with lateralized eyes – a greater proportion of visual input to SC originates from the contralateral eye due to eye placement. Our study investigated VTA and SNc DA neurons activity, which is affected by lateralized illumination of the eyes of male albino rats anesthetized with urethane. After SC disinhibition with bicuculline microinjection, most of the recorded DA neurons exhibited responses to monocular light stimulation, showing differences when the ipsilateral or contralateral eye was stimulated in relation to the recording site. The proportion of excitatory and inhibitory responses, as well as the response dynamics (i.e., latency and duration), depended on whether the eye on the same or contralateral side to the recording site was stimulated. Observed differences in DA neurons response proportions and dynamics to lateralized stimuli may influence DA release in the basal ganglia, potentially shaping animal behavior and motivation.

EXPRESSION AND EFFECT OF RESISTIN ON GNRH LEVEL. IN VITRO STUDY ON MOUSE HYPOTHALAMIC GT1-7 NEURONAL CELL LINE

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Resistin is an adipokine involved in the regulation of lipid and glucose metabolism, adipogenesis and reproduction. Recent studies indicated an important role of resistin in maintaining brain homeostasis, but its role in the hypothalamus secretory function is still unknown. The aim of the present study was to examined firstly gene and protein expression of resistin and its receptors ROR1, CAP1 and TLR4, and then the effect of resistin on the viability, levels of PCNA (proliferating cell nuclear antigen) and GnRH in the mouse hypothalamic GT1-7 cells (*in vitro* model of GnRH-secreting neurons). The gene and protein expression of resistin, ROR1, CAP1 and TLR4 were analysed by real-time PCR, Western blot, and immunocytochemistry, respectively. GT1-7 cells were treatment with resistin (0.1, 1, 10 ng/ml) and cell viability was analysed using alamarBlue®, PCNA transcript expression, as well as gene and protein levels of GnRH by real-time PCR, Western blot, and ELISA. Statistical analysis employed one-way ANOVA, followed by Tukey›s test (n=5; $p<0.05$). The results showed the expression of gene and protein of resistin and its receptors as well as their co-localization with GnRH in GT1-7 cells. Additionally, the inhibitory effect of resistin on GT1-7 cells viability, PCNA transcript level and GnRH secretion were observed; with no effect on GnRH gene expression. Our results demonstrate for the first time expression of resistin system in mouse hypothalamic neuronal cells and its important role in the *in vitro* regulation of GnRH secretion.

EXPRESSION OF OREXIN RECEPTOR 2 AND GLUTAMATE RECEPTORS IN SELECTED CANCER CELL LINES

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Emerging evidence suggests a role for glutamate and orexins in cancer biology. The expression of nervous system-related receptors, including orexin receptors (OXR) and glutamate receptors (NMDA, AMPA), has been reported in several cancers. The effect of NMDA receptors has been shown to down-regulate the proliferation of lung cancer cells. In digestive cancers expressing OXR1, its activation has been shown to lead to cell apoptosis. On the other hand, a strong association between OXR2 expression and cervical cancer progression has been demonstrated, suggesting its potential as a therapeutic target. In this context, we aimed to determine the expression of OXR2 and AMPA receptors in selected melanoma (skin and uveal), thyroid and breast cancer cell lines. Melanoma cells are particularly predisposed to express these receptors as they originate from neural crest cells. Our results confirmed OXR2 expression in all melanoma, thyroid and breast cancer cell lines analysed. Expression of the AMPA receptor subunit – GluA1 was only detected in breast cancer cells and selected melanomas. To our knowledge, this is the first report of OXR2 expression in melanoma cells. As OXR2 expression has not been reported in melanocytes, it may play a role as a target in melanoma therapy.

ROLE OF SODIUM GLUTAMATE IN STRUCTURAL CHANGES OF HYPOTHALAMIC NUCLEI IN AN EXPERIMENT

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"Glutamate-induced obesity" is a term that has been causing scientists to debate for many years. Since the hypothalamic nuclei are responsible for energy and lipid metabolism, it was reasonable to analyze the morphological and morphometric changes in the hypothalamic nuclei under the influence of sodium glutamate

and its absence (in an experiment of white rats). The study material consisted of macro- and micropreparations of the hypothalamus of male Wistar rats. Sodium glutamate was administered orally to male rats once a day. Material sampling was carried out at 6, 8, 10, 12 weeks of the experiment. Analysis of histological sections stained with hematoxylin and eosin was performed. Large neurons were found in the dorsomedial and ventromedial nuclei of the hypothalamus with vacuolated perikaryon cytoplasm, hypochromic neurons and neurons with picnotic nuclei after prolonged administration of sodium glutamate. After discontinuation – the nuclei of certain neurons were picnotic, with some lysed nuclei. Long-term administration of sodium glutamate leads to deep changes in the microstructural organization of the hypothalamic nuclei in experimental animals, which are not compensated by discontinuation of the specified dietary supplement.

NEUROENDOCRINE REGULATION OF PORCINE PITUITARY CELLS FUNCTION: OMENTIN-1 EXPRESSION AND *IN VITRO* EFFECT ON TROPIC HORMONES SECRETION

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Omentin-1 (OMNT1) is a novel adipokine that mediates important anti-inflammatory, antioxidative, and anti-apoptotic effects. It also regulates endothelial dysfunction and reproduction. Our previous study discovered the OMNT1 gene and protein expression in the porcine anterior pituitary (AP) cells. Nevertheless, OMNT1's role in neurohormonal processes is unclear, so the present study aims to investigate OMNT1 localization and its impact on tropic hormone (GH, PRL, ACTH, TSH, LH, FSH) secretion in porcine AP cells. APs were isolated from mature pigs to explore OMNT1 co-localization with tropic hormones using immunohistochemistry. In *in vitro*, AP cells were treated for 24 h with OMNT1 at increasing doses of 10, 50, and 100 ng/ml combined or not with hypothalamic liberins to study tropic hormones mRNA and protein expression by RT-qPCR and ELISA, respectively. Statistical analysis employed one-way ANOVA, followed by Tukey's test ($n=5$; $p<0.05$). The results showed OMNT1 immunolocalization with tropic hormones (except ACTH) in AP cells. Also, OMNT1 (50 ng/ml) upregulated LH, FSH, PRL, and ACTH expression, while at 10 ng/ml, combined with TRH, it affected TSH, and at 100 ng/ml inhibited PRL expression. OMNT1 also modulated hormone secretion, stimulating LH (10 and 50 ng/ml) and inhibiting FSH (50 ng/ml) induced by GnRH. In conclusion, our study shows OMNT1 protein localization in pig's AP. Its regulatory role on tropic hormones suggests a potential neuromodulatory role of OMNT1 in the hypothalamic-pituitary axis, requiring further investigation into underlying molecular mechanisms.

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COMPARATIVE MORPHOLOGY OF THE CEREBELLUM OF THE COMMON NOCTULE (*NYCTALUS NOCTULA*) AND THE BARN SWALLOW (*HIRUNDO RUSTICA*)

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The cerebellum of *Nyctalus noctula* and *Hirundo rustica* was studied according to generally accepted methods. It was found that the weight of the cerebellum of the common noctule is 16.2% of the brain weight, and that of the barn swallow is 15%. The relative volume of the cerebellum (in % of the cerebral volume) of the swallow is larger than that of the noctule (14.9% and 11%, respectively). Also, the relative area of the cerebellar cortex (as a percentage of the cerebral area) is larger in the bird than in the noctule, 31% and 23.6%, respectively. At the same time, the average absolute and relative thickness of the cerebellar cortex and its individual layers in the common noctule (366±18.7 μm; 522) significantly exceeds that of the barn swallow

(285±15.9 μm; 274). Also, the bat has a higher CFI index, than the bird (23.55 and 3.28, respectively), which indicates a larger number of cerebellum lobes and is explained by the presence of hemispheres. Thus, the swallow's cerebellum is characterized by more complex worm differentiation, larger relative area and volume, and less cortical thickness than that of the common noctule.

POSTER SESSION I – SYNAPTIC PLASTICITY

25th April, 2024 (Thursday), 13:15–14:30

EXPANSION MICROSCOPY AS A TOOL FOR DISENTANGLING INFLUENCE OF MATRIX METALLOPROTEINASE 9 ON THE DENDRITIC SPINE MORPHOLOGY AND FUNCTION

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Dendritic spines, small protrusions on neuronal dendrites, are crucial for the organization of excitatory synapses. Their structure and molecular composition evolve during development and undergo dynamic changes in response to learning. Matrix metalloproteinase 9 (MMP9) is a secretory gelatinase well-known for its involvement in affecting spine structure in response to learning. MMP9 is stored in synaptic vesicles, from which it is released into the extracellular space to digest proteins and orchestrate synaptic signaling cascades. However, the co-occurrence of MMP9 and its target proteins within these synaptic vesicles—critical for understanding the synchrony of their release and subsequent action—remains elusive, largely due to the limitations imposed by the small size of dendritic spines and the resolution of conventional light microscopy. To address this challenge, we utilized expansion microscopy, a super-resolution technique that physically enlarges specimens. This process entails embedding the specimen in a hydrogel, followed by digestion and isotropic expansion in an aqueous environment. Employing a combination of expansion microscopy and immunofluorescent staining enabled us to visualize the spatial distribution of MMP9 within dendritic spines using a conventional confocal microscope. Our ongoing research aims to explore the colocalization of MMP9 with potential targets, such as brain-derived neurotrophic factor and insulin-like growth factor binding protein 2.

INPUT-SPECIFIC MODULATION OF GABAERGIC PLASTICITY IN CA1 PYRAMIDAL CELLS BY THE EXTRACELLULAR MATRIX

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The extracellular matrix (ECM) of the brain plays a pivotal role in regulating synaptic plasticity. The maturation of the ECM, particularly the formation of perineuronal nets enveloping parvalbumin (PV) interneurons, imposes constraints on excitatory synaptic plasticity in adulthood. Notably, these constraints can be reversed to a juvenile-like state by enzymatic treatment. Our study utilized patch-clamp recordings to investigate the effects of hyaluronic acid or chondroitin sulphate digestion on GABAergic transmission in synapses connecting PV or somatostatin (SST) interneurons and CA1 pyramidal cells (PCs). We employed an optogenetic approach to selectively activate PV and SST inputs while synaptic currents (IPSCs) were measured from PCs. Enzymatic removal of ECM constituents did not impact the amplitude or kinetic parameters of inhibitory transmission. However, it induced a subtle deepening of burst-induced depression in PV-PC synapses. We then analysed NMDA-dependent heterosynaptic long-term inhibitory plasticity. In SST-PC synapses, NMDA-iLTP was specifically impaired following chondroitinase treatment (sham: 125.9±7.6%, n=15; after digestion: 106.1±4.5%, n=16, p=0.03). Conversely, hyaluronidase treatment selectively impaired iLTP in PV-PC input (sham: 116.6±4.7%, n=16; after digestion: 100.4±5.3%, n=10, p=0.01). Collectively, these findings underscore the crucial role of the brain ECM in shaping inhibitory plasticity by exerting control over input-specific long-term modifications at distinct GABAergic synapses.

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REGULATION OF HIPPOCAMPAL INHIBITORY TRANSMISSION AND PLASTICITY BY D1/D5 DOPAMINE RECEPTORS

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Neuromodulation by dopamine is widely recognized as a key factor both in the regulation of hippocampal excitatory synaptic plasticity and in memory processes. However, the involvement of dopaminergic receptors signaling in the plasticity of GABAergic synapses is still unexplored. We therefore addressed the question whether dopamine D1-like receptors could modulate inhibitory synaptic transmission and plasticity in hippocampal brain slices. First, we performed recordings of miniature inhibitory postsynaptic currents (mIPSCs) using patch-clamp technique from pyramidal cells in the presence of dopamine D1/D5 receptors antagonist (SCH23390) or agonist (SKF38393) and we have revealed that usage of these compounds had opposite effects on the mIPSCs amplitude (SCH23390: 87±7 %, n=7; SKF38393: 113±4 %, n=6; relative to baseline). Then, we induced inhibitory LTP (iLTP) by NMDA treatment in control conditions (mIPSCs amplitude: 127 ± 4%, n=9) and after blocking or enhancing the activity of dopamine D1/D5 receptors. Interestingly, we have observed that the application of SCH23390 led to conversion of iLTP to iLTD (84±5%, n=7), while SKF38393 preserves iLTP (111±4%, n=5). In conclusion, our data indicate that dopamine D1-like receptor signaling interfere with GABAergic transmission and plasticity in hippocampus.

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THE INVOLVEMENT OF THE RELAXIN-3/RXFP3 SYSTEM IN THE CONTROL OF THE DENTATE GYRUS ACTIVITY – IMPLICATIONS FOR ANXIETY-RELATED DISORDERS

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Alternations in the ventral hippocampus dentate gyrus (vDG) functioning are closely linked to anxiety disorders. vDG receives dense innervation from the nucleus incertus (NI), a stress-sensitive brainstem structure and a major source of relaxin-3 (RLN3) in the brain. RLN3, through its receptor, RXFP3, affects stress and anxiety-related behaviors. However, its impact on vDG neuronal activity remains unexplored. Therefore, we explored possible influence of RXFP3 activation on rat vDG neuronal activity *ex vivo*, and examined related neuroanatomical substrates, both in rats and humans. Whole-cell patch-clamp recordings showed that RLN3 reduced vDG granule cell excitability. Viral vector based neural tract-tracing indicated similar innervation of the hilus and inner-molecular layer of vDG by NI-originating and RLN3-positive fibers, suggesting NI as a major source of this neuropeptide in vDG. HiPlex in situ hybridization (ISH) revealed RXFP3 mRNA expression in vDG hilar interneurons, but not in granule cells, in rats. Importantly, in human postmortem tissue, ISH also revealed RXFP3 mRNA expression in anterior DG GABA-ergic hilar interneurons. Our findings suggest that NI-originating RLN3 innervation of vDG can directly activate RXFP3 on hilar interneurons, altering granule cell excitability. These effects of RLN3/RXFP3 signaling likely regulate stress and anxiety-related behaviors.

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NUCLEUS INCERTUS MODULATION OF SOMATOSTATIN INTERNEURONS IN THE DENTATE GYRUS-MEDIAL SEPTUM AXIS

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Somatostatin-expressing GABAergic interneurons (SOM) of dentate gyrus (DG) involve hilar interneurons (HILs) that innervate the medial septum (MS). Both DG and MS are heavily innervated by GABAergic neurons originating in the stress-sensitive brainstem nucleus incertus (NI), the main source of relaxin-3 (RLN3) in the brain. NI originating RLN3 innervation of DG is prominent in the ventral part of the DG (vDG), associated with anxiety behavior. Yet, the characteristics of NI-vDG-MS axis, as well as HILs involvement in this pathway remain unknown. HiPlex in situ hybridization (ISH) studies revealed that neurons expressing RXFP3 mRNA in the rat vDG co-expressed vesicular GABA-transporter (vGAT) and SOM mRNA. Importantly, in human anterior hippocampal sections ISH also showed co-localization of vGAT, RXFP3 and SOM mRNA. Viral vector based neural tract-tracing studies confirmed that SOM DG neurons innervate MS. Additionally, tract-tracing results showed that single NI RLN3+ neurons innervate both MS and vHPC. Our findings are first to show the involvement of SOM interneurons in RLN3 signaling in the vDG, and that MS and vDG are controlled by NI originating RLN3 innervation. Our research contributes to molecular characterization of SOM vDG interneurons, which are a crucial elements of the circuits engaged in stress and anxiety control.

Funding: The National Science Centre Poland: UMO-2023/49/B/NZ4/01885, UMO-2018/30/E/NZ4/00687; MiniGrant2023_ID.UJ.

ELUCIDATING THE ROLE OF NUCLEUS INCERTUS AND INTERPEDUNCULAR NUCLEUS IN FINE-TUNING THE VENTRAL DENTATE GYRUS ACTIVITY: IMPLICATIONS FOR ANXIETY CONTROL

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Ventral hippocampal dentate gyrus (vDG) is strongly involved in the control of stress, anxiety and social interactions. vDG is densely innervated by highly stress sensitive brainstem nucleus incertus (NI) and midbrain interpeduncular nucleus (IPN). NI is the main source of relaxin-3 (RLN3) neuropeptide, and activation of RLN3 cognate receptor RXFP3 in the vDG, was shown to induce anxiety and social avoidance. However, the neuronal mechanisms underlying RLN3/RXFP3 signalling in the vHPC, as well as neurochemical characteristics of NI neurons innervating vDG are still not fully understood. Similarly, the nature of the IPN-vDG connection remains completely unknown. Stereotaxic injections of fluorescent retrograde tracers into the vDG of Sprague Dawley rats revealed that NI neurons innervating vHPC are mainly RLN3-positive and their projections are mainly ipsilateral. At the same time vHPC-innervating neurons were observed in observed in the lateral, caudal, rostral and dorsomedial subnuclei of the IPN, remaining under NI control. Multi-electrode array (MEA) *ex vivo* recordings unveiled both inhibitory and excitatory influence of RLN3 on the vDG network activity. Taken together these observations shows that vDG remains under control of both NI and IPN, shedding light on the neurochemical and neurophysiological underpinnings of anxiety and social interactions.

Funding: The National Science Centre, Poland: UMO-2023/49/B/NZ4/01885; UMO 2021/41/N/NZ4/04499.

GADOLINIUM INFUSION TO THE NARES PRODUCES ANOSMIA AND ELECTROPHYSIOLOGICAL CHANGES IN THE OLFACTORY BULB OF FREELY MOVING RATS

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Olfactory sensory neurons deliver sensory input from the nasal epithelium to the olfactory bulb (OB). Our goal was to examine the role of sensory input from the nasal epithelia on electrophysiological activity in the OB. To accomplish this we developed a gadolinium model of anosmia. Rats (N=10/group) were bilaterally implanted with electrodes to the OB. Gadolinium (3 mg/side) or saline was infused to both nares. Anosmia was assessed using the hidden cookie test. Rats were tested every other day for 15 days. Local field potentials from the OB were recorded after each hidden cookie test. Gadolinium infusion increased time taken to find the hidden cookie compared to control rats. This lasted around 10 days. Electrophysiological recordings revealed gadolinium-infusion to the nares reduced the amplitudes of respiration rhythm (1-10 Hz) and gamma (40-80 Hz), compared to saline-infused rats. Hidden cookie test performance and changes in nasal respiration rhythm positively correlated. Together these findings demonstrate that intranasal gadolinium infusion can be used as a safe model to produce anosmia. Further we show that sensory input arising from the nasal epithelium is critical for the generation of respiratory and gamma rhythms in the OB.

Funding: Supported by the National Science Centre.

ALTERATIONS IN EXCITABILITY, SPONTANEOUS EXCITATORY POSTSYNAPTIC ACTIVITY AND MORPHOLOGY OF DORSAL RAPHE SEROTONERGIC CELLS OF 5-HT7 RECEPTOR KNOCK-OUT MICE

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The 5-HT7 receptor is involved in many physiological and pathological processes, including spatial navigation, circadian rhythm regulation, pain perception and the development of mood disorders. Since the pathophysiology of major depressive disorder is thought to include disturbances in serotonin metabolism, it is of great interest to study the main site of serotonin production – the dorsal raphe nucleus (DRN), especially as the role of the 5HT7 receptor in this area remains largely obscure. In this study, we aimed to evaluate the effect of 5-HT7 receptor knock-out on cell membrane properties and excitatory synaptic activity in the DRN. Using whole-cell patch clamp electrophysiological protocols, we examined spontaneous excitatory synaptic currents and intrinsic excitability of serotonergic DRN cells of male 5-HT7 knockout and wild-type mice. The cells were identified by immunostaining for tryptophan hydroxylase II and each recorded neuron was filled with biocytin to allow examination of cell morphology using Sholl analysis. 5-HT7 receptor knockout increased the basal amplitude of sEPSCs and decreased the excitability of TPH+ neurons. In addition, a slight increase in the complexity of axodendritic arborizations was observed in 5HT7-KO mice. We hypothesize that these changes in DRN projection neurons may affect the release of serotonin in target structures.

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DYNAMIC S-PALMITOYLATION OF SYNAPTIC PROTEINS ASSOCIATED WITH NEURONAL PLASTICITY

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S-palmitoylation (S-PALM) is a type of lipid post-translational modification of proteins unique among other lipidations due to its reversible nature. It has been estimated that about 40% of synaptic proteins can undergo S-PALM. S-palmitoylation may modulate localization and function of synaptic proteins. However, the time-course of this process, protein-specificity and the role of S-PALM in scaling the efficacy of excitatory synapses remain largely unknown. Here we studied dynamic changes of synaptic proteins' S-PALM following pharmacological induction of long-term synaptic potentiation (LTP) in hippocampal neurons with

either NMDAR co-agonist glycine or a mixture of rolipram, forskolin and picrotoxin. We employed Acyl-Biotin Exchange assay and investigated the differences in S-PALM profiles of proteins at 20 min and 1 h following LTP in *in vitro* and *ex vivo* preparations. Our results indicate that both palmitoylation and depalmitoylation occur post enhanced neuronal activity in time- and protein-dependent manner. Further research in this area may shed more light on the S-PALM's role in healthy brain function and contribute to the understanding of diseases of the nervous system that negatively affect cognitive functioning in people.

Funding: Research funded by the Polish National Science Centre (grant 2019/34/E/NZ4/00387).

POSTER SESSION I – PAIN

25th April, 2024 (Thursday), 13:15–14:30

UNLOCKING THERAPEUTIC POTENTIAL: INVESTIGATING THE IMPACT OF 5-HT7 RECEPTOR ACTIVATION ON DORSAL HORN SYNAPTIC TRANSMISSION

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Neuropathic pain remains one of the most challenging health issues nowadays. Complex etiology, chronic state and limited treatment options result in high demand for new, efficient therapies. 5-HT7R is a serotonin receptor subtype, localized in pathways connected to neuropathic pain and is shown to be involved in nociceptive mechanisms activated in animal models used to study chronic pain. In the present study, we aimed to determine the modulatory effects of 5-HT7 receptor activation on synaptic transmission in mouse dorsal horn spinal cord neurons, a region associated with pain transmission. Utilizing whole-cell patch clamp recordings, we assessed the effects of a new 5-HT7R agonist CPL 298 on inhibitory and excitatory synaptic transmission as well as intrinsic membrane properties of recorded neurons in lamina II of the dorsal horn. Our results suggest that activation of 5-HT7 receptors in the dorsal horn of the spinal cord modulates both inhibitory and excitatory neurotransmission, which may have therapeutic potential in the treatment and/or prevention of chronic pain.

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THE EFFECTS OF E-98, A NOVEL HISTAMINE H3 RECEPTOR ANTAGONIST, ON NERVE INJURY-INDUCED DEFICITS IN LOCOMOTOR ACTIVITY AND MEMORY PERFORMANCE IN NEUROPATHIC MICE

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Neuropathic pain is caused by the lesion or disease of somatosensory nervous system and may be characterized by both sensory and affective impairments. Histamine H3 receptor (H3R) has been proven to play a role in cognition, mood disorders, and pain modulation. We aimed to assess the effect of a novel H3R antagonist (E-98), on pain (von Frey) anxiety (open field, OF) and memory performance (novel object recognition, NOR) in neuropathic mice. Mice underwent chronic constriction injury (CCI) (model of neuropathic pain) and received E-98 (10 mg/kg; twice daily, 7 days, following day 7th). We collected the hippocampus for high-performance liquid chromatography (HPLC) analysis of monoamines (NA, DA, 5-HT). E-98 produced an analgesic effect. Neuropathic mice exhibited lower rearings. In T2 (NOR), E-98-treated animals explored novel objects significantly longer. The time spent exploring a familiar object in T2 was higher in the vehicle-treated group, and E-98 did not influence this parameter. The HPLC analysis did not reveal any changes in monoamine levels. Our studies showed that CCI influenced animals' locomotor activity and memo-

ry performance, and the E-98 treatment reversed this effect. The novel H3R antagonist did not affect hippocampal monoamine's level, suggesting a different yet undefined mechanism of neuropathy-related affective impairment.

Funding: Work was financed by a grant from the National Science Centre, Poland, SONATA 2019/35/D/NZ7/01042.

BLOCKAGE OF CCR2 AND CCR5 AS A POTENTIAL THERAPEUTIC TARGET FOR DIABETIC NEUROPATHIC PAIN

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Chemokines and their ligands are known to be involved in nociceptive transmission in neuropathic pain including diabetic neuropathy. Among them CCR2 and CCR5 together with their ligands seem to be associated with pathomechanism of developing neuropathic pain. Therefore, our study aimed to examine the changes of these factors in parallel with hypersensitivity accompanying diabetic neuropathy. Moreover, we studied if and how cenicriviroc, a CCR2 and CCR5 antagonist, influences pain symptoms. The experiments were performed on male and female Swiss albino mice with streptozotocin (STZ; 200 mg/kg, intraperitoneally)-induced model of diabetic neuropathy. Pain-related behavior was assessed by the von Frey and cold plate tests. An analysis of the mRNA expression of CCR2 and CCR5 ligands was performed by qRT-PCR. Cenicriviroc was injected intraperitoneally 2 h before behavioral tests on day 7 after STZ injection. The result shows that on day 7 after STZ administration, the blood glucose level was increased, and at the same time mechanical and thermal hypersensitivity developed. In male mice, we observed increased mRNA levels of *Ccl2, Ccl5,* and *Ccl7* while in female mice additional *Ccl8* and *Ccl12* increased levels were noted. Moreover, we demonstrated that cenicriviroc alleviates STZ-induced hypersensitivity. Based on these results, we suggest that targeting CCR2 and CCR5 is a potent therapeutic solution in novel pain treatments for diabetic neuropathy.

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OXALIPLATIN-INDUCED NEUROPATHY IN MICE – POSSIBLE ROLE OF CCR5 AND ITS LIGANDS

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Recently, involvement of some chemokines in the development of neuropathic pain has been noted; however, participation of the CCR5 ligands in oxaliplatin-induced neuropathy still needs to be studied. The goal of our study was to examine if CCR5 ligands (CCL3, CCL5, CCL7 and CCL8) evoked pain-related behavior and whether their levels are changed in oxaliplatin-induced neuropathy. The experiments were performed on male Swiss albino mice: naive and with oxaliplatin (10 mg/kg, intraperitoneally)-induced model of peripheral neuropathy. The study was conducted using behavioral tests (von Frey/ cold plate) and RT-qPCR analysis of the spinal cords on day 7 and 14 after oxaliplatin administration in mice. The results of our studies provide evidence that the intrathecal administration of CCL3, CCL5, CCL7 and CCL8 induces mechanical and thermal hypersensitivity in naive mice. Importantly, the RT-qPCR analysis showed elevated levels of CCL5 and CCL7 mRNAs in the spinal cord on day 7 after oxaliplatin administration. Taken together, our results suggest an important role of two CCR5 ligands (CCL5 and CCL7) in the development of thermal and tactile hypersensitivity. Additionally, our biochemical studies revealed that they may also participate in hypersensitivity development observed in oxaliplatin-induced neuropathy. CCR5 may become a potential therapeutic target for pain management, but further research is necessary

Funding: The research was funded by the National Science Centre, Poland grant OPUS 22 2021/43/B/NZ7/00230 and statutory funds from the Maj Institute of Pharmacology Polish Academy of Sciences.

THE EFFECTS OF HISTAMINE H3 RECEPTOR ANTAGONIST, PITOLISANT ON NOCICEPTIVE TRANSMISSION IN NEUROPATHIC PAIN MODEL AND INFLAMMATORY RESPONSE OF GLIAL CELLS IN PRIMARY CULTURES

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Initiating and sustaining an inflammatory response largely depends on glial cell activation, which is a significant factor in the pathophysiology of chronic pain. Our study aimed to determine the analgesic effects of histamine H3 receptor (H3R) antagonist, pitolisant (PIT), in neuropathic mice and its influence on glial cells activation in primary cultures. The effect of a single intraperitoneal injection of PIT (1, 5, 10, 20 mg/kg) on mechanical stimuli (von Frey test) was assessed on mice subjected to chronic constriction injury (CCI) at day 14th after surgery. Anti-inflammatory effects of PIT were examined in LPS-treated (100 ng/mL) primary microglial and astrocyte cell cultures. Nitric oxide (NO) production was determined by Griess assay. Cytokine (IL-6, IL-1β, IL-10) and cell markers (Iba1, CD206) levels were quantified by ELISA and Western blot, respectively. We observed PIT's dose- and time-dependent analgesic effects. PIT (0.01, 0.1, 1.0, 10 μM) did not affect NO production by both cell types. PIT (10 μM) did not affect cytokine levels in microglia; however, it reduced the Iba1 level. We detected increased IL-1β and decreased IL-10 levels in astrocytes. The results demonstrate an analgesic property of PIT in neuropathic animals, while in cell cultures, modulation of glial cell activation.

Funding: This research was financed by grant SONATA 2019/35/D/NZ7/01042 from the National Science Centre, Poland.

COMPARING TECHNICAL AND BIOLOGICAL REPETITIONS IN THE MORPHOMETRIC ANALYSIS OF PERIPHERAL NERVES IN DIABETIC NEUROPATHY

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This study compares biological (BR) and technical repetitions (TR) in assessing sciatic nerve morphometry in diabetic mice across wild-type (WT), Diaph1 knockout (DKO), and Diaph1-RAGE knockout (DRKO) models, examining statistical methodologies' impact on neuropathy interpretations. Six months after the onset of streptozotocin-induced diabetes, WT, DKO, and DRKO mice were analyzed for nerve fiber metrics. BR used averages from individual animals; TR considered each measurement independently. TR underscored significant morphometric differences, particularly in axon and fiber diameters between diabetic DKO and diabetic WT. At the same time, BR illuminated diabetic DRKO's higher G-ratio *vs.* diabetic WT, suggesting varied impact scales. Unlike BR's broader deformation analysis, TR revealed more structural deformations in diabetic DKO. Both acknowledged DRKO's neuroprotection *via* stabilized axon and fiber diameters, G-ratios, and fiber counts. Only TR analysis showed a difference in myelin-to-axon area ratio between diabetic WT and diabetic DRKO. TRs offer a detailed lens for detecting minute morphometric differences and genotype-specific neuroprotective mechanisms against diabetic neuropathy, which BRs may not capture due to their aggregated data approach. However, BRs excel in elucidating inter-individual variability and broader genotype effects. Combining both methods could enhance understanding of neuropathic changes and gene-related neuroprotection in diabetes.

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POSTER SESSION I – NEUROLOGICAL DISORDERS

25th April, 2024 (Thursday), 13:15–14:30

GRASPING THE MICROSTRUCTURAL PARAMETERS OF THE BRAIN IN A HETEROGENEOUS MULTI-SITE ENVIRONMENT: A FEDERATED LEARNING APPROACH

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Medical data privacy concerns and heterogeneity in data acquisition protocols make creating and publishing large datasets for machine learning (ML) difficult. Federated learning (FL) allows separate institutions to train a common ML model without sharing data. This research examines the FL-based approach to estimate brain microstructural properties from diffusion magnetic resonance imaging (MRI) data. The study compares the performance of a traditional deep learning method with that supported with the FL technique. To estimate the diffusion tensor imaging (DTI) microstructural parameters (i.e., FA, MD), the U-Net model was used on three publicly available datasets (CamCan, HCP WU-Minn, and ZJU) and one private. Three FL algorithms were evaluated to improve the model's generalizability from different sources: the standard FedAvg and FedMedian, and the MRI data-specific FedCostWAvg. The ability of a network to generalize in traditional deep learning relies heavily on the dataset it was trained on. However, when using basic FL techniques, the model generalization is improved (MSE=00381). Moreover, implementing FedCostWAvg significantly enhances the accuracy of the estimated FA parameter (the average MSE decreased from 0.00398 to 0.00361). These findings highlight the crucial role of FL in improving the security of medical data and the generalization of the model.

Funding: The numerical experiment was possible through computing allocation on the Ares and Athena systems at ACC Cyfronet AGH under the grants PLG/2023/016117 and PLG/2024/016945. This research is supported by the European Union's Horizon 2020 research and innovation programme under grant agreement Sano No 857533 and the project of the Minister of Science and Higher Education "Support for the activity of Centers of Excellence established in Poland under Horizon 2020" on the basis of the contract number MEiN/2023/DIR/3796. Tomasz Pieciak acknowledges the Polish National Agency for Academic Exchange for grant PPN/BEK/2019/1/00421 under the Bekker programme and the Ministry of Science and Higher Education (Poland) under the scholarship for outstanding young scientists (692/STY/13/2018).

DIFFUSION-RELAXOMETRY MULTICOMPARTMENT SIMPLE HARMONIC OSCILLATOR-BASED RECONSTRUCTION AND ESTIMATION MAGNETIC RESONANCE SIGNAL REPRESENTATION

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The multiparametric magnetic resonance imaging allows to disentangle the different water microenvironments that contribute to the acquired signal. To analyze such multiparametric signals one can use the continuum modeling approach which transforms the signal into a set of coefficients corresponding to compartments characterized by different parameters. The possible compartments are described by the so-called kernels representing processes present during the signal evolution. Considering the diffusion-relaxometry acquisitions majority of the works use the one-dimensional first-order diffusion signal expansion represented by the apparent diffusion coefficient as the diffusion part of the kernel. This work proposes the use of the three-dimensional simple harmonic oscillator-based reconstruction and estimation as the diffusion representation in the diffusion-relaxometry signal analysis. To define the objective function used in the coefficient estimation task the network least absolute shrinkage and selection operator and alternating direction method of multipliers were used. The proposed method was compared with the diffusion-relaxation correlation

spectrum imaging and sparsity promoting iterative joint non-negative least squares approaches. A significant improvement in the signal approximation was achieved. The method allows to estimate the indices associated with the geometrical parameters of the nerve fibers and also separate the free water contribution in the orientation distribution function reconstruction.

MAGNETIC RESONANCE SPECTROSCOPY THERMOMETRY (MRST) IN THE BRAIN TUMORS

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1H magnetic resonance spectroscopy (1HMRS) thermometry (MRSt) is an innovative method enabling localized non-invasive brain temperature measurements. However its use in brain temperature measurements in tumors has been scarce. MRS is a technique used for measuring metabolites levels in brain tumors as key biomarkers. In our study unsuppressed water peak in conjunction with metabolite peaks data from MRS spectrum was used in order to estimate temperature within brain tumors. Calibration datasets were generated using phantom filled with water solution of chosen metabolites (NAA 12.5 mM, creatine 10 mM and choline 3 mM). *In vivo* data was collected from 10 preoperative adult patients with brain lesions with voxels placed both within lesioned tissue and contralaterally. Temperature measurements were calculated with individual metabolites as reference and with an amplitude weighted averaging combining all measurements. MRSt temperature measurement method demonstrated a similar overall temperature increase in the lesioned tissue compared to healthy tissue. Our findings suggest the feasibility of introducing temperature as a novel biomarker in MRS studies of brain tumors.

CLINICAL APPLICATION OF THE MIDDLE CEREBRAL ARTERY BLOOD WAVEFORM ANALYSIS BY USE OF THE FOURIER TRANSFORM

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Transcranial Doppler (TCD) examination of the middle cerebral artery (MCA) blood flow is frequently used in neurosurgery in multiple clinical scenarios concerning cerebrovascular diseases. However, a limited number of parameters are typically used in MCA waveform analysis. The aim of the study was to evaluate novel spectral parameters of the MCA waveform and assess their variability in terms of common cardiovascular risk factors. 80 patients' (56.23% females) aged 57.21±13.61, admitted to the neurosurgery unit, were prospectively enrolled. A detailed medical history was collected. Each patient underwent TCD examination of the MCA bilaterally. Envelopes of 5 registered MCA flow waveforms were transformed into the frequency domains using the Fourier transform, and the following parameters were calculated: spectral coefficient, spectral entropy, and spectral spread. We found significant associations between spectral parameters of MCA waveform and diagnosed hypertension, smoking, and dyslipidemia. Patients with hypertension had significantly lower spectral coefficient (8.05±10.51 *vs.* 13.47±13.32; p=0.02). In the multivariate linear regression model, spectral entropy and spectral coefficient remained independently associated with hypertension (R=-0.97; 95% CI: [-1.83;-0.10]; p<0.01; R=-2.69; 95% CI: [-5.39;-0.35]; p=0.04). Our findings suggest that traditionally used neurosonological parameters might be supplemented by an analysis of proposed spectral parameters. We also provide evidence of the clinical significance of these parameters.

MOTOR CORTEX MEDIATES ASSOCIATIONS BETWEEN STRIATAL DOPAMINE DEFICIENCY AND UPPER EXTREMITY MUSCLE STIFFNESS IN PARKINSON'S DISEASE: A MULTIMODAL STUDY USING PET/CT, EEG, AND MYOMETRY

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The underlying mechanism of muscle stiffness in Parkinson's disease (PD) is poorly understood, and no direct relationship exists between dopamine deficiency and rigidity. The study involved fifteen patients with right-sided mild PD symptoms. All subjects were assessed by: (i) positron emission computed tomography with an estimation of striatal [18F]Fluorodopa uptake ratio ([18F]FDOPA PET/CT) to evaluate dopaminergic degeneration; (ii) resting EEG recorded after bimanual anti-phase index finger movement from which we calculated event-related synchronization of the beta band; and (iii) the resting muscle stiffness of upper extremity measured by myometry. Mediation analysis were conducted using structural equation models to examine the impact of motor cortex activation in putative associations between dopamine deficiency and upper extremity muscle stiffness. PD patients exhibited significantly lower muscle stiffness of right first dorsal interosseous (FDI) than the left FDI. The activation of the motor cortex was positively correlated with the muscle stiffness of the right FDI and also positively associated with putaminal dopaminergic dysfunction. Structural equation models indicated that motor cortex activation mediated the association between putaminal dopamine depletion and muscle stiffness of right FDI. The motor cortex did not significantly mediate associations between putaminal dopamine depletion and muscle stiffness of left FDI. Impaired muscle stiffness of the right upper extremity associated with putaminal dopaminergic deficiency seems to be mediated to some extent by the motor cortex, what might suggest cortical compensations.

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TARGETED SENSORY TRAINING HELPS TO EXTEND THE LIMITS OF STABILITY: TWO CASE STUDIES

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In stroke patients with hemiparesis, the asymmetrical position of the trunk is often characterized by a one-sided tilt or impaired mobility to one side. Postural tilt and predominant loading can be seen on either the paretic side or non-paretic side. Dynamic sitting balance in the early post-stroke stages varies across cases and thus requires individualized intervention. Recent studies have shown that additional sensory input enhances rehabilitation when added to standard motor-skill training. Visual feedback and proprioceptive stimulation can positively modify neural mechanisms, facilitate the improvement of motor performance, and promote effective motor learning. Two subacute stroke patients with cerebral lesions of vascular origin underwent personalized training (8 days, 20 min/day), which included 8 postural tasks based on visual biofeedback using the center of pressure position projected on a screen. The tasks were carried out while sitting on the force plate, and the patient trained trunk mobility in both frontal and sagittal planes, focusing on the paretic side. Unilateral vibration (80 Hz, 1 mm, 15 s) to the quadratus lumborum was applied in two tasks. After 8 days of training, the functional limits of stability in the frontal plane were extended by approximately 53% on the paretic side in both stroke patients.

Funding: This work was supported by the grant APVV-20-0420.

DIFFERENCES IN THE COURSE OF THE DISEASE BETWEEN PATIENTS WITH YOUNG- AND LATE-ONSET MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is an immune-mediated demyelinating disease, typically diagnosed among young adults. According to recent reports, the course of MS might be determined by age at disease onset. The aim of this study was to compare clinical picture in groups of adult patients with MS onset before and after 40 years of age. The retrospective observational study included adult patients diagnosed with MS. The cohort was divided into two groups depending on the age of onset: 18-40 years (young-onset MS; YOMS) and at or later than age of 40 (late-onset MS; LOMS). Together 84 patients were included: with YOMS (n=70) and LOMS (n=14). Mean age at diagnosis was 29,47 ± 6,21 in YOMS and 43,93 ± 2,79 years in LOMS. There was dominance of women in YOMS (82,86% *vs.* 64,29%), however with no statistical significance. In the YOMS group, most cases represented relapsing-remitting type of MS (RRMS) while in the LOMS group there was a predominance of primary-progressive MS. Later onset patients had significantly more frequent urination disorders (p=0.008). Clinical picture of MS is different depending on the age of onset. Most cases of YOMS represent RRMS. LOMS is associated with more frequent urinary dysfunction.

DIAGNOSTIC PERFORMANCE OF PLASMA P-TAU212 IN ALZHEIMER'S DISEASE

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Plasma phosphorylated-tau (p-tau) biomarkers have found utility in clinical trials for anti-amyloid drug therapies for Alzheimer's disease (AD). Plasma p-tau levels are increased in AD, and their decrease is observed after drug treatment. However, it is unknown if p-tau212 is a useful biofluid-based biomarker for AD since no method exists for its quantification. Here, we developed and validated a novel blood p-tau212 assay and assessed its biomarker potential in cohort with *in vivo* diagnosis of AD neuropathology. Using in-house Simoa immunoassay we measured p-tau212 levels in plasma in Slovenia Memory Clinic Cohort n=149. Plasma p-tau212 and p-tau217 had statistically not different AUCs to distinguish Aβ-SCD from Aβ+ AD-dementia (AUC=92.5% [95% CI=87.0%-97.9%] *vs.* 95.6% [95% CI=91.7%-99.4%]; DeLong test P=0.232) and to separate Aβ+ AD-dementia from Aβ- non-AD MCI (AUC =89.2% [95% CI=88.2%-96.2%] *vs.* AUC=87.8% [95% CI=78.2%-97.2]; De Long test p=0.8119). Positive predictive value (PPV) for Aβ positivity *vs.* SCD were 94.7% for p-tau212 and 98.1% for p-tau217. The negative predictive values (NPVs) were 72.4% and 74.2% respectively. As the newest member of the plasma AD biomarker toolbox, plasma p-tau212 is useful for AD diagnosis and differentiation diagnosis. Blood-based p-tau212 will be a cost-effective and simple-to-implement alternative to *in vivo* and autopsy-based evaluations for AD neuropathological changes.

TAU PHOSPHORYLATION AS A DYNAMIC PROCESS ACROSS PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS: CLINICAL IMPLICATIONS OF PLASMA P-TAU217 IN NEWBORNS, ACUTE NEUROLOGICAL DISORDERS AND ALZHEIMER'S DISEASE

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Among the fluid biomarkers for Alzheimer's disease (AD) diagnosis, plasma p-tau markers, particularly p-tau217, have shown high accuracy for the differentiation of AD from healthy controls and other neurodegenerative conditions. In addition, findings that plasma p-tau217 is increased in amyloid PET positive, but tau PET negative, cases have led to the assumption that plasma p-tau primarily reflects brain amyloidosis, and therefore only is changed in AD. In this multicentre study, we aim to explore levels of plasma p-tau217 in different age groups and across diverse acute and chronic neurological conditions. Using the Simoa HD-X platform, we measured plasma p-tau217 in healthy newborns (n=55), healthy younger (n=60) and older (n=30) controls, AD (n=60), acute ischemic stroke, AIS [20], cardiac arrest (n=20) and traumatic brain injury, TBI (n=20). Across the different groups, newborns had the highest concentrations of plasma p-tau217 (10.19 +/- 3.92 pg/ml). There were no significant differences between young and older controls. Levels in AD were significantly higher than in the older control group (3.43 +/- 1.44 and 1.57 +/- 0.45 pg/ml, respectively) and showed a high diagnostic accuracy identifying AD (AUC: 0.92). Acute conditions such as cardiac arrest and TBI, but not AIS, had similar or higher levels of p-tau217 as in AD at admission. However, p-tau217 levels decreased rapidly in the first 24 hours after admission in patients with cardiac arrest and TBI. Our findings suggest that tau phosphorylation is process present in both physiological and pathological processes across the lifespan. High plasma p-tau in newborns might indicate an important role of tau phosphorylation in neuronal plasticity in the earliest stages of brain development. High plasma p-tau in acute conditions may be due to a temporary opening of the blood-brain barrier, with release of p-tau from the extracellular space to blood. While plasma p-tau217 is a very efficient biomarker for detecting AD pathology, tau phosphorylation, secretion and clearance can be affected in a variety of physiological and pathological conditions, necessitating further investigations to identify a wider set of conditions worth considering in the impending clinical implementation of blood biomarkers.

GLIAL FIBRILLARY ACIDIC PROTEIN IN ALZHEIMER'S DISEASE PATHOLOGY

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In the Alzheimer's disease (AD) biomarkers have become increasingly important for various clinical purposes tracking the progression of the disease. The GFAP is an astrocytic cytoskeleton intermediate filament protein and concentrations of GFAP are higher in areas surrounding Aβ plaques and increased with tau accumulation in the brains of patients with AD. Measuring levels of GFAP in the blood and CSF can provide insights

into the extent of neurodegeneration pathology in AD. This study intends to evaluate how effectively the concentrations of GFAP in the blood and in CSF can differentiate individuals with CSF biomarker-confirmed AD in comparison to CSF biomarker-negative healthy control group. Plasma and CSF concentrations of GFAP were measured by single molecule array (Simoa) assay. The quantitative assessment of classical biomarkers (Aβ-42, Aβ-42/Aβ-40, tau, and pTau181) in the CSF of patients with possible AD according to the Erlangen Score algorithm (ER 2 and 3) and controls (ER 0) were performed by Lumipulse. Significantly higher plasma concentrations of GFAP in CSF and Plasma were noticed in AD patients compared to controls. The results of the present study indicate that plasma GFAP has better diagnostic accuracy than CSF.

IP-MS METHOD OPTIMISATION FOR TAU PROTEIN PROFILING IN TAUOPATHIES

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Alzheimer's disease (AD) originates from two major brain changes: extracellular plaques of amyloid beta, and intraneuronal tau protein accumulations called tangles. Our question is, if tau accumulations associated with amyloid beta plaques are different regarding their molecular composition when compared with tangles that form independently of amyloid beta. If our hypothesis is correct, we expect to find differences in the way tau is processed by pinpointing cleavage sites or modifications that are disease specific. Specific aims are to analyse brain material from AD and other tauopathies using immunoprecipitation-mass spectrometry (IP-MS) and different extraction methods. Method optimisation is always the first step towards addressing the given research question. This step includes optimisation of tau protein digestion into peptides, by introducing different enzymes and finding the most optimal reaction time. Here, we report that the most optimal time for tau protein digestion is 18 h when using trypsin. Next steps cover optimisation of the amount and ratio of labelled protein standards for tau protein isoforms for best MS readouts. We believe this work is essential to improve our understanding of why tau accumulations develop in neurodegenerative dementias, and the work should give clues on novel biomarkers and therapeutics.

RIGHT HEMISPHERE HYPOTHESIS OF EMOTION PROCESSING IN MCI/AD PATIENTS

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Understanding and using emotional communication is a complex task integrating the language and cognitive skills. The right hemisphere hypothesis focuses on the lateralization of emotion processing indicating the domination of the right hemisphere in the adequate emotion processing. Theory has been studied within different groups of subjects. Current research analyses understanding and communication of the emotional communicates within the group of elderly subjects (N=25). The relations between the cognitive capacity, language fluency and understanding of humor were analysed. The standardised methods of evaluation like: MMSE, verbal fluency tests and RHLB were used. The results show different patterns of humor understanding in group of healthy elderly persons, mild cognitive impairment and Alzheimer's disease patients. The prosody of speech and emotional prosody shows different level among the above-mentioned groups. The education level and the cognitive abilities show correlations with the level of emotional prosody, humor understanding and prosody of speech. The capabilities of active emotional communication was investigated by observation of the facial expressions of the subjects. The relations between dominating emotion and the humor understanding and ability to differentiate the prosody were investigated.

ALPHA-AMYLASE AS A PREDICTOR OF PSYCHOLOGICAL THERAPY RESPONSE IN ANXIETY

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The sense of mental well-being is related to the activity of several biological systems. Investigating them allows us to define conditions needed to maintain an adequate mental health. The enzyme – Salivary alpha amylase (sAA), is considered a marker of the response of the autonomic nervous system which has a greater sensitivity than heart rate, blood pressure or cortisol. The sAA activity increases in the presence of a psychological stressor, especially of a psychosocial nature, and is related to the level of subjectively experienced anxiety. This study analyzed the characteristics and relationships of the enzyme with subjective measures describing the level of anxiety in a sample of 130 people. The subjects took part in a therapeutic intervention. Alpha amylase was tested before and after the intervention. The analyzes showed a relationship between the initial level of sAA activity and the level of physiological flexibility of the person. The initial level of sAA activity turned out to be a predictor of the future outcome of therapeutic interventions. ROC analysis indicated the possible future use of baseline sAA activity level as a diagnostic indicator. Analyzes also showed an association of sAA with generalized anxiety disorder. However, the method requires refinement in further research.

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THE POTENTIAL ROLE OF HEALTHY EATING IN STUDENTS' ANXIETY LEVEL

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Anxiety is a condition which is present in every student's life due to a lot of exams, trying to manage academic and personal life and many others. Unfortunately, a large part of students do not lead a healthy lifestyle including nutritious food and sport. We perceive nutritious food as a high intake of fruits, vegetables, omega 3 acids, whole grains products and minimizing the consumption of processed meals with high fat and carbohydrates index. The analysis made by Aucoin et al. (2021) revealed the associations between more fruits and vegetables, omega 3 acids, vitamins, microelements consumption and less anxiety. In order to examine the potential role of healthy eating in students' anxiety level, we investigated the group of students (19-26 years old). To measure the consumption of roughage we used Dietary Screener Questionnaire (DSQ) and for the anxiety level – State-Trait Anxiety Inventory (STAI). Our study reveals a positive correlation between unhealthy food habits and the apprehension level. Although, more studies are needed to explore the impact of nourishment on anxiety.

CORRELATION BETWEEN ELEVATED INTERLEUKIN-6 LEVELS AND COGNITIVE FUNCTIONS IN YOUNG ADULTS

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Most studies focus on the analysis of cognitive function in older adults or in neurodegenerative diseases, paying little attention to the impairment of these functions in young people. In our study, we wanted to examine the effects of pro-inflammatory cytokines on cognitive function in young adults. We collected a group of 49 college students aged 20-25 and examined the following parameters: body fat, BMI, waist-to-hip ratio, IL-6 and TNF-alpha blood levels. We also conducted cognitive tests: TMT, face association test, Stroop test. Among all the subjects, we identified a group of 13 women who had elevated levels of IL-6. Then, after processing the results, we found correlations between reduced cognitive test scores and an increase in the waist-hip ratio, and elevated levels of IL-6. Based on the available literature and the results of our study, it can be assumed that interleukin-6 reduces cognitive function in young people. This study suggests that it would

be appropriate to look more closely at other pro-inflammatory cytokines, as well as anti-inflammatory cytokines based on their effects on cognitive function in young individuals.

SENSITIVITY OF GAMMA-RANGE AUDITORY STEADY-STATE RESPONSES TO AWARENESS FLUCTUATIONS DURING GENERAL ANESTHESIA

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Previous studies found consistent attenuation of gamma-range responses to auditory stimulation during consciousness loss under general anesthesia. Our goal was to replicate and extend the assessment of 40-Hz auditory steady-state responses (ASSR) sensitivity to consciousness changes and exploring envelope following responses (EFR) to wide-band chirp modulated stimulation across various frequencies, including both low-gamma and high-gamma frequencies. We studied 26 patients undergoing propofol-remifentanil TIVA TCI. Auditory stimulation involved click-based 40-Hz and wide-band chirp-modulated protocols under three conditions: pre-anesthesia, anesthesia maintenance, and post-awakening. EEG data were recorded using a 64-channel amplifier system at 1024 Hz. Anesthetic agent concentrations and anesthesia depth were monitored with target-controlled infusion systems, and bispectral index (BIS). EEG analysis focused on inter-trial phase clustering (ITPC) from 7 fronto-central channels, using cluster-based nonparametric permutation testing on envelope curve data. Under constant 40-Hz stimulation, we found a significant difference in grand average ITPC responses between averaged pre-and post-anesthesia conditions and anesthesia (clusterstat=602.2, $p<0.001$, [-0.03-0.65 s]). In wide band stimulation, the ITPC response, particularly in the low-gamma range (28-50 Hz), indicated consciousness loss during anesthesia (clusterstat=64.28, $p<0.001$). Notably, the significant difference between averaged responses before and after anesthesia and anesthesia conditions held only for low-gamma frequencies, with no significant difference in the high-gamma range. Despite sensitivity of 40-Hz ASSR and low gamma EFR to consciousness loss, these measures appear insensitive to BIS and propofol concentration. We confirmed consistent attenuation of 40-Hz ASSR responses during general anaesthesia-induced consciousness loss. In wide-band stimulation, the most discriminative part of the EFR response was in the low-gamma range (28-50 Hz), emphasizing its selectivity for consciousness loss. However, no significant differences were found in BIS index or propofol concentration during deep anesthesia, indicating limited utility for anesthesia depth monitoring. This may be due to the marked reduction in ITPC parameter at the point of consciousness loss.

PARSONAGE-TURNER SYNDROME COMPLICATED BY PHRENIC NERVE PALSY

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Parsonage-Turner syndrome, a rare neuropathy characterized by brachial plexus inflammation potentially involving the phrenic nerve palsy resulting in diaphragmatic paralysis and pulmonary dysfunction, with 1.64 per 100,000 rate of incidence yearly. A 39-year-old patient was admitted to the Department of Neurology at Uniwersytecki Szpital Kliniczny w Poznaniu due to right brachial nerve inflammation complicated by phrenic nerve palsy, manifesting as right upper limb pain and breathing difficulty. An X-ray revealed a high-positioned left diaphragmatic dome on X-ray (2022). The patient's medical history indicated right brachial plexus inflammation complicated by phrenic nerve palsy eight years earlier (2013). On admission, the patient reported persistent fatigue and pain of the upper limb. Despite overall good physical condition, with intact upper and lower limb reflexes and normal neurological examination, atrophy of the right biceps, supraspinatus, and infraspinatus muscles was observed. Further imaging, including CT scan of the head, chest, and abdominal cavity and MRI of the cervical spine, was done to exclude proliferative processes, and blood tests to rule out malignancy. A diagnosis of Parsonage-Turner syndrome complicated by phrenic nerve palsy was established based on clinical and imaging findings. The patient was discharged in

a good condition with a planned treatment including Encorton. To our best knowledge, this is the only case that illustrates a rare instance of a long gap period relapse of Parsonage-Turner syndrome on the contralateral side of the body.

DOES A STROKE MAKE YOU LESS EMPATHETIC? ON AFFECTIVE AND COGNITIVE EMPATHY IN THE AFTERMATH OF STROKE

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Clinical experience suggests that stroke may lead to impaired social cognition, including impaired affective and cognitive empathy. However, the available scientific information on this topic is inconclusive. It is unclear whether the impairment affects both types of empathy or only cognitive or affective empathy. The aim of this study was to use the Multifaced Empathy Test to investigate the extent to which stroke survivors show impairments in understanding the emotional states of others and in affective empathy. Fifty-one people in the subacute phase of their first stroke and 25 demographically matched people undergoing rehabilitation in five hospitals in Lesser Poland were studied. Statistical analysis showed that post-stroke patients had statistically significantly lower affective empathy scores (M=5.49; SD=1.73) than controls (M=6.29; SD=1.31), $t_{(74)}=2.42$; $p<0.05$, especially for positive valence pictures $t_{(74)}=3.16$; $p<0.01$. There were no statistically significant differences between groups for cognitive empathy. The study suggests that despite the cognitive understanding of another person's situation, the reported level of affective empathy may be weakened after the stroke.

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WHARTON'S JELLY-DERIVED MESENCHYMAL STEM/STROMAL CELLS OBTAINED FROM DIFFERENT PATIENTS SECRETE DIFFERENT NUMBERS OF EXOSOMES – A COMPARATIVE STUDY

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Mesenchymal stem/stromal cells derived from Wharton's jelly of human umbilical cord (WJ-MSCs) exhibit unique immunomodulative and neuroprotective properties and are therefore considered as a potential tool in the treatment of various neurological disorders. Their therapeutic potential mostly relies on their secretome – WJ-MSCs secrete different factors that are either secreted into the environment as a soluble secretome or are encapsulated within extracellular vesicles (EVs), particularly exosomes. The ability to secrete immunomodulative and neuroprotective factors usually varies significantly between donors, which correlates with different numbers of released exosomes. Therefore, we performed a comparative study of the ability to secrete exosomes by WJ-MSCs obtained from different donors. Umbilical cords were obtained from full-term deliveries and MSCs were then mechanically isolated from Wharton's jelly. The cells were then cultured until 3rd passage in standard culture medium. Next, the standard medium was removed, WJ-MSCs were rinsed with double-filtered PBS (0,1 μm) and a medium without platelet lysate was added for 24 h. After 24 h, cell culture medium containing exosomes secreted by WJ-MSCs was collected and exosomes were isolated by ultracentrifugation. The isolated exosomes were suspended in double-filtered PBS and NTA analysis was performed. The analysis revealed that WJ-MSCs obtained from different donors secrete different numbers of exosomes, which in the future may potentially have an impact on the efficiency of cell therapies dedicated for individual patients.

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POSTER SESSION I – LANGUAGE AND PSYCHEDELICS

25th April, 2024, 13:15–14:30

NEURAL UNDERPINNINGS OF SENTENCE READING IN DEAF, NATIVE SIGN LANGUAGE USERS

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Deaf, native signers who use sign language on a daily basis have different language and sensory experience from hearing individuals, hence, reading processes are not the same in those two groups. Previously, the neuronal basis of the reading in deaf, native signers were mainly investigated at the word level and still relatively little is known about neural underpinnings of reading at the sentence level. Our study used functional magnetic resonance imaging (fMRI) to investigate brain activity while performing a sentence reading task (Semantic Judgment Task) in deaf, native signers and hearing adults. Similar activation in both groups were observed in the typical left perisylvian reading network areas: the left middle temporal gyrus (MTG) and the left inferior frontal gyrus (IFG). However, differences were also found: increased activity in left occipitotemporal and right frontal and temporal regions in deaf, relative to hearing readers. Functional connectivity analysis revealed enhanced coupling between the left IFG and the left MTG in hearing but not in deaf group. The analysis of lateralization indices showed more left-lateralized reading-related activation in the STG in the deaf readers. In conclusion, our study showed shared and distinct patterns in brain activity in deaf and hearing when reading sentences.

MORE DEMANDING SPEECH PRODUCTION ENGAGES MORE LANGUAGE-SPECIFIC PROCESSING, BUT NOT GENERAL COGNITIVE CONTROL RESOURCES

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Speech production is a complex process engaging both language-specific and domain-general resources. However, it is unclear to what extent increasing task difficulty affects engagement of language-specific or domain-general mechanisms. In this study, we addressed this question using a verbal fluency task (VF) in which participants are asked to generate words in response to either semantic or phonetic cue, with phonetic fluency being shown more difficult. Forty-one participants performed semantic and phonetic fluency in an fMRI experiment. Additionally, we used two functional localizer tasks to identify the language-specific and domain-general networks in the brain. For each subject, we created a set of functional ROIs and subsequently, we assessed the response of these two networks to both VF tasks. Our results showed that differences between conditions are linked mainly to the increased engagement of the left-lateralized language network. Although both conditions engaged the multiple-demand network, we found no differences between them in this network. Our support the claim, that differences in performance between the VF versions result from specific language requirements rather than general task demands. Altogether our results show that while the multiple-demand network supports the execution of demanding speech production tasks, the production demands reflect language-specific processing.

Funding: This research was possible thanks to the grant from the National Science Centre awarded to Zofia Wodniecka (OPUS 2017/27/B/HS6/00959).

IS THERE EVIDENCE FOR THE NEURAL NOISE HYPOTHESIS IN DYSLEXIA? INSIGHTS FROM EEG AND MRS RESULTS

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According to the neural noise hypothesis of dyslexia, reading difficulties stem from an imbalance between excitatory (glutamate, Glu) and inhibitory (gamma-aminobutyric acid, GABA) activity in neural networks. Specifically, increased Glu levels in dyslexia were suggested. In the current work, we tested both indirect measures of the excitatory-inhibitory ratio from the EEG power spectrum in 120 Polish adolescents and young adults (60 with dyslexia, 60 controls) and direct Glu and GABA concentrations from magnetic resonance spectroscopy (MRS) at a 7T MRI scanner in half of the EEG sample. Previous works have shown associations between flatter slope of the EEG power spectrum and greater dominance of excitation over inhibition, and between greater GABAergic activity and increased EEG beta power. Based on the Bayesian statistics, we have found no evidence for group differences in the indirect measures of the neural noise (exponent and offset of the signal's slope, as well as beta power) tested both at rest and during an auditory language task. Similarly, no evidence for group differences was found in Glu and GABA concetrations in the left superior temporal sulcus derived from MRS. Our results indicate poor adequacy of the neural noise hypothesis in dyslexia.

Funding: This study was supported by the National Science Centre grant OPUS (2019/35/B/HS6/01763) awarded to prof. Katarzyna Jednoróg.

FMRS STUDY ON READING-RELATED METABOLITE CHANGES

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Functional magnetic resonance spectroscopy (fMRS) is a non-invasive technique used to measure changes in metabolite concentrations in response to various stimuli. While it is a powerful tool for gaining deeper insights into the mechanisms accompanying brain activations, it still remains relatively novel, lacking clear guidelines for optimal data acquisition and analysis. Most of existing studies have focused on changes in the visual cortex in response to simple visual stimuli. In our innovative approach, we focus on metabolite changes induced by reading-related stimuli within individually localised brain regions involved in the reading process. Moreover, we extend the investigation by incorporating fMRS data acquisition with varying delays between stimulation and signal acquisition, aiming to study the glutamate response function. 59 adolescents and young adults aged 15-24 years participated in fMRS experiment on a 7T scanner. In the superior temporal sulcus 500 and 1000 ms after stimulus presentation we observed changes in glutamate (for 500 ms, t=-2,099, p=0.041; for 1000 ms, t=-2,114, p=0.040). Additionally, N-acetylaspartate (NAA) changes were detected in the medial prefrontal cortex 500 ms and 1000 ms after stimulation (for 500 ms, t=-2.714, p=0.009; for 1000 ms, t=-2.800, p=0.007).

Funding: This study was funded by the Polish National Science Center OPUS grant (2019/35/B/HS6/01763) awarded to Katarzyna Jednoróg.

PREDICTION ERROR REPRESENTATIONS IN VISUAL WORD RECOGNITION

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Explicit computation of prediction error has been proposed as a key element of predictive coding, an architecture that naturally integrates bottom-up and top-down information. It has been hypothesized that this could lead to increased stimulus representations when prior expectations conflicts with sensory input (Blank and Davis, 2016). In this fMRI study, we test this hypothesis within the context of visual word recognition. We manipulated the signal strength of visually presented words (low *vs.* high noise), as well as prior information (visual words were preceded by an auditory word that was unrelated, semantically related, or the same word). Using forward encoding models, we investigated whether stimulus information was stronger when the input was clear and mismatching with prior expectations, therefore generating a strong prediction error. Preliminary results do not directly confirm this hypothesis: stimulus information in the visual ventral stream was not stronger for mismatching than matching conditions. However, we did find stimulus information patterns consistent with prediction error coding in the inferior frontal lobes. The results show that findings from Blank and Davis do not generalize to visually presented stimuli and thereby challenge their prediction error coding model.

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NEURAL ENTRAINMENT TO A SPEECH-TYPICAL RHYTHM IN DOGS

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Ethological works suggest that dogs outperform other species in their readiness to respond to human vocal communicative signals, including speech. But whether this readiness of dogs is supported by neural tuning to characteristic spectral or temporal properties of natural speech, is currently not understood. To test this, we conducted an auditory electroencephalography (EEG) study (N=27), comparing dogs' neural entrainment to auditory streams of intact speech *vs.* sine-wave replica with natural (4 Hz) *vs.* fast (9 Hz) syllable presentation rates, in a 2x2 design. We expected that tuning to spectral and temporal properties of natural speech would lead to higher inter-trial coherence (ITC) values for intact speech and 4 Hz streams, respectively. Dog brains exhibited higher ITC values for 4 Hz than 9 Hz streams ($p=0.001$), but ITC values did not differ for intact speech *vs.* sine-wave streams, and there was no spectral by temporal naturalness interaction. These results suggest that dog brains are tuned to a speech-typical auditory rhythm but not to the spectral properties of speech. Further studies with other species need to reveal whether this tuning to the 4 Hz rate in dogs is a consequence of domestication or of living with humans, or it is more general across vocal mammals.

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DISTRIBUTION OF VISUAL ATTENTION DURING THE PROCESS OF PERCEIVING DOG SILHOUETTES: DIFFERENCES BETWEEN EXPERTS AND NOVICES. AN EYE-TRACKING STUDY

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Plenty of eye-tracking studies comparing experts and novices in a certain field of knowledge have shown significant differences between these two groups in the way they process the stimuli and distribute visual attention on them. This study aimed to investigate whether similar dependence occurs in the field of cynology – the knowledge of dogs. To accomplish this, we examined 33 individuals – 7 experts (experienced Judges, Canine Assistants or Breeders registered in the Canine Association in Poland) and 26 novices (individuals without professional experience in cynology). Each participant completed an information questionnaire and then underwent an eye-tracking examination. Every participant was presented with 20 images of silhouettes and heads of purebred dogs and dogs resembling purebred dogs. The participants were compared in terms of the distribution of attention to each stimulus, the duration of stimulus observation, as well as chosen eye-tracking indicators during the perception of these stimuli - the number of saccades and fixations. All participants directed most of their attention towards the dogs' heads. However, experts in cynology looked at the dogs much more holistically. They paid significant amount of attention to the areas of the front and rear legs, as well as the tail and torso. Their attention was also distributed more evenly on the dogs' silhouettes. Novices focused mainly on the area of the dogs' heads. Depending on the specific silhouette of the dog, their attention also extended to the areas of the legs or torso of a certain dog, but it was distributed significantly less evenly. We can clearly observe that experts in the field of cynology looked at the stimuli more holistically, paying attention to every element of the dogs' silhouettes with their attention being relatively evenly distributed. Novices, on the other hand, focused mainly on the dogs' heads and certain elements characteristic of the particular silhouette of the dog.

Funding: SWPS University in Warsaw.

DOES L2 USE ALWAYS HINDER SUBSEQUENT L1 SPEECH PRODUCTION? AN EXPLORATION OF DIFFERENT L2 LANGUAGE USAGE DURING COMPREHENSION AND PRODUCTION

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In bilingualism research, the "L2 after-effect" describes the challenge of native language (L1) lexical access following second language (L2) use. We explored the constraints of the L2 after-effect: (1) is it elicited only by production, or also comprehension, in L2, and (2) to what extent does the complexity of the L2 task modulate it? We analyzed how different L2 tasks—ranging from reading aloud to picture naming (i.e., single-word reading, narrative reading, and picture naming)—affect the subsequent L1 retrieval in a picture naming task in Polish-English bilinguals (n=149). Our findings revealed no significant effects of the reading tasks in L2 (compared to L1) on L1 production. In contrast, naming pictures in L2 (compared to L1) hindered the consecutive picture naming in L1. These results show that the L2 after-effect is elicited by an active production task but not the passive reading tasks in L2. The next step in exploring the boundaries of the L2 after-effect is to check whether it's affected by the complexity of an active production task in L2. These insights advance our understanding of bilingual language processing and inform theoretical models, highlighting the differential impact of various language tasks on language control.

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PHONEME AWARENESS DEVELOPMENT IN PRESCHOOL CHILDREN IN SHALLOW ORTHOGRAPHY

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The relationship between phoneme awareness and reading proficiency, particularly in pre-reading stages, is a complex and debated topic. This study focuses on exploring phoneme awareness by examining phonemic analysis in pre-reading children (N=250, aged 3.5-6.5, 48% girls) in a shallow orthography (Serbian) to determine the dynamics of its development. Three phonemic analysis tasks were explored – recognizing the first, second, and last letter in a word. These tasks are typically used to test phoneme awareness. Our results show significant developmental differences in phonemic analysis ability among pre-reading children. Success rates varied significantly between age groups, with the most substantial differences observed between the oldest (5.5-6.5) and youngest (3.5-4.5) groups. Success in identifying the first letter in a word predicted success in identifying the second letter, but not the last letter in a word. Task correctness in identifying the first letter was significantly greater than success in other tasks in all age groups, but age-specific variations were observed, showing that phonemic awareness tasks may measure different levels of phoneme awareness development. Patterns of developmental outcomes within age groups were analysed, suggesting that phonemic analysis is a continuous, rather than a discrete ability.

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EXPLORING THE IMPACT OF COGNATES ON THE ENGAGEMENT OF LANGUAGE CONTROL

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Studies on bilingual language use demonstrate a difficulty in speech production in the native language (L1) following production in a second language (L2). This so-called L2 after-effect manifests itself in a picture naming paradigm through longer naming latencies for L1 following L2 naming and possibly reflects engagement of language control mechanisms. The effect has been reported in experiments on noncognates, as cognate presence could increase language co-activation. However, the exact impact of cognates on language control has not been studied. We investigated whether inclusion of cognates indeed impacts the magnitude of L2 after-effect. Two experimental groups completed two sessions of picture naming. In the exposure block, cognates constituted 80% of stimuli in one group and 20% of stimuli in another group. The measurement block remained the same across groups and did not include cognates. The preliminary results show a clear L2 after-effect in both groups. However, the magnitude of the effect is bigger in the 80% cognate stimuli group. Slower word retrieval after naming cognates could be explained by an increased language competition following the increased language co-activation. The results should inform our understanding of mechanisms underlying the L2 after-effect and have methodological implications for future studies investigating language control.

CHARACTERIZING DIFFERENT MODES OF AUDITORY PERCEPTION

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The dynamic attending theory suggests that the temporal regularities within behaviorally relevant sensory streams can be exploited to selectively direct our attention and enhance perception. It is proposed that attention operates in various modes of processing, contingent on the stimulus and task structure, as the continuous allocation of attentional resources is metabolically expensive. Recent evidence indicated that the "rhythmic mode" functions optimally at approximately 1.5 Hz in the auditory domain. However, some recent studies did not find any behavioral advantage of dynamic attending. Furthermore, it remains unclear how different modes of attention adjust with varying tasks and whether these modes are dependent on different processing stages (e.g., perceptual, or linguistic). To investigate this, we carried out a series of nine deviant detection experiments with short (<7 sec) or long (~1 min) auditory streams, consisting of pure tones or syllables, presented at rates ranging from 0.5 to 6.5 Hz. We identified a rhythmic mode of operation—characterized by optimal performance accuracy at ~1.5 Hz during perceptual tasks involving long auditory streams, irrespective of the attended perceptual feature. Conversely, we observed no such advantages for short auditory streams. We further generalized these results using a model of coupled oscillators. Additionally, these benefits were not evident in syllabic categorization tasks for either short or long streams. Our findings reveal that a rhythmic mode of operation at 1.5 Hz naturally arises during the perception of long auditory streams and is specific to the processing stage.

DIFFICULTY OF SOLVING NONVERBAL SYLLOGISMS REFLECTED IN MIDFRONTAL THETA POWER

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Syllogisms have a long history of being used to test fluid intelligence but the ability to properly judge them is affected by language barriers and existing beliefs. Nonverbal syllogisms have been developed to avoid these issues. In two of our experiments with nonverbal syllogisms, participants were exposed to either two, three, or four premises about spatial relations between objects in different pictures, and then had to judge whether a picture with a conclusion aligned with these premises. We examined to what extent task performance related to fluid intelligence and measured the electroencephalogram to examine whether task complexity is reflected in midfrontal theta power. In the first experiment conclusions were always a direct combination of the presented premises, while in the second experiment, conclusions could also be based on indirect combinations of the presented premises. Together, the results indicated that the ability to properly judge nonverbal syllogisms is indeed related to fluid intelligence. Furthermore, increased midfrontal theta power was observed while evaluating the conclusions which increased as a function of task complexity. These findings indicate that tasks with nonverbal syllogisms provide us with a tool that may enhance our understanding of fluid intelligence and its underlying brain dynamics.

SETTING THE STAGE FOR INNER TRANSFORMATION: UNRAVELING THE INTERPLAY OF CONTEXTUAL FACTORS AND THE INTENSITY OF EGO DISSOLUTION IN PSYCHEDELIC EXPERIENCES

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Psychedelic substances have the potential to induce profound alterations in cognition, emotionality, and sensory perception. However, the quality and intensity of their subjective effects exhibit high intra- and inter-individual variability. Therefore, the aim of this cross-sectional study was to investigate how internal and external contextual factors are related to the subjective effects of a psychedelic experience, specifically with the intensity of ego-dissolution. Participants of an online survey (1761 in total; 1495 LSD users and 1231 psilocybin mushrooms users) reported their motivations for past use of a given substance, frequency of use in different environments and social contexts, and filled out an Ego Dissolution Inventory. Robust linear regression analysis revealed that ego-dissolution experiences were more intense in participants using psychedelics for spiritual purposes and less intense in those reporting curiosity as a motivation. Moreover, the ego-dissolution was more intense when psychedelics were consumed in one's own home, in natural settings, at festivals, or during ceremonies. Furthermore, regarding social context, greater intensity of ego-dissolution was observed when psychedelics were used alone, with a partner, a friend, or a guide. Therefore, our study contributes to better understanding of how contextual factors shape subjective psychedelic experiences, which is essential for advancing the psychedelic-assisted therapies.

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FEATURE-BASED AND END-TO-END APPROACHES FOR EEG SIGNAL CLASSIFICATION OF INDIVIDUALS WITH DYSLEXIA AND TYPICAL READERS

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Dyslexia, a neurodevelopmental disorder characterized by reading and spelling difficulties, has been a topic of research for over a century. However, a clear-cut cause and an unambiguous diagnostic rule have yet to be established. The prevalence of dyslexia varies between 5% and 17.5% of the population, depending on the adopted diagnostic criteria. The impact of reading and writing difficulties extends beyond learning, affecting social development and the overall mental well-being of individuals. Machine-learning techniques are being presented as a potential way to automate the process of diagnosing many disorders. Here, we use electroencephalographic signals recorded during a listening task from both individuals diagnosed with dyslexia and typical readers, aiming to find the optimal algorithm that distinguishes between the two groups. Two approaches were employed for this purpose: end-to-end, in which two neural networks (EEGNet, Deep4Net) were trained independently, and feature-based classifiers, which received multiple features from three different domains (time, frequency, and connectivity) as input. Presented results reflect the exploration of a comprehensive set of input data and a comparison of the obtained outcomes.

DO EMOTIONAL CLIMATE CHANGE STORIES INFLUENCE CLIMATE-FRIENDLY DECISIONS? BEHAVIORAL AND FMRI STUDY

Dominika Zaremba[1]*, B. Kossowski1, M. Wypych[1], Katarzyna Jednoróg[2], J. M. Michałowski[3], C.A. Klöckner[4], M. Wierzba[1], Artur Marchewka[1]

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It was previously shown that emotions can drive climate action. 160 participants read Emotional Climate Change Stories eliciting either anger, hope, or neutral state. Then, they made a series of decisions between monetary rewards (egoistic) and reducing CO2 emissions (climate-friendly) in the Carbon Emission Task. Initial analyses showed no group differences in behavior nor neuronal activity. However, pooling the data from all participants revealed that the number of climate-friendly choices decreased with the size of monetary rewards but increased with the level of CO2 emission reduction. In general, egoistic choices lead to activations in brain areas associated with reward processing (caudate nuclei), self-awareness (precuneus), and emotion processing (cingulate gyrus, insula). Interestingly, previous research associated these regions with altruistic, not egoistic behaviors. On the other hand, climate-friendly choices activated parts of the executive network, including MFG and angular gyrus, implicated in studies on delayed gratification and moral judgements. We did not find evidence for the influence of emotional stories on behavior and brain activity in climate action. Climate-friendly choices may not completely align with altruistic decisions, as they involve immediate personal loss but contribute to long-term gains for both individuals and society. We propose to position the topic of climate action at the intersection of prosocial and delayed gratification research.

Funding: The research leading to these results has received funding from the Norwegian Financial Mechanism 2014-2021, project: "Understanding patterns of emotional responses to climate change and their relation to mental health and climate action taking" No. 2019/34/H/HS6/00677.

IMPACT OF TRADITIONAL AND CONTEXTUAL AUDIO DESCRIPTIONS ON THE PERCEPTUAL ENGAGEMENT WITH SELECTED ARTWORKS: A STUDY ON INDIVIDUALS WITH NO ART HISTORY BACKGROUND

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This study investigates the effects of two types of audio description – traditional and contextual – on the reception of four selected works of art, as well as the presentation method: listening during viewing, listening before viewing or reading the description before viewing the painting. The research involved 58 participants without a formal art education, using an eye-tracking methodology. Data were analyzed using a two-way analysis of variance in a 2×3 design. Results indicate that traditional audio description significantly increases fixations on areas of interest within the paintings. Furthermore, listening to audio descriptions while viewing the painting emerges as crucial. Our findings underscore potential disparities in art perception based on the type of audio description employed. These insights contribute to understanding the efficacy of audio descriptions in enhancing engagement with visual art.

POSTER SESSION II – DEVELOPMENT

26th April, 2024 (Friday), 14:00–15:15

EMBRYONIC PROGENITOR CELLS DEVELOP DIFFERENT PHENOTYPES WHEN EXPOSED TO SPECIFIC ENVIRONMENTAL CONDITIONS *IN VITRO*

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Different environmental conditions activate diverse differentiation pathways in progenitor cells thus different types of cells could be generated. To understand the influence of specific environmental conditions on embryonic progenitor cells (EPCs) fate, the cells dissected from the embryonic brainstem were grown *in vitro* in the presence of either Shh/FGF4 (S) or EGF/bFGF (E). Isolated cells effectively proliferated, creating neurospheres (S1 and E1), capable to form secondary neurospheres (S2) or monolayers (E2). Bioinformatic analysis of transcriptomes showed significant differences in gene expression of EPCs grown under different conditions. We found that in S1 the most upregulated genes were related to neurogenesis and nervous system development as well as axon growth processes, while in S2 the upregulated genes were related to the organization of genetic material in the cell as chromatin and nucleosome formation. Higher expression of genes involved in neurogenesis was also found in the E1 *vs.* E2 cells. Next, the differentiation fate of pre-treated groups of cells either in neural or glia-promoting medium was investigated, which also indicated significant differences in their progeny characteristics. Concluding, EPCs adopt different phenotypes *in vitro*. Whether neural progenitor cells would be able to differentiate in specific *in vivo* conditions should be investigated next.

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DIFFERENTIATION OF WHARTON'S JELLY-DERIVED HUMAN MESENCHYMAL STEM/STROMAL CELLS INTO A GLIAL COMMITTED CELL LINEAGE

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Brain damage caused by neuronal and glial cell death or dysfunction leads to several neurodevelopmental disorders, such as aberrant formation of the brain's white matter. The search for an effective therapy began with attempts to differentiate human mesenchymal stem/stromal cells (MSCs) into glial lineage cells. MSCs, obtained from the Wharton's Jelly (WJ) of the umbilical cord up to 24 hours after birth, were at first cultured under physiologically normoxic conditions, in standard culture medium. On the second day after seeding, the medium was changed to induce glial commitment of the cultured cells. Accordingly, MSCs were cultured at different culture densities with the addition of the mitogen PDGF-AA to the culture medium or in the serum-free medium conditioned by mixed primary glial culture derived from neonatal rats. After 2-3 weeks in differentiating medium, the cells were used for morphological, immunocytochemical and molecular analyses to verify their phenotype. The preliminary results indicate that WJ-MSCs have the potential to undergo the differentiation process and will be used to elaborate a protocol for the efficient derivation of cells of glial phenotype from WJ-MSCs.

Funding: Supported by the National Science Center (NCN) in Poland, grant: 2022/47/O/NZ4/01161.

TGF-B AND WNT SIGNALING PATHWAYS CAN BE POTENTIALLY INVOLVED IN THE REGULATION OF PROLIFERATION AND DIFFERENTIATION OF RAT SPINAL CORD EPENDYMAL CELLS

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In the adult mammalian spinal cord, the central canal ependymal zone is a niche of neural progenitor cells (ependymal NPCs) that might be a potential source of cells useful in therapy of spinal cord injuries. In lower vertebrates after spinal cord injury, those cells proliferate and differentiate into neurons which participate in the restitution of lost motor function. However, in mammals after spinal cord injury ependymal cells differentiate mainly into astrocytes forming a glial scar that often limits neural regeneration. The aim of our study was to identify genes and/or signaling pathways that can potentially control the proliferation and differentiation of rat spinal cord ependymal NPCs after injury. To achieve that we selectively collected ependymal cells from the tissue sections of the spinal cord central canal of injured and control rats and compared their transcriptomes. Bioinformatic analysis identified genes specifically upregulated in ependymal cells that participate in the control of TGF-β and WNT signaling pathways in injured rat spinal cords. Moreover, we identified Klf5 and Elf3 as two transcription factors uniquely upregulated in central canal cells. Understanding the molecular mechanisms involved in the proliferation and differentiation of ependymal NPCs may contribute to the development of new therapies for spinal cord injury treatment based on the manipulation of their fate.

Funding: The National Science Center MINIATURA 4 Grant (2020/04/X/NZ3/00185).

INHIBITION OF AUTOPHAGY SUPPRESSES OLIGODENDROCYTE MATURATION *IN VITRO* – LESSONS FOR NEONATAL ASPHYXIA MODELLING STUDIES

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The process of autophagy is involved in the survival and maintenance of every cell. Its disruption, especially deficits, can lead to pathophysiological changes in tissues and cause various diseases, including cancer and neurodegenerative disorders. Recently, it has been shown that dysregulation of autophagy may be involved in the brain damage and hypomyelination that develop after neonatal asphyxia. In this study, we investigated the process of autophagy in primary cultures of neonatal rat oligodendrocytes and oligodendrocyte progenitor cells (OPCs). We exposed them to different oxygen-glucose deprivation (OGD) procedures to mimic hypoxia-ischemia in the neonatal brain. To inhibit lysosomal degradation, we tested chloroquine treatment of cell cultures. OGD performed on OPCs and lasting 40 min did not induce massive autophagy when p62 and LC3-II were detected by immunoblot. The 24 h incubation with 25-100 uM chloroquine induced cell death, while 6 h incubation at 5-25 uM concentrations efficiently inhibited autophagic flux and affected oligodendrocyte differentiation. Further research will shed light on the prospect of using pharmaceuticals that modulate the autophagy process to treat the consequences of neonatal asphyxia.

Funding: Supported by National Science Center in Poland, grant: 2021/03/Y/NZ4/00214.

POSTER SESSION II – NEUROPSYCHIATRY

26th April, 2024 (Friday), 13:15–14:30

THE ROLE OF NEUROMODULATORY EFFECT OF DYNORPHIN SIGNALING IN SOCIAL MEMORY STORAGE

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Maintaining complex social relationships is a fundamental ability for humans and other group living animals. Social dysfunction is present in many neuropsychiatric disorders. Social memory, i.e., the ability to recognize familiar conspecifics, plays a crucial role in maintaining appropriate social relationships. Previous studies indicate the involvement of the kappa opioid system in the formation of social memory traces. In particular, it was demonstrated that prodynorphin, κ opioid receptor (KOR) ligand, knockout mice (Pdyn -/-) retain social memory traces longer than their wild-type littermates. However, the mechanism underlying this phenomenon is not known. The question remains which of the KOR expressing neurons (serotonergic or oxytocinergic) react to dynorphin in a way that erases the social memory trace. To test this, we examined social memory in two mouse strains with selective inactivation of KOR receptors on serotonin or oxytocin expressing neurons (Oprk1Tph2CreERT2 and Oprk1OxtCre strain, respectively). In our preliminary experiments Oprk1OxtCre mice, but not Oprk1Tph2CreERT2, maintained a social memory trace for a longer period than animals from the control group, recapitulating the Pdyn -/- mice phenotype. These results suggest that the modulation of oxytocin signaling by the dynorphin/KOR system plays a major role in the erasure of social memory trace. Therefore, further research is necessary to fully understand the role of the interplay between dynorphin and oxytocin signaling in social memory retention.

Funding: The National Science Centre, Poland OPUS 2019/35/B/NZ7/03477.

SOCIABILITY ALTERATIONS IN THE NOVEL MODEL OF EARLY-LIFE INFLAMMATION ARE MEDIATED *VIA* THE MMP-9 PATHWAY

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Our study investigates the role of matrix metalloproteinase-9 (MMP-9) an extracellular protease, a key player in synaptic plasticity, in behavioral consequences of early postnatal inflammation. We administered a single injection of bacterial lipopolysaccharide (LPS, 0.05 mg/kg) or saline to postnatal-day-7 mice. Two hours post-administration, TIMP-1 serum levels were elevated in both sexes compared to saline controls. MMP-9 levels were elevated in males but not females treated with LPS, as demonstrated by Luminex® immunoassay. Brain MMP-9 activity was assessed using gel zymography protocol, revealing heightened activity in the hippocampi of both sexes two hours post-LPS injection. After six hours, elevated MMP-9 activity was observed only in male cortices. To further investigate MMP-9's role, we conducted behavioral assessments on adult wild-type (WT) animals and MMP-9 knockout (KO) littermates following LPS injection on P7. WT males exhibited a decreased interest in odors from unfamiliar animals but increased socializing with familiar cage mates post-immune challenge. In contrast, WT females displayed heightened interest in unfamiliar social stimuli and reduced sociability within known groups. Remarkably, these effects were absent in MMP-9 KO animals. Our results suggest MMP-9's involvement in long-term sociability alterations following immune activation, but further investigation into underlying molecular mechanisms is necessary.

Funding: 'BRAINCITY – Centre of Excellence for Neural Plasticity and Brain Disorders' project of Foundation for Polish Science (FNP).

A NOVEL XANTHONE DERIVATIVE OF PIPERAZINE, HBK-1A, SHOWS AFFINITY TOWARDS 5-HT1A RECEPTORS AND EXHIBITS ANTIDEPRESSANT-LIKE EFFECTS IN MICE

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Serotonin 5-HT1A receptors have recently gained a lot of attention in the field of neuropharmacology due to their association with the neuropathology of depression, anxiety, and cognitive impairments. Several studies suggest that xanthone derivatives of piperazine, which possess an affinity for 5-HT1A receptors, exhibit antidepressant-like effects. Considering that despite years of investigation, research on antidepressant drugs still poses a significant challenge, here we aimed to evaluate the preliminary pharmacological properties of HBK-1a, a novel xanthone derivative of piperazine. In the *in vitro* radioligand binding assays, we assessed the affinity of HBK-1a for 5-HT1A receptors in the rat hippocampus and for adrenergic α1 and β1 receptors in the rat cortex. Moreover, we investigated its ability to induce antidepressant-like effects in the forced swim test and its influence on spontaneous locomotor activity in mice. Our results demonstrate that HBK-1a shows moderate affinity towards 5-HT1A and α1-adrenergic receptors. At a dose of 10mg/kg, HBK-1a significantly reduced the immobility time in the forced swim test. The compound did not influence spontaneous locomotor activity in mice, which excludes the possibility of changes in locomotor activity influencing the results. Our findings confirm that piperazine xanthone derivatives exhibit antidepressant-like properties, however further research is required.

STABILITY OF SOCIAL BONDS OVER TIME-MEASURED IN MICE TESTED UNDER SEMI-NATURALISTIC CONDITIONS

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Social mammals – including people – function as a part of a group for most of their lives. However, social relationships change over time. The ability to assess the dynamics of such shifts is crucial for understanding of neuronal mechanisms underlying social relationships. To investigate the stability of social bonds over time, we used groups of mice kept in the computer-controlled experimental environment (Eco-HAB) in which they could move freely form social bonds. Eco-HAB system enables measuring the time each pair of mice within the group spends together voluntarily on each day, as reflected by the variable called in-cohort sociability. Further, we used this measure to design the autocorrelation-based algorithm for the assessment of the stability of the social bond between any given two animals over time. We show that mouse dyads do form stable relationships. Moreover, about 2/3 of the tested pairs developed constant level of spending time together. Additionally, we show that for all individual animals, the mean values of in-cohort sociability are very close to each other, which means that all animals form social bonds to the same extent, however, with different individuals. We present an approach to measuring the formation of social bonds in animals over time.

DEVELOPMENT OF COMPUTATIONAL TOOLS FOR ECO-HAB FIELD – AN AUTOMATED BEHAVIORAL ASSAY LOCATED IN THE WILD HABITAT

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To accelerate the research on spontaneous social behaviors that reliably activate specific, evolutionarily established neural pathways, we developed a new field assay and accompanying analytical tools. Eco-HAB Field is an automated-testing environment located in the wild habitat. It consists of 8 subterritories, connected *via* underground corridors equipped with the RFID antennas, providing continuous recording of behavior in groups of mice. It enables testing behavioral patterns relevant for surviving and thriving in varying natural conditions, as well as social interactions and their stability over time with high ecological accuracy. We show that the developed methodology not only provides access to naturalistic patterns of behavior under naturalistic conditions but also is characterized by high data collection validity. To demonstrate the latter, we developed custom Python scripts for analyzing the potential antennas' misreadings and skipped registrations, thus determining influence of such events on reliability of the collected data. We established that corrupted data segments are rare, relatively evenly distributed over time, and constitute less than 1% of total registrations. Our results confirm Eco-HAB Field as a reliable approach to studying neural underpinnings of behaviors crucial for survival and success across different environmental conditions tested in groups of mice.

HOW THE PRELIMBIC CORTEX ENCODES SOCIAL BONDS – THE EFFECTS OF MANIPULATION OF THE MAIN CELL POPULATIONS

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Understanding the role of the prelimbic cortex (PL) in encoding social attachment remains a challenge. This study investigates the functional role of various neuronal classes in the PL, including pyramidal cells (Pyr), parvalbumin- (PV+), somatostatin- (Sst+), and vasoactive intestinal peptide- (VIP+) expressing interneurons, in the processing of familiar and novel social stimuli. We employed chemo/optogenetics and automated behavioral testing in Eco-HAB® system, which allows automated, individualized measurement of voluntary behavior, while manipulating the activity of specific neuronal populations in the PL. Our evaluation focused on animals' responses to known conspecifics and their interest in novel social stimuli. The results indicate that inhibiting Pyr and activating PV+ interneurons in the PL reduce sociability by diminishing the time voluntarily spent with cagemates. Interestingly, Pyr inhibition also increases interest in novel social stimuli, a behavior not observed in animals with activated PV+. Furthermore, VIP+ cell activation mirrors the functional role of the PV+ but to a lesser extent. Conversely, Sst+ activation disrupts interest in both familiar and novel social stimuli indiscriminately.These findings underscore the diverse roles of different PL neuronal classes in processing familiar and novel social information. Importantly, the study emphasizes the crucial role of PV+ neurons in selectively encoding familiarity.

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ADAPTIVE AVOIDANCE OF AGGRESSIVE CONSPECIFICS AND SEROTONIN STATUS IN MICE

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Altered central serotonin (5-HT) signalling has been associated with anxiety disorders, among other clinical indications. Human studies indicate a positive correlation between severity of social anxiety symptoms and 5-HT synthesis in the amygdala and dorsal anterior cingulate cortex (ACC). Polymorphisms in the gene encoding tryptophan hydroxylase (Tph2), the rate-limiting enzyme for 5-HT synthesis, are not only linked to elevated 5-HT levels in the amygdala and ACC, but also associated with increased amygdala reactivity to emotional stimuli. Animal studies further support the idea that alterations in 5-HT neurotransmission cause changes in threat responsiveness. Tph2 gene expression in the dorsal raphe nucleus (DRN) is reported to be upregulated by acute stress. Whereas chronic social stress increases Htr1a and Slc6a4, the gene that encodes the 5-HT transporter (SERT), expression in the DRN, amongst other 5-HT changes. In this study, we aimed to investigate in mice if short-term exposure to social aversion that results in adaptive social avoidance would also lead to elevated tissue levels of Tph2 mRNA in the midbrain raphe nucleus and of levels of 5-HT and its major metabolite in projection regions involved in emotional stimulus processing.

ESTABLISHING THE UNIFIED, AUTOMATIC, UNBIASED PLATFORM FOR CHARACTERIZATION OF SOCIAL BEHAVIOR IN MICE

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Validation of any biological intervention developed for tackling the root or symptoms of neuropsychiatric disorders requires proper tools. Disturbances of social behavior is a hallmark of many psychiatric conditions, such as depression, anxiety and schizophrenia. Capturing and quantifying broad range of social behavior simultaneously within a single tool is therefore essential, as it would allow for registration and clustering of groups of behavior specific for particular disorders. Such method would be of great advantage for better translational studies. Here, within Same-NeuroID project, we implemented a pipeline for efficient characterization of complex social behavior in mice. We call it Same-SocialBox. In the setup animals are housed together in a semi-naturalistic environment with proper bedding, food and water access, and with night-day cycle. Animals are recorded for long hours to ensure a capture of diverse behavior. SLEAP.ai is used for pose estimation of recorded animals and extracted coordinates are processed by deepOF software to create set of features. These features are then used to "feed" models of both supervised and unsupervised learning for complex behavior classification.

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GLUCOCORTICOID SIGNALING IN ASTROCYTES MEDIATES MOLECULAR EFFECTS OF CHRONIC STRESS IN MICE

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Stress is an adaptive reaction of the organism to alterations of the environment. The stress response is coordinated by the hypothalamus-pituitary-adrenal (HPA) axis, largely through secretion of glucocorticoids (GCs). Glucocorticoids receptors (GRs) act primarily as transcription factors activated by increased levels of GCs, such as those observed upon stress. Growing evidence suggest that astrocytes play an important role in mediating central effects of GCs. Astrocytes sense local synaptic activity, they regulate neurotransmitter homeostasis, and signal back to the synapse, securing physiological performance of neural networks. Our group showed that GR deletion in astrocytes affects the formation of aversive memory, which correlated with the changes in the expression of metabolic genes. Here, we examined GR-dependent transcriptional effects of chronic social defeat stress in astrocytes. We isolated astrocytes from 2 brain regions relevant for stress response and found differential effects of CSDS in the two brain structures examined, with certain overlap. We identified a significant contribution of the GR to these changes. Furthermore, elimination of GR from astrocytes abolished vast majority of CSDS-induced changes, while other molecular pathways, previously unaltered by CSDS, were affected in GR astroKO mice. We conclude that GR signaling in astrocytes mediates transcriptional effects of chronic stress in these cells.

Funding: This work was supported by the NCN OPUS grant 2021/41/B/NZ3/04099 ‚AstroSyCo'.

THE EFFECT OF REPEATED ADMINISTRATION OF VORTIOXETINE ON FEMALE MICE BEHAVIOR IN THE UNPREDICTABLE CHRONIC MILD STRESS MODEL

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Depression, a highly prevalent mental health condition, presents a significant challenge to healthcare, especially for women, who experience twice the prevalence compared to men. However, despite the availability of various treatment options, there are notable variations in treatment responses. In this study, using the unpredictable chronic mild stress (UCMS) model, we aimed to assess the efficacy of vortioxetine in female mice, focusing on its effects on recognition memory and anhedonic behavior. Female C57BL/6 mice underwent 6 weeks of UCMS, while a control group remained unstressed. Daily administration of vortioxetine at a dosage of 5 mg/kg began during the final 14 days of the study. Depressive-like behavior was assessed using the sucrose preference test, while cognition was evaluated using the object recognition test. We observed the successful induction of anhedonia after the third week of UCMS, with a more pronounced effect evident by the fourth week. Furthermore, repeated administration of vortioxetine effectively reversed anhedonia in female mice. However, an antidepressant did not attenuate recognition memory deficits. While our findings indicate the potential of vortioxetine to reverse anhedonia in female mice, its effect on memory was not present, suggesting possible differences in the treatment response depending on the sex.

Funding: This study was conducted as part of a research project funded by the National Science Centre, Poland (grant 2019/34/E/NZ7/00454).

CHANGES IN SENSITIVITY TO REWARDS AND OPIOID SIGNALLING DURING ADOLESCENCE

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Adolescence is a period of intense brain reorganization, accompanied by heightened reward sensitivity. Though endogenous opioid system is implicated in this phenomenon, the specific mechanisms remain elusive. We have discovered that in the social conditioned place preference test (social CPP) the social reward temporarily decrease in mid-adolescence male C57BL/6 mice. This decrease appears to be specific to social domain since we did not observe similar results in another natural reward (food CPP). The social reward result is in contrast to cocaine reward (cocaine CPP) that peaks during mid-adolescence. Treatment with a selective κ-opioid receptor antagonist, norbinaltorphimine (i.p., 10mg/kg), induced a drop in social reward in early adolescent mice. Furthermore, using qPCR we investigated changes in the relative mRNA expression of the μ, δ and κ-opioid receptors (*Oprm1*, *Oprd1* and *Oprk1*, respectively) and the opioid peptide precursors prodynorphin (*Pdyn*) and preproenkephalin (*Penk*) in key areas of the brain's reward system areas (prefrontal cortex (PFC), nucleus accumbens (NAc), dorsal striatum (DS)). We found a decrease in expression of (mRNA) *Pdyn* in mid-adolescent mice in the PFC and DS. The relative expression of (mRNA) *Oprd1* in NAc appears to increase with age. Taken together, these data shows the developmental changes of sensitivity to the rewards across mice adolescence and point at κ-opioid signalling as potential mechanism shaping adolescent social behavior.

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THE ROLE OF NGF-SENSITIVE INTERPEDUNCULAR NUCLEUS (IPN) NEURONS IN CIRCUITS CONTROLLING SOCIAL BEHAVIOR: ANATOMICAL AND FUNCTIONAL STUDIES OF THE NUCLEUS INCERTUS–IPN–VENTRAL HIPPOCAMPAL AXIS

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The midbrain interpeduncular nucleus (IPN) plays a significant role in social behavior and anxiety control. IPN neurons highly express the nerve-growth factor (NGF) receptors – TrkA and are densely innervated by the stress-sensitive nucleus incertus (NI). NI is a the primary source of relaxin-3 (RLN3), and it innervates the ventral hippocampus (vHPC), vital for social behavior and anxiety signalling. However, the relationships within of the NI-IPN-vHPC axis remain unknown. Fluorescent in situ hybridisation showed that GABAergic IPN neurons co-express TrkA and RLN3 receptor (RXFP3) mRNA. Neural tract-tracing unveiled extensive RLN3 projections from the NI to the IPN. Whole-cell patch clamp recordings demonstrated that RXFP3-selective agonist A2 induces outward currents in IPN neurons, and multielectrode array recordings revealed both excitatory and inhibitory NGF action within the IPN. Furthermore, tract-tracing studies revealed dense IPN originating innervation of the vHPC, particularly from the rostral and lateral nuclei, that at the same time are strongly innervated by the NI. Taken together, our findings show that NGF-sensitive IPN neurons innervating vHPC receive innervation from NI and remain under the control of RLN3/RXFP3 system, implicating important role of NI-IPN-vHPC axis in the control of social interactions and anxiety.

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UNRAVELING THE ROLE OF NUCLEUS INCERTUS IN STRESS AND REWARD PROCESSING: AN INTEGRATED STUDY OF ELECTROPHYSIOLOGY, ANATOMY AND IMMEDIATE EARLY GENE EXPRESSION

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The brainstem nucleus incertus (NI) is involved in modulating stress response and aversive stimuli processing. It is also a primary source of the stress related neuropeptide relaxin-3 (RLN-3). NI innervates ventral tegmental area (VTA), a key component of the brain's reward system. By tracing neural pathways using a retrograde viral vector, the NI-originating innervation of the VTA was confirmed within the midbrain of Sprague-Dawley rats. Immunohistochemical staining indicated that only a small percentage of neurons in the NI, which contain the RLN-3, also extend projections to the VTA, implying a specialized connectivity pattern between these regions. Behavioral experiments have shown increased activity in NI neurons, as indicated by c-Fos expression, in response to painful stimuli. This highlights the NI's involvement in processing adverse conditions, bolstering its role in stress response. Electrophysiological recordings further reveal excitatory reactions of NI neurons to painful stimuli, and intriguingly, the response direction of some neurons varied in correlation with alternating brain states, indicating dynamics in the information processing that takes part within the NI. This dynamic information processing within the NI contributes to understanding stress and reward mechanisms, providing potential therapeutic avenues for stress-related disorders.

Funding: The National Science Centre in Poland, UMO-2022/45/N/NZ4/03171.

UNRAVELLING THE ROLE OF NUCLEUS INCERTUS IN STRESS AND REWARD PROCESSING: ANATOMICAL AND FUNCTIONAL INSIGHTS FROM RAT MODEL

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The brainstem nucleus incertus (NI) is involved in modulating stress response and aversive stimuli processing. It innervates ventral tegmental area (VTA) and rostromedial tegmental nucleus (RMTg) – the primary inhibitory input to the VTA dopaminergic (DA) neurons. In order to visualise the circuit's anatomy, retrogradely transported viral vectors, carrying genes for fluorescent proteins, were unilaterally injected into the RMTg of Sprague-Dawley rats. The results revealed that, unlike the ipsilaterally innervated VTA, the RMTg receives bilateral innervation from the NI. The following electrophysiological recordings in urethane-anesthetised rats were preceded by injections of two viral vectors: one retrograde, carrying Cre recombinase gene, to the VTA or RMTg and another, carrying Cre-dependent genes for an excitatory opsin, which targeted the NI. The results revealed functional effects of NI-originating innervation on the two midbrain structures. Lastly, preceding behavioral experiments, retrograde viral vectors carrying YFP were injected bilaterally into the animals' RMTg. Following a stress-induction procedure in operant conditioning chamber, a series of immunostaining was performed. The resulting data provide insight into the presumed overlap between c-fos-reactive NI subpopulation and the neurons innervating the RMTg. Altogether, this suggests that NI-originating innervation of midbrain structures forms a complex system involved in stress and reward processing.

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UNRAVELING THE ROLE OF NUCLEUS INCERTUS-INTERPEDUNCULAR AXIS IN NOVELTY-RELATED BEHAVIORS

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Accurate discrimination between new and familiar stimulus is crucial for adaptive responses, with disruptions strongly linked to neuropsychiatric disorders. Stress significantly impairs novelty related responses. Thus, we investigated how the stress-sensitive brainstem nucleus incertus (NI), which is the primary source of the neuropeptide relaxin-3 (RLN3), may control the interpeduncular nucleus (IPN), which is crucial in signaling novelty preference. Multiplex in situ hybridization revealed RXFP3 mRNA expression in dopaminergic D1 and cholinergic α5 receptor mRNA-expressing IPN neurons, implicated in novelty and familiarity signaling, respectively. Patch-clamp recordings combined with optogenetic stimulation showed direct NI originating, inhibitory innervation of IPN in male rats. Viral tract-tracing unveiled NI-IPN neurons projecting to regions controlling stress and novelty related behaviors. Behavioral studies showed that chemogenetic activation of NI-IPN axis increased exploration time and reduced grooming in the open field test. Our findings suggest NI involvement in stress-related novelty preference control, and sheds light on the neuronal mechanisms underlying stress-related impaired novelty preference.

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HBK-15 DEMONSTRATES ANXIOLYTIC-LIKE PROPERTIES AND FACILITATES ACTIVE STRESS-COPING IN FEMALE MICE

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Anxiety disorders stand among the most widespread mental health challenges, impacting approximately 4% of the worldwide population. Central to this is stress, which, especially when coupled with ineffective coping mechanisms, can augment anxiety levels, and compromise therapeutic outcomes. Given that women experience anxiety more frequently than men, biological sex should be regarded as a potential variable in effective treatment development. Therefore, our study examines the effects of HBK-15, a novel multimodal compound, on anxiety-like behaviors and acute stress-coping in female mice. Animals were given a single dose of HBK-15 and then underwent the four-plate test to measure its anxiolytic-like properties. Another group of mice underwent the forced swim test to evaluate how HBK-15 influenced the stress-coping strategy. At a dose of 0.15 mg/kg, HBK-15 significantly elevated the number of punished crossings in the four-plate test. Meanwhile, administration of 0.3 mg/kg resulted in a 20% decrease in immobility time during the forced swim test. Our results demonstrate that HBK-15 exerts an anxiolytic-like effect on female mice. Moreover, it promotes an active coping strategy following acute stress exposure. Although in both cases the effect was observed in a narrow dose range. Such a dual-action profile holds promise for advancing therapeutic approaches in anxiety treatment.

Funding: This study has been conducted as part of a research project financed by the National Science Centre, Poland (grant number 2019/34/E/NZ7/00454).

HBK-10, A MULTIMODAL COMPOUND, DEMONSTRATES ANTIPSYCHOTIC-LIKE AND ANTIAMNESIC PROPERTIES IN MICE

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Schizophrenia is a severe mental disorder defined by disturbances in thought processing and perception of reality, leading to a lifelong disability. Although conventional antipsychotic therapy can alleviate symptoms, such as hallucinations and delusions, addressing memory deficits remains a challenge. Therefore, there is an urgent need to develop novel antipsychotics with additional procognitive properties. Building on our previous study on HBK-10, a multimodal compound targeting the D2 and 5-HT1A receptors, we aimed to further explore its antipsychotic-like and antiamnesic activity. First, we conducted the MK-801- and amphetamine-induced hyperlocomotion tests. Subsequently, we performed an object recognition test with test phase 15 min and 24 h after the administration of compounds, using MK-801 to impair memory. In all experiments, we employed male CD-1 mice. HBK-10 at higher tested doses showed antipsychotic-like activity, reducing hyperlocomotion caused by both MK-801 and amphetamine. Additionally, at doses of 1.25, 5 and 10 mg/kg, it reversed MK-801-induced short-term recognition memory impairments. Considering its antiamnesic effect on long-term recognition memory, only the dose of 0.625 was active. Our study reveals HBK-10's antipsychotic-like and antiamnesic properties, encouraging further research.

Funding: This study was financed by the Jagiellonian University Medical College (grant number N42/DBS/000288 and N42/DBS/000329).

EFFECT OF A NOVEL 2-METHOXYPHENYLPIPERAZINE DERIVATIVE, HBK-10, ON RECOGNITION MEMORY IN MICE

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Cognitive deficits of varying severity have often been observed across neuropsychiatric conditions. Memory impairments significantly deteriorate the daily functioning of the patients and may affect the effectiveness of the used medications. Hence, there is an urgent need for therapies that improve cognitive performance. Our previous research has identified HBK-10, an antagonist of 5-HT1A and D2 receptors, as a promising compound with demonstrated antidepressant-like properties in mice. To further investigate, our study concentrated on determining the effect of HBK-10 on short-term, intermediate, and long-term recognition memory using the object recognition test in CD-1 mice. Our findings indicate that HBK-10, within a dosage range of 0.625 to 10 mg/kg, does not significantly impair short- and long-term recognition memory in mice. However, at doses of 0.625 and 5 mg/kg, it adversely affects intermediate recognition memory. This calls for more research to thoroughly explore the full potential of HBK-10.

Funding: This study was financed by the Jagiellonian University Medical College (grant number N42/DBS/000288).

POSTER SESSION II – NEURODEGENERATION

26th April, 2024 (Friday), 14:00–15:15

GENERATION OF SH-SY5Y CELL LINE STABLY EXPRESSING EGFP AND MRUBY2 REPORTER GENES *VIA* 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 research models, which do not accurately represent living organisms. Widely used neuronal model SH-SY5Y neuroblastoma cell line is commonly used in undifferentiated state that is not representative of mature neurons. Differentiated SH-SY5Y neural-like cells are distinguished from undifferentiated ones by their neural marker expression, neurite formation and halt of proliferation. We established a dual-reporter SH-SY5Y cell line expressing EGFP and mRuby2, which could be used for gene editing tool screening, evaluating tool efficiency in differentiated and undifferentiated cell states at the single cell level. The dual-reporter system was generated by template knock-in *via* CRISPR-mediated HDR into the safe harbour AAV1 locus of SH-SY5Y cells. Donor template and CRISPR-Cas were transfected *via* lipofection. In the template plasmid, mRuby2 was positioned near its own promoter, for easy visualization upon successful transfection. EGFP, along with the puromycin resistance gene, was driven by the cell's endogenous promoter, which ensured EGFP expression only after a successful integration into the genome. Furthermore, we assessed SH-SY5Y differentiation conditions for neural-like cell generation.

ESTABLISHING BRAINSTEM NORADRENERGIC AND SEROTONERGIC CULTURES: A NOVEL APPROACH FOR MODELING NEURODEGENERATIVE DISORDERS

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Brainstem is a midline structure comprised of numerous nuclei. Notable among these nuclei are the locus coeruleus (LC), rich in noradrenergic neurons, and the nuclei raphes (NR), predominantly composed of serotonergic neurons. These neurons are linked with the regulation of mood, arousal, stress responses, sleep-wake cycles, and cognitive functions. Despite their significance, they remain largely understudied in the context of Parkinson's disease (PD), despite being among the major cell groups affected by degeneration in this condition. Establishing methodology for isolating and culturing primary noradrenergic and serotonergic neurons holds promise for advancing our understanding of their involvement in PD etiology. Brainstem was isolated from embryonic mice at days 15-18 and specific fragments located within the fourth ventricle were excised followed by a cell dissociation procedure and plated onto polyornithine-coated 96-well plates in neurobasal medium with B-27 supplement. After 7 or 14 days, the cells were fixed with 4% PFA and stained by immunofluorescence method to visualize a noradrenergic (NET/DBH marker) or serotonergic neurons (TPH marker). Fluorescent imaging confirmed successful culturing of primary noradrenergic and serotonergic neuronal populations for prolonged periods of time. Established protocols hold significant potential for investigating Parkinson's disease-related pathology across diverse neuronal types, opening new avenues for further research exploration.

Funding: This work was supported by the statutory funds of the Maj Institute of Pharmacology, PAS, Poland.

DIFFERENTIAL EXPRESSION OF THE PH-SENSING RECEPTORS TDAG8 AND GPR4 IN HUMAN AND MOUSE OLIGODENDROCYTES: IMPLICATIONS FOR MULTIPLE SCLEROSIS RESEARCH

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Acidosis is a distinctive feature of demyelinating lesions in multiple sclerosis (MS) in the central nervous system (CNS). The cellular response to acidic pH is primarily regulated by a family of G protein-coupled proton-sensing receptors, including OGR1, GPR4, and TDAG8, which are inactive under alkaline conditions and maximally activated in an acidic environment. Genome-wide association studies have linked a locus within the TDAG8 gene to autoimmune diseases, including MS. We found an upregulation of TDAG8 expression in MS plaques, distinguishing it from GPR4 or OGR1. This led to a detailed exploration of TDAG8 expression and function in oligodendrocytes using *in vitro* and *in vivo* models in mice and humans. Surprisingly, we observed significant upregulation of TDAG8 in human MO3.13 oligodendrocytes during maturation and in response to acidic conditions. However, its deficiency did not impact normal myelination in the mouse CNS, and TDAG8 expression remained unchanged under demyelinating conditions in mouse organotypic cerebellar slices. Notably, we found no expression of TDAG8 in primary mouse oligodendrocyte progenitor cells (OPCs), in contrast to its presence in primary human OPCs. These findings highlight substantial species differences in the expression of the proton-sensing receptor TDAG8 in OPCs, underscoring the limitations of the models employed in comprehending the role of TDAG8 in myelination. Despite these model-specific constraints, our results suggest a potential role of TDAG8 in human myelination, implicating its involvement in the pathophysiology of MS, and provide valuable insights into the judicious selection of models for future scientific investigations.

Funding: This project received funding from the National Science Centre, Poland, grant registration number: 2019/33/B/NZ4/03000 (AR).

DELTA9-TETRAHYDROCANNABINOL PROTECTS FROM SPATIAL MEMORY IMPAIRMENTS IN A STREPTOZOTOCIN-INDUCED INFLAMMATION MODEL OF ALZHEIMER'S DISEASE IN RATS

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Recent studies demonstrated that delta9-tetrahydrocannabinol (THC) prevents neurodegenerative processes occurring in animal models of Alzheimer's disease (AD) and protects from inflammation-induced cognitive damage in old mice. In the present study we investigated an influence of intraperitoneal injections of THC at a dose of 5 mg/kg b.w. for 7 consecutive days on spatial memory, measured as a latency to reach the platform and total swimming distance before escaping onto the visible platform in the Morris water maze test (MWM) in rats with the streptozotocin (STZ)-induced inflammation model of AD. In the STZTHC group a significantly shorter ($p<0.05$) total distance (25947.23±2968.37 cm; mean±SD) rather than in the STZTHC solvent group (32016±3580.99 cm) was observed. As compared to the control VEHTHC solvent group, both the latency to reach the platform (2.58 ± 1.17 s) and total distance (22144.88 ± 3025.34 cm) were significantly ($p<0.05$) longer in the STZTHC animals. Moreover, increased total distance ($p<0.05$) but not latency in the STZTHC solvent rather than VEHTHC solvent (22144.88±3025.34 cm) animals was noticed. The seven-day THC (5 mg/kg b.w.) injections could improve spatial memory disorders, as indicated by decreased total swimming distance in the MWM in rats with the inflammation-induced AD model.

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EXPLORING THE NEUROPROTECTIVE POTENTIAL OF PAPE-1 IN CELLULAR ALZHEIMER'S DISEASE MODEL: A NOVEL APPROACH BASED ON TARGETING NON-NUCLEAR ESTROGEN RECEPTOR SIGNALING

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Alzheimer's disease (AD) presents a serious challenge in neurodegenerative disorders due to the accumulation of amyloid-β (Aβ), leading to neuronal dysfunction and cognitive decline. Estrogen receptors (ERs) have emerged as potent mediators of neuroprotection against AD, with non-nuclear ER activation considered safer than nuclear activation. This study investigates PaPE-1, a compound activating non-nuclear ER pathways, for its neuroprotective effects in AD. To model AD, we used mouse primary neocortical cell cultures exposed to Aβ. PaPE-1 was applied with 24 hour-delay and the treatment lasted for 6 hours. The presence of extracellular Aβ aggregates and changes in the expression of AD-related markers (Rbfox, Ache, Apoe, Chat, Ngrn) confirmed the adequacy of our model. We showed that Aβ-induced cell death involves apoptosis-specific pathways. PaPE-1 influenced the expression of AD-related markers and decreased apoptotic cell death in terms of caspase-3 activity. PaPE-1 exerts regulatory control over apoptosis at different stages, including DNA methylation, mRNA expression, and protein level of Bcl2/BCL2 and Bax/BAX. This study highlights PaPE-1's neuroprotective potential and unveils its novel mechanisms of action, supporting the therapeutic promise of targeting non-nuclear ER signaling pathways in developing innovative AD therapies.

Funding: The National Science Centre of Poland, grant number 2020/39/NZ7/00974.

INHIBITION OF JNK PROVIDES NEUROPROTECTION AGAINST 6-OHDA TOXICITY IN PARKINSON'S DISEASE *IN VITRO* MODEL

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Parkinson's disease (PD) is a neurodegenerative disorder caused by death of dopaminergic neurons. The main molecular mechanism underlying PD is oxidative stress, which may be induced by pro-oxidants like 6-hydroxydopamine (6-OHDA). JNK is a major pro-apoptotic kinase involved in pathogenesis of many diseases, and it was also reported to have a key role in PD. The present study aimed to investigate the effect of pharmacological JNK inhibition in cellular model of PD.The study was conducted on SH-SY5Y cells differentiated with retinoic acid. Neurodegeneration was induced by treatment with 6-OHDA. Cells were treated with JNK inhibitor V either before or after 6-OHDA-induced damage. The cell viability was measured by XTT assay, genotoxicity – by comet assay, and the mRNA expression level of specific genes – by RT-qPCR analysis. Inhibition of JNK significantly improved cell viability, even when the inhibitor was applied after 6-OHDA-induced damage. The protective effect of JNK inhibition was also observed against 6-OHDA genotoxicity. Gene expression analysis revealed a significant downregulation of MAPK10, XBP1 and DDIT3 by JNK inhibitor. The results obtained indicate neuroprotective effects of pharmacological JNK inhibition against 6-OHDA-induced damage. Thus, JNK inhibitors could potentially be applied for the selective treatment of PD.

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ER STRESS INHIBITION RESCUES NEURODEGENERATION IN THE COURSE OF PARKINSON'S DISEASE – AN *IN VITRO* STUDY

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Neurodegeneration in Parkinson's disease (PD) is associated with accumulation of α-synuclein and induction of Endoplasmic Reticulum (ER) stress in dopaminergic neurons, which activates the PERK branch of the UPR signalling pathway. PERK orchestrates neural cell apoptosis *via* upregulation of specific pro-apoptotic genes, which makes it a perfect target for development of novel treatment strategies against PD. The pri-

mary objective of the study was to evaluate the effectiveness of the selected small-molecule PERK inhibitor LDN-87357 (LDN) in PD *in vitro* model. XTT assay was used for the cytotoxicity analysis. SH-SY5Y cells were exposed to LDN at 0.75-100 μM, 50 μM 0.1% DMSO (solvent for LDN) and 500 nM ER stressor, thapsigargin (Th). Cells treated with Th only served as a positive control, whereas untreated cells as a negative control. qPCR was performed to assess the mRNA expression levels of specific ER stress related pro-apoptotic genes including DDIT3, BAX, ATF4 and GADD34 and anti-apoptotic gene BCL-2. Cells were treated with LDN at 0.75 or 50 μM, 0.1% DMSO, 500 nM Th or with LDN+Th. Untreated cells constituted a negative control. XTT test demonstrated no cytotoxic effect of investigated PERK inhibitor towards SH SY5Y cells. Importantly, the viability of cells exposed to Th was significantly increased upon pretreatment with LDN. qPCR revealed a significant decrease in the expression of pro-apoptotic genes, and an increase in anti-apoptotic genes expression in SH SY5Y cells with induced ER stress conditions, as compared to only Th-treated cells. To effectively treat PD, new drugs which directly target the molecular pathways involved in pathophysiology of the disease need to be developed. We may assume that targeting PERK *via* small-molecule inhibitors, such as LDN-87357, may contribute to development of a novel targeted therapy against neurodegenerative diseases, that would provide neuroprotection and have no cytotoxic effect.

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GHRELIN RECEPTOR AGONIST MK-0677 RESCUES MOTOR IMPAIRMENTS AND PROTECTS SUBSTANTIA NIGRA DOPAMINE NEURONS IN MOUSE ALPHA-SYNUCLEIN AGGREGATION MODEL

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Parkinson's disease (PD) is neurodegenerative disorder which motor symptoms are connected with progressive loss of dopamine neurons. Another sign of PD is Lewy Pathology which formation and transmission are linked with alpha-synuclein's (a-syn) prion properties. We have previously demonstrated that activation of Akt and Src pathways by neurotrophic factors reduce accumulation of a-syn. Here our goal was to determine if activation of those pathways by Ghrelin Receptor agonist MK-0677 will be also protective. Mice injected into striatum with prion a-syn fibrils (PFFs) were treated with saline (SAL) or MK-0677 at different doses for either 1 or 4 months, followed by behavioral tests and immunostaining for markers of dopamine neurons and a-syn aggregates. After 1 month PFF+SAL mice exhibited impaired motor coordination on multiple static rod test which was reversed by MK-0677 at 1 mg/kg and 2 mg/kg. PFF+SAL group had decreased number of TH+ neurons, rescued by MK-0677 at 0.2 mg/kg, 1 mg/kg and 2 mg/kg. Number of a-syn aggregates in TH+ cells increased in 0.2 mg/kg dose, decreased in 2 mg/kg. After 4 months MK-0677 at 2mg/kg clearly decreased amount of a-syn aggregates in TH+ cells. Our results strongly support further investigations of GHS-R agonist for treatment of PD at early stages.

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INFLUENCE OF GPR84 ACTIVATION ON CELL DEATH MECHANISMS IN MICROGLIAL CELLS

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The GPR84 receptor, an orphan G-protein-coupled receptor, is expressed in various immune cells, including microglia, the resident macrophages of the central nervous system (CNS). Microglia play a significant role in the pathophysiology of CNS disorders. While the activation of GPR84 is associated with the regulation of inflammatory processes, the precise mechanism remains elusive. As microglial death and its consequences serve as a means of communication within the CNS, our study aims to investigate the effects of GPR84 activation on the regulation of pyroptosis and apoptosis pathways in human microglial cells. Employing a pharmacological approach, we analysed gene expression associated with pyroptosis and apoptosis using RT-qPCR. We observed an increase in GPR84 expression during microglial apoptosis, whereas its expression decreased during pyroptotic cell death. Interestingly, treatment with DL175 (a GPR84 agonist) resulted in increased expression of

the main pyroptotic factor, NLRP3, in control cells, but decreased expression during pyroptosis. Additionally, altered expression of caspase genes was noted in HMC3 cells following GPR84 activation. These findings suggest that GPR84 may regulate microglial cell death by modulating pyroptosis and apoptosis through distinct mechanisms, contributing to our understanding of its role in CNS immune response regulation.

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ASTROCYTE HETEROGENEITY AND MOLECULAR MARKER VISUALIZATION IN THE RAT BRAIN

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Astrocytes – star-shaped glial cells support neurons structurally and energetically, but also coordinate their functions in e.g., memory or compensatory processes. Astrocytes are naturally heterogeneous and vary in terms of localization, morphology, protein expression and activation state. In this study, we documented those differences in the cerebral cortex, striatum and substantia nigra. To observe this heterogeneity *in vivo*, immunohistochemically stained brain sections were examined in a rat model for selective, prolonged astrocyte dysfunction by constant infusion of fluorocitrate and in a 6-OHDA dopaminergic system lesion model. Astrocyte-specific GFAP, glutamine synthetase and s100β protein expression were detected. In astrocyte depletion model, activated astroglia surrounded lesioned area probably creating a „glial scar". In contrast, neuronal degeneration did not affect astrocytic markers. Regional differences in cell density and shape were visible in particular markers. Marker protein expression showed that astrocytes tailor their morphology to specific brain parts, most probably to perform region and neuron type-dependent functions. Observed variability also hints at functional flexibility and indicates necessity to co-detect multiple markers to better understand molecular context of changes. Astrocyte-specific markers have already been put into discussion as perspective tools for neurodegenerative disease diagnostics.

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INTERPLAY OF NORADRENERGIC TRANSMISSION AND ASTROCYTIC REACTIVITY IN NEURODEGENERATION: INSIGHTS FROM CELLULAR AND ANIMAL MODELS

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Neuroinflammation and glial reactivity contribute to dopaminergic neuron degeneration in Parkinson's disease. Noradrenergic enhancement shows promise as a neuroprotective strategy against dopaminergic cell loss, partly by reducing glial activation. We investigated whether noradrenergic transmission is mediated by astrocytes. We induced a reactive phenotype in primary mouse astrocytes using IL-1α-TNFβ or IL-1β-TNFβ treatment, leading to characteristic changes: altered morphology, decreased GFAP expression, increased proliferation, and Nf-kB translocation to the nucleus. Cytokine stimulation increased monocarboxylate transporter expression, indicating metabolic changes, confirmed in seahorse studies. In midbrain neuronal cultures, cytokine treatment didn't affect TH+ dopaminergic neuron numbers, but co-culturing with astrocytes led to dose-dependent TH+ neuron reduction, mitigated by α-adrenergic receptor agonists. In mouse models mimicking Parkinson's disease (PD), progressive noradrenergic cell degeneration and phenotypic changes occurred without TH+ cell loss in the SN/VTA but with increased neurodegenerative markers, GFAP expression, and astrocytic chemokines. Elevated genes in the SN included among other Sgk1, an astrocytic GR-dependent gene. Our results provide data on the possible negative influence of noradrenergic degeneration on SN/VTA, confirming the neuroprotective role of noradrenaline, possibly also mediated by astrocytes. Primary astrocytes after IL-1α-TNFβ or IL-1β-TNFβ treatment acquire reactivity and are a useful model for *in vitro* research.

Funding: 2019/35/N/NZ7/03300 financed by the Polish National Science Center.

EXPLORING THE ROLE OF HIPPOCAMPAL ASTROCYTES IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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Astrocytes are implicated in several cellular and synaptic mechanisms that play a crucial role in different pathophysiological and behavioral phenotypes linked to Alzheimer's disease (AD). Our aim is to elucidate the contribution of astrocytes in different AD phenotypes, opening a window to new treatments against cognitive deficits in AD. In this study, we used male and female APP/PS1 mice as a model of AD. First, we set up a behavioral analysis combining EzTrack® and DeepLabCut™ with handmade Python scripts. Notably, we observed sex- and genotype-dependent effects in different cognitive domains. Second, we used *in vivo* fiber photometry to investigate whether astrocyte calcium dynamics are linked with memory alterations. Animals at five-months-old were operated and infused with pZac2.1 gfaABC1D-cyto-GCaMP6f virus in dorsal and ventral hippocampus. After 4 weeks, animals performed the behavioral paradigms in a within-subjects design (novel object recognition and light-tone sensory preconditioning). Our preliminary data suggest sex- and/or genotype-dependent differences in hippocampal calcium dynamics at different phases of the behavioral tasks. Overall, this data suggests a direct link between astroglial calcium dynamics and the behavioral differences found in an AD' animal model, which should be further confirmed with causal experiments.

THE EFFECTS OF EXPRESSION OF WILD-TYPE AND E46K- MUTATED A-SYNUCLEIN ON *DROSOPHILA MELANOGASTER* BEHAVIOR

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α-Synuclein (α-Syn) is a protein encoded by SNCA gene, involved in the regulation of synaptic vesicle trafficking and neurotransmitter release. However, mutated form of α-Syn has high ability to aggregation and it is a major component of protein inclusions known as Lewy bodies, which are hallmarks of synucleinopathies including Parkinson's disease (PD). In our studies we used *Drosophila melanogaster* as a model of familial PD linked with mutation of SNCA. Insects do not express synuclein, however using transgenic flies we were able to prepare flies with expression of human wild-type and E46K-mutated α-synuclein in glial cells and neurons, respectively. Previous research, has shown that E46K α-synuclein caused remarkable climbing defects, as well as reduced survivorship. However, there is still much that remains unknown about the role of α-synuclein. In the present project, we compared the effects of expression of wild-type and E46K-mutated α-synuclein on behavior of young and old flies.

THE EFFECT OF THE PARK MUTATION ON FUNCTIONING OF CENTRAL CIRCADIAN OSCILLATOR IN OLD *DROSOPHILA MELANOGASTER*

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Parkinson's disease (PD) is the second most common neurodegenerative disorder. One of the early onset form of PD is associated with mutations in the park gene, which is constitutive among species. PARKIN starts the process of ubiquitination and degradation of damaged mitochondria on the pathway called mitophagy, which disruption leads to increase oxidative stress which causes cell death. There are strong evidences about connection between PD progression and disruptions of the circadian machinery. One of the main models in chronobiology is *Drosophila melanogaster* due to its simplified clock system consisting of 150 neurons divided into 7 groups, including the sLNv neurons that release PDF (Pigment Dispersing Factor) neurotransmitter crucial for circadian activity pattern. In this study, we tried to investigate how ageing contributes to circadian disruptions caused by park mutation. First, we examined the locomotor activity and sleep profiles of young and 30-day-old park mutants. Then, we isolated brains at two time points, at the be-

ginning of the day and the night, and using anti-PDF immunostaining we visualized sLNv neurons to analyse daily axonal plasticity. Young PD model flies exhibited reduced sleep time and increased sleep fragmentation, along with disrupted rhythmicity in sLNv neuron axons complexity. Compared to those results, old flies showed decreased activity amplitude during the day. We also observed changes in the branching pattern of sLNv neurons. Overall, our results showed that PD model flies have disrupted circadian clock and observed changes increase with age.

INCREASED SUSCEPTIBILITY TO PARACETAMOL TOXICITY IN *DROSOPHILA MELANOGASTER* PARKINSON'S DISEASE MODEL

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Paracetamol is a popular over-the-counter analgesic and antipyretic drug. Despite being considered relatively safe it can have toxic effects *via* one of its metabolites called N-acetyl-p-benzoquinone imine (NAPQI). NAPQI depletes reduced form of glutathione and binds to cellular macromolecules resulting in oxidative stress and cytotoxicity. In our study we investigated the effect of paracetamol on Canton-S (wild type control), w1118 (genetic background control) and park1 (mutation in park gene, model of early-onset autosomal recessive Parkinson's disease (PD)) flies. For park1 strain experiments were performed separately on individuals that were homo- or heterozygous for the mutation. Young flies were exposed to 100 mM paracetamol for 24 h and then collected for gene expression analysis or transferred back on the standard cornmeal medium for survival assay. Exposure to paracetamol increased mortality of homozygous mutants, but did not affect heterozygotes or control flies. There were also changes in the expression levels of *gstd2* (glutathione S-transferase D1) gene, genes related to oxidative stress response: *sod1* (superoxide dismutase 1) and *trxr1* (thioredoxin reductase 1) and dopamine-pathway-related genes: dat (dopamine transporter) and ple (tyrosine hydroxylase). Since the toxic effects of paracetamol are especially detrimental for PD-modelling *Drosophila* strain these results suggest that mutation in park gene may increase susceptibility to toxic effects of otherwise safe drug.

LIGHT IMPACT ON SURVIVAL IN PARK MUTANT *DROSOPHILA MELANOGASTER*

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The Earth rotation around the Sun provides dramatic changes in light conditions during the day and night. Most of organisms is light-sensitive, and keep diurnal or nocturnal life style. Light has both, positive and negative effects on an organism; from being a regulator of circadian rhythms to being a factor in ROS production, which can lead i.e., retina degeneration. *Drosophila melanogaster* is a great model for studying molecular and cellular mechanisms of human diseases such as Parkinson's disease. Short lifespan and simple behavior causes that this organism is commonly used in neurobiology of aging. In our study we tried to investigate how different light conditions affect survival of fruit flies. We used males coming from different strains: wildtype CantonS, white mutants and park mutants (both homozygous and heterozygous). We used three different light settings; 12 h of light : 12 h of darkness (LD12:12), constant darkness (DD) and 12 h of light : 12 h of dim light (L-dim). The last conditions simulated light pollution in the dark phase observed in urbanized areas. Experiment started with 30 males per genotype. Survival was checked every day starting from emergence until the death of the last fly in the group. Experiment was repeated three times. We observed statistically significant differences between flies kept under different light regimes. Our results suggest that presence of light may shorten the lifespan, which may be connected with increased oxidative stress levels.

INSULIN SIGNALING DYSREGULATION IN ALZHEIMER'S DISEASE PATHOGENESIS

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Despite extensive research over many years, there is still no consensus on the etiology and pathogenesis of Alzheimer's disease (AD), making it difficult to establish effective treatment and/or prevention strategies. Insulin has been observed to be significantly involved in cell survival, metabolic function and neuronal plasticity. In the present study, the age-dependent expression of insulin (Ins1) and its receptor (Insr) in the frontal cortex and hippocampus of control and transgenic APP NL-F/NL-F mice was examined using real-time polymerase chain reaction. Due to the involvement of adaptor proteins in the insulin pathway, the expression of Irs1, Irs2, Shc-1 and Grb2 was also investigated. It was found that in the AD model studied, the mutation significantly affects the expression patterns of genes involved in insulin signalling, with different effects depending on the brain region studied and the age of the animals. These changes are dynamic and may play a key role in AD pathology, especially given their occurrence early in animal development. Further exploration of the mechanisms underlying these regulatory dysfunctions may lead to the development of new therapies or preventive measures for AD.

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THE EFFECTS OF EXOSOMAL TETRASPANINS OVEREXPRESSION AND SILENCING IN *DROSOPHILA MELANOGASTER* CIRCADIAN NETWORK

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Exosomes have been widely recognised as communication vesicles that transfer bioactive proteins and RNAs between cells under normal and pathophysiological conditions. In this study, we investigate at the cellular and behavioral levels whether this type of cellular communication is subject to circadian regulation in the fruit fly *Drosophila melanogaster*. We used transgenic flies with the targeted expression of GFP-tagged mammalian tetraspanin (Tsp), CD63, to examine its daily expression in neurons and glial cells. We also examined the prominent output of *Drosophila* circadian clock, the circadian rhythm of locomotor activity, in flies with silenced expression of Tsp42Eg and Tsp42Ee in neurons and glial cells of the circadian network. For this study we used confocal microscopy and the Drosophila Activity Monitoring System (DAMS). We found daily changes in CD63 expression in glial cells of *Drosophila* brain. We also detected changes in the daily and circadian pattern of locomotor activity of flies expressing CD63 (with overexpression of tetraspanins) and flies with silenced expression of Tsp42Eg and Tsp42Ee. This implies circadian regulation of this type of cellular communication and suggests that exosomal communication may be an important part of the functioning of the circadian clock/network.

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MITOCHONDRIAL PROTEIN DYNAMICS: KEY PLAYERS IN ISCHEMIC PRECONDITIONING FOR NEUROPROTECTION AGAINST CEREBRAL IR INJURY

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Ischemic preconditioning (IPC) triggers endogenous neuroprotection to defend against subsequent, more severe ischemia. IPC takes advantage of brain plasticity for its neuroprotective purposes, especially for energy and redox homeostasis. Mitochondria sense and respond to diverse harmful stresses, aiding cells in adaptation and resilience, with proteins being a primary focus of their defensive mechanisms. In our

study, 33 hippocampal and 15 cortical mitochondrial proteins exhibited different susceptibility to IPC and ischemia-reperfusion (IR). IPC upregulated glyceraldehyde-3P dehydrogenase and glutamine synthetase in the hippocampus while downregulating isocitrate and succinate dehydrogenase. Peroxiredoxins (Prx) stand out among antioxidant enzymes, with Prx5 and Prx6 levels declining post-IPC but escalating after IR, notably in CA1 and CA3 hippocampal regions. IPC elevated ATP synthase subunit beta and Mn superoxidase dismutase in cortical mitochondria, alongside enhanced ATP synthase, glutathione peroxidase and glutathione reductase activities. Conversely, IR downregulated cytochrome c reductase aconitate hydratase and pyruvate dehydrogenase. Hippocampal proteins exhibit ROS sensitivity, particularly impacting Prx pathways, leading to energy metabolism dysregulation post-IPC. In contrast, the cortex maintains mitochondrial antioxidant availability during cerebral IR injury, indicating region-specific responses to IPC and IR, crucial for targeted neuroprotective strategies.

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ABSENCE OF THE MITOCHONDRIAL CHAPERONE TRAP1 RESULTS IN ALTERED MITOCHONDRIAL DYNAMICS IN THE BRAIN

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Neuronal cells depend on mitochondrial activity to maintain membrane excitability, neurotransmission, and synaptic plasticity. Production of ROS can cause mitochondrial DNA damage. The most common mutation is the oxidation of guanine to 8-oxo guanine. The accumulation of mutations in mtDNA can lead to the impairment of mitochondria function. Fusion and fission determine the mitochondrial morphology and adapt it to the metabolic needs of the cells. Therefore, these two processes are crucial to optimize mitochondrial function. TRAP1 is a mitochondrial chaperone protein that belongs to the HSP90 family. This protein is involved in protection against oxidative stress and regulation of mitochondrial dynamics. In a knock-in mouse model of Trap1 (p.Gln639Ter), the expression level of this protein is significantly reduced and the behavior of mouse mutants is affected. We isolated mitochondrial DNA from the brains of mutant and WT mice. MtDNA was sequenced to compare the amount of the mutations accumulation in different genotypes. Moreover, we isolated hippocampal and cortical mitochondria to investigate the levels and phosphorylation status of proteins involved in fission and fusion.

DAILY CHANGES IN THE MITOCHONDRIA NETWORK IN THE RETINA OF *DROSOPHILA MELANOGASTER*

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Circadian rhythms are daily fluctuations in behavior and physiology, generated by internal timekeeping mechanisms and entrained by environmental cues. Our research focuses on the retina as it possesses a functional circadian clock mechanism and represents a hallmark for neurodegeneration and senescence. Using *Drosophila melanogaster* as a model organism, we aim to elucidate the involvement of the circadian clock in mitochondrial network within the retina. Indeed, these findings serve as a foundation for exploring the impact of circadian disruption on mitochondrial function in the context of neurodegeneration. In this study we investigated daily changes in the number of mitochondria in specific photoreceptor type. We used transgenic flies in which mitochondrial-tagged fluorescent proteins were expressed under control of specific Rhodopsin type. Heads were collected at four time points and cryosections were prepared. Next, fluorescent signal was enhanced using immunostaining with anti-RFP antibodies. Finally, we analysed fluorescent intensity and the number of particles in the photoreceptor cell bodies and terminals, respectively. Our data suggest that mitochondria number in the retinal cells changes during the day.

THE EFFECT OF AGING ON RETINA VULNERABILITY TO UV-INDUCED DNA DAMAGES IN *DROSOPHILA MELANOGASTER*

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Light intensity and composition changes throughout the day, which provides circadian clock synchronization. However, intense light induces production of reactive oxygen species which results in the physical and chemical changes in DNA structure. The retina is at the highest risk of light-induced DNA damages due to its phototransduction function and high level of metabolic processes. Although retina possess many protective mechanisms, they weaken with aging. In addition, the level of retinal DNA damage depends on the time during the day, when it is exposed to UV radiation, because the protective mechanism against the light is controlled by circadian clock. In this study we investigated the consequences of UV radiation on *Drosophila melanogaster* retina in the morning (ZT1) and in the evening (ZT13). To investigate whether protective mechanisms change their effectiveness with age we used young (5-7 days) and old (30 days) wild type Canton-S flies. They were kept under the normal light condition (12 h of light and 12 h of darkness, LD 12:12) and decapitated at selected time points. Brains cryosections were immunostained using the anti-8-hydroxyguanosine primary antibodies to mark DNA breaks, which were then measured by comparing the reaction intensity using ImageJ. In young flies, more severe changes were observed after evening UV exposure. However, in old flies this difference between timepoints was not statistically significant, which suggest that age-related molecular changes in the circadian clock may affect retina vulnerability to light-dependent degeneration.

AGING INSIGHTS THROUGH THE FRUIT FLIES EYES: THE EFFECT OF AGING ON THE RHYTHMS OBSERVED IN THE VISUAL SYSTEM OF *DROSOPHILA MELANOGASTER*

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The aging process of the retina significantly impacts its structure, function, and susceptibility to degeneration, ultimately affecting overall health and visual function. Understanding this process offers valuable insights into age-related visual impairments and holds profound implications for neuroscience, given the close relationship between retinal and brain aging. *Drosophila melanogaster*, with its easy genetics, short lifespan, well-defined retinal structure, conserved molecular and genetic pathways, serves as an ideal model for such investigations. A general decline in neuron function is associated with aging. This study examines whether specific changes occur also in photoreceptor neurons, particularly in *Drosophila's* R1-R6 cells. These alterations may include molecular shifts affecting presynaptic proteins like Bruchpilot (BRP), crucial for calcium channels aggregation in the synaptic active zone and neurotransmitter release. Consequently, synaptic transmission relies on BRP, with decreased levels resulting in weaker transmission. BRP expression was previously shown to be regulated by both, light and circadian clock, expressing distinct pattern – reaching maximum at the beginning of the day (ZT1) and night (ZT13). To investigate possible changes in the retina rhythmicity during aging we collected old flies at specific time points throughout the day (ZT1, ZT4, ZT13, ZT16). We cryosectioned heads and immunostained them with anti-BRP antibodies. Analysis of confocal images showed that aging retina maintains daily presynaptic protein profile observed in young flies. These results highlight the need for further investigation into the molecular mechanisms underlying age-related changes in *Drosophila's* retina.

BLOCKING OF DIAPH1 SIGNALLING AFFECTS THE ULTRASTRUCTURE OF THE RETINA

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Diaphanous homolog 1 (Diaph1) is a protein crucial in neural tissue development, especially actin polymerization and microtubule formation. Lack of Diaph1 leads to neurodevelopmental disorders such as blindness, deafness, microcephaly, and seizures. The study aimed to compare the retinal structure of wild-type (WT) C57BL/6 mice with Diaph1 knockout (DKO) mice. Retinas from six mice (three WT, three DKO) were fixed in 2.5% glutaraldehyde and 1% paraformaldehyde, post-fixed in 2% osmium tetroxide, dehydrated, and embedded in Epon 812. Morphometric analysis on semi-thin sections stained with toluidine blue was performed across five layers: Inner Plexiform Layer (IPL), Inner Nuclear Layer (INL), Outer Plexiform Layer (OPL), Outer Nuclear Layer (ONL), and Photoreceptor Layer (PL) using CaseViewer. Statistical results highlighted significantly thinner OPL and PL in DKO mice (OPL: 11.94±3.62 µm DKO *vs.* 14.67±3.56 µm WT; PL: 44.80±4.85 µm DKO *vs.* 49.98±7.97 µm WT). The results highlighted Diaph1's essential role in retinal cilia formation. The OPL layer is a complex structure that consist of dendrites and axons of many neuronal cells, thus the impact of Diaph1 knockout requires further investigation.

NEGATIVE EFFECTS OF MATERNAL SMOKING ON RETINOPATHY OF PREMATURITY

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A disorder associated with premature birth, called retinopathy of prematurity (ROP), is a neurovascular disease of the retina. The oxygen-induced retinopathy (OIR) is a well-established model of ROP characterized by vessel abnormalities. There are several factors which can result in premature birth, such as smoking during pregnancy. Our aim was to examine the vulnerabilities of maternal smoking on OIR. C57BL/6 laboratory mice were used in this experiment. During the pregnancy mice had to smoke two times a day. To induce OIR, pups were exposed to hyperoxia from postnatal day (PD) 7-12 then returned to room air. On PD17 retinas were isolated. Isolectin GS-IB4 was used to label the endothelial cells of the retinas, then a computational tool was used for further quantitative analysis of the retinal vascular networks. Several antibodies were detected and quantified by western blotting of pooled retinas distributed by treatment groups. Our computational analysis of retinal vasculature showed quantitative changes in several parameters as well as in case of the protein expressions examined by western blotting compared to control conditions. Based on our results we showed that maternal smoking caused a greater degree of retinal damage in ROP.

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THE PROTECTIVE EFFECT OF PACAP38 IN TYPE 2 DIABETIC RETINAL DISEASE

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Type 2 diabetic retinal disease (T2DRD) is a leading cause of permanent blindness in the diabetic population. Pituitary adenylate cyclase-activating polypeptide (PACAP) has neuroprotective effects. One of the isoforms, PACAP38 has an impact against the apoptotic signaling pathways and creates an anti-inflammatory environment in the retina. Our aim was to test the possible retinoprotective effect of topical administration of PACAP38 in type 2 diabetic animal model. Type 2 diabetes was induced in Wistar rats with the combination of streptozotocin administration and high-fat diet. All rats were treated topically two times a day for 4 months, accordingly. Diabetes model was validated by fasting oral glucose tolerance test and C-peptide ELISA test. Electroretinography (ERG), optical coherence tomography (OCT), immunohistochemistry, and vessel analysis were performed in the retinal samples. Our ERG results showed that the visual function of PACAP38-treated diabetes group was preserved. The OCT measurements correlated with the ERG data where the total retinal thickness was preserved in the diabetes+PACAP38 group. The retinal microvascular structure and the ganglion cell number were also protected. Topically administered PACAP38 has displayed its potent neuroprotective effect against T2DRD, therefore it could be a promising therapeutic approach for the treatment of the disease.

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POTENTIAL NEW TREATMENT TARGET IN BACTERIAL KERATITIS

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Bacterial keratitis is an infection of the corneal tissue caused by various bacterial species. Keratitis is still responsible for the most sight-threatening lesion. Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide, known for its neuroprotective and anti-inflammatory effects, which are mainly mediated through PAC1 receptor (PAC1R). The aim of our research is to investigate the protective role of the PAC1R in endotoxin-induced keratitis model in mice. In our study, we induced bacterial keratitis in a CD1-IGS mouse strain by intraperitoneal injection of lipopolysaccharide (LPS). To investigate the role of PAC1R, half of the animals were treated intravitreally with a PAC1R antagonist, maxadilan. 24 h after injection, optical coherence tomography (OCT) and routine histology were performed. Cytokine arrays were executed to map inflammatory pathways. Five weeks after the LPS administration, a four-step scoring system was used to determine the degree of keratitis. Based on OCT and histology results, maxadilan attenuated the increase of central corneal thickness and inhibited the activation of inflammatory cytokines. Five weeks later the group receiving LPS and treated with maxadilan showed less severe keratitis. Our results suggest that targeting the PAC1R could be a promising therapeutic approach for the treatment of bacterial keratitis.

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EFOP-3.6.2-16-2017-00008; "The role of neuroinflammation in neurodegeneration: from molecules to clinics''; and Higher Education Institutional Excellence Programme of the Ministry of Human Capacities in Hungary: 20765/3/2018/FEKUTSTRAT, 2020-4.1.1-TKP2020—FIKP III. Project No. TKP2020-IKA-08 has been implemented with the support provided from the National Research, Development and Innovation Fund of Hungary, financed under the 2020-4.1.1-TKP2020 funding scheme.

EFFECT OF TRIS(2,3-DIBROMOPROPYL) ISOCYANURATE ON MOUSE HIPPOCAMPAL NEURONAL CELLS

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Tris(2,3-dibromopropyl) isocyanurate (TBC) is one of the novel brominated flame retardants (NBFR), widely used in industry. Current data showed significant bioaccumulation of TBC in the environment and living organisms. Because it has been showed that TBC is a lipophilic substance, while nervous tissue is rich in fat, so probably TBC can pass through the blood-brain barrier. To date, TBC is also known as an endocrine disruptor which may have a particularly negative effect on the nervous system of the human and animals. This may be important for the induction of inflammatory processes that cause disorders and development of neurodegenerative diseases. Therefore, the aim of our research was to evaluate the effect of TBC treatment on the mouse hippocampal neuronal cell line (HT-22) *in vitro* as a model cells. It is also important to understand the mechanism of action of TBC. The basic parameters of the research were changed in HT-22 cells after use TBC with cotreatment. Additionally, we analyzed the effect of TBC and cotreatment on the expression of proteins related to inflammatory processes. Our results indicate the involvement of TBC in these processes, which may indicate a negative impact on neuronal cells.

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TITANIUM(IV) OXIDE NANOPARTICLES SURFACE-MODIFIED WITH SALICYLIC AND 5-AMINOSALICYLIC ACID AFFECT LIPID AND PROTEIN OXIDATION IN THE BRAIN OF WISTAR RATS

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The broad use of titanium(IV) oxide (TiO2) particles in various products, and toxicity indicators of particles with diameters<100 nm (nanoparticles, NPs), inspire scientists to find a suitable, non-toxic replacement. An effective approach to diminish TiO2 NPs toxic impact might comprise altering their physicochemical properties by surface modification. Therefore, commercially available TiO2 NPs were surface-modified with antioxidants: salicylic acid (SA-TiO2) or 5-aminosalicylic acid (ASA-TiO2), with a goal to compare their ability to reduce oxidative stress, specifically levels of lipid peroxidation (LPO) and advance oxidation protein products (AOPP) in the brain of Wistar rats. Oxidative stress markers were determined in whole cell brain extracts, isolated 14 days following acute oral intake of either vehicle (V, 2.5 ml 0.01 M HCl) or TiO2/SA-TiO2/ASA-TiO2 NPs (1000 mg/kg dissolved in V). The results showed that LPO levels were evenly elevated in all TiO2 treated groups relative to the V group. However, AOPP levels in ASA-TiO2 group were similar to V group and significantly lower compared to TiO2 and SA-TiO2 groups; suggesting that this modification moderates some of the TiO2 NPs-induced toxicity. Additional experiments are required to investigate their effects on toxicity mechanisms and fully elucidate the potential of ASA-TiO2 as TiO2 NPs substitute.

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ELASTIN-DERIVED PEPTIDE AS A POTENTIAL NEURODEGENERATIVE FACTOR

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Elastin is present in many tissues e.g., brain. It is well-described that elastin-derived peptides (EDPs) are created during age due to elastin decay. The increasing amount of EDPs during aging correlates with the first symptoms of many neurodegenerative diseases. Therefore, the study aimed to determine the impact of EDP on basic parameters of neuroblastoma-derived neurons, together with determining its ability to induce neurodegeneration in these cells as well as engagement of certain roles of the specific histone deacetylase (HDAC) in this process. The obtained results show no significant changes in the cells during dose-response analysis after 24h and 48h of treatment, however, the confocal microscope-based analysis proved the ability of the EDP to induce morphological changes in the neurons i.e., shortening axons' length. Furthermore, the changes in the antioxidant enzymes were detected in the tested time intervals of treatment. Lastly, the increased expression of HDAC and tubulin-related proteins were observed. Summarizing, the results show – for the first time – that tested EDP can cause neurodegeneration phenotype in neurons with potential engagement of specific HDAC. However, more studies are needed in this field.

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EXPLORING THE NEUROPROTECTIVE POTENTIAL OF A NOVEL THIRD-GENERATION TSPO LIGAND IN TAUOPATHY

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The 18 kDa Translocator protein (TSPO), formerly recognized as the peripheral benzodiazepine receptor (PBR), has been considered a positron emission tomography (PET) biomarker for various types of neuroinflammation. While it has been demonstrated that TSPO ligands may decrease the level of beta-amyloid peptide associate in Alzheimer's but their role for tau pathology remains unexplored. To investigate this aspect, we conducted an analysis of the influence of the third-generation TSPO ligand, BBMP regarding the progression of the tau transgenic mice neuropathology. In pursuit of this objective, we conducted an analysis of the impact of the third-generation TSPO ligand BBMP (2-(5-bromo-2-oxo-1,3-benzoxazol-3(2H)-yl)-N-methylN-phenylacetamide) on development of neuropathology in TauTg. Analysis were made through MR and PET imaging and immunohistochemistry/autoradiography. The *in vivo* animal neuro-imaging results were corroborated with immunohistochemistry to analyse markers associated with inflammation (TSPO, Controller of the complement cascade (1q/C1q), microglial tauopathy marker (AT8) and the neuronal survival (NeuN), in the brain sections obtained from the mice that underwent scanning.The administration of BBMP significantly reduced atrophy during the 6 to 10-month period, resulting in a 50% reduction in cortical and hippocampal volumes in comparison to TauTg mice administered with the vehicle. Administering BBMP to TauTg mice resulted in a decrease in average concentration levels of the three assessed inflammatory markers. Distance-based redundancy analysis revealed a strong correlation (80%) between the variation in inflammatory markers among groups and C1q (0.996). The indicators of neuroinflammation/degeneration in cortex and hippocampus exhibited a negative association with inflammatory markers. In conclusion, our data point to a safeguarding role of new generation TSPO ligands in tauopathies, with the potential to lower neuroinflammation/degeneration, and brain atrophy.

ANALYSIS AND FUNCTIONAL CHARACTERIZATION OF ALTERNATIVELY SPLICED NOVEL ISOFORMS OF HUMAN GENES ENCODING SMALL HEAT SHOCK PROTEIN 8 AND DECIPHERING THEIR POTENTIAL ROLE IN NEUROPROTECTION

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HSPB8 also known as the alpha-crystallin C chain, protein kinase H11 or small stress protein-like protein HSP22 is a small heat shock protein. This protein functions as a chaperone in association with Bag3, a stimulator of macroautophagy. It intervenes in the governance of cell proliferation, apoptosis, and carcinogenesis. Mutations in this gene have been linked with various neurodegeneration. HSPB8 manoeuvres its role by expediting autophagy by inhibiting the deposition of misfolded proteins in afflicted cells. Ameliorating the discerning attempt of misfolded proteins by HspB8-BAG3-Hsp70 to autophagy might also result in reduced delivery to the proteasome by the BAG1-Hsp70 complex so that the probable proteasome overwhelming is reduced. With the help of bioinformatics, we have predicted novel exons of the human HSPB8 gene. The addition of novel exons in the mature RNA transcript resulted in the removal of the essential residues of the HSPB8 protein. These novel isoforms can be analysed to understand their role in neuroprotection and several other processes in which HSPB8 plays a cardinal role. These novel isoforms can also be targeted for therapeutic purposes by developing splice-switching antisense oligonucleotides (SSOs) in order to regulate their functioning.

POSTER SESSION II – PSYCHOPHYSIOLOGY

26th April, 2024 (Friday), 14:00–15:15

GRAPH ANALYSIS OF THE GUILT NETWORK HIGHLIGHTS ASSOCIATIONS WITH SUBCLINICAL ANXIETY AND SELF-BLAME

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Maladaptive forms of guilt, such as excessive self-blame, are common characteristics of anxiety disorders. Nevertheless, despite understanding the anatomy of the guilt processing circuitry, it is currently unknown how its network-level interactions are related to subclinical anxiety and self-blaming behavior. To fill this gap, we used resting-state functional and diffusion-weighted magnetic resonance imaging (MRI) data to construct the guilt networks in 78 young healthy adults, and subsequently investigated associations of their graph theory parameters with these two phenomena. Increased functional contributions (higher clustering coefficient, local efficiency and strength) of the left superior anterior temporal lobe (sATL) were a common feature for individuals with higher self-blaming and trait-anxiety, while functional isolation (lower clustering coefficient and local efficiency) of the left inferior frontal gyrus pars opercularis and insula was related to higher trait-anxiety. Trait-anxiety was also linked to the structural network's global parameters (mean clustering coefficient), with the circuitry's architecture favouring increased local information processing in individuals with increased anxiety levels. Previous research suggests aberrant interactions between conceptual (sATL) and affective (fronto-limbic) regions underlie maladaptive guilt and the current results align and expand on this theory by detailing network changes associated with self-blame and trait-anxiety.

RELATIONSHIPS BETWEEN INDIVIDUAL DIFFERENCES IN REINFORCEMENT SENSITIVITY, CAFFEINE CONSUMPTION AND SELF CONTROL

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Current knowledge of Gray's Reinforcement Sensitivity Theory (RST) and stimulating substances is mainly focused on drugs and alcohol. Relationships between BIS/BAS and caffeine have not yet been researched. The study explored relationships between RST, caffeine consumption, and self-control in 187 Polish adults aged 18 to 30 years old. A Polish version of the RSQ (Reinforcement Sensitivity Questionnaire), a Polish version of the SCS (Self-Control Scale) and a self-made caffeine intake questionnaire were used. Questionnaires were sent out online in the form of a survey.

Relationships between caffeine and BIS/BAS scores were not determined. No relationships between caffeine intake and self-control were found. There were no differences between subjects with high and low scores on the sensitivity to reward (BAS) scale in caffeine intake. There was a moderate negative correlation between the sensitivity to punishment (BIS) scale and self-control. Additionally, there were significant differences between people with high and low BIS scores; people with low BIS had higher scores on a self-control scale than people with high BIS. Individuals with high BIS might be driven by the avoidance of risk and punishment, which takes away control of their own actions. The study highlights the lack of research between RST and caffeine intake.

EXAMINING INTOLERANCE OF UNCERTAINTY IN AN AFFECTIVE NEUROSCIENCE FRAMEWORK

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This study, aims to examine the relationship between the level of intolerance for uncertainty and the affective neuroscience personality traits. The sample is a total of 174 participants, aged between 18-25, female (112) and male (62) in Turkey. It was used a non-experimental cross-sectional and correlational design in this study. Demographic data were collected using a Demographic Information Form, Affective Neuroscience Personality Scale and Intolerance of Uncertainty Scale were used to data collection. Positive correlations were identified between intolerance of uncertainty and emotions such as sad, anger, fear and care, elucidating the emotional associations of uncertainty in the affective neuroscience personality scale. It is planned that this study be expanded into a cross-cultural investigation by collecting data from Norway in the future. This proposed research aims to explore tolerance to uncertainty within the context of cross-cultural affective neuroscience, focusing on the influence of culture on the regulation of basic emotional systems. By explaining how tolerance for uncertainity is influenced by cultural context and how it relates to emotions in affective neuroscience, intends to contributes to improving cross-cultural understanding and insights into its implications for mental health outcomes like anxiety disorders, guiding interventions to enhance resilience and coping mechanisms.

WHO IS RESISTANT TO SLEEP DEPRIVATION?

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Sleep deficit results in a variety of neurocognitive effects, impaired emotional recognition and psychosocial functioning. This study explores individual differences in vulnerability to sleep deprivation in terms of subjective socio-emotional and cognitive functioning. Thirty healthy volunteers (mean age 23.4 ± 3.7 years) participated in three sleep conditions: full-rest sleep/baseline (B), chronic partial sleep deprivation (C), and acute/total sleep deprivation (A). Two sets of subjective questionnaires assessed individual traits (chronotype,

sensitivity, and personality dimensions) and well-being measures including sleepiness, physiological symptoms, irritation, cognitive attenuation, positive and negative affectivity, and pleasure experience. Results indicated varying physiological symptoms, irritation, and cognitive attenuation across conditions, with total sleep deprivation showing the largest effects. Differences in pleasure were observed between full-rest and chronic sleep deprivation conditions, participants reported less pleasure in the latter. As far as subjective well-being is concerned, total sleep deprivation seems to be a more difficult experience than chronic sleep restriction. Resistance to chronic sleep restriction is linked to morning orientation, low sleep need, low sensitivity, and high extraversion. Resistance to total sleep deprivation is associated with low circadian rhythm amplitude and lower levels of sensitivity, neuroticism, agreeableness, and openness to experience. These findings contribute to a better understanding of the individual response to sleep loss.

Funding: The research was supported by the grant from the Polish National Science Centre No 2018/29/B/HS6/01934.

EXPLORING CIRCADIAN RHYTHM DISTINCTNESS: IMPLICATIONS FOR NEGATIVE EMOTIONALITY AND PUNISHMENT PROCESSING

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Several studies found behavioral and neural differences corresponding to chronotypes. However, the impact of other dimensions of the circadian rhythm is unclear. This study explored how circadian rhythm distinctness (subjective amplitude) influenced reward and punishment processing. We examined 37 healthy participants aged 20-30. Distinctness was measured using the Morningness-Eveningness Stability-Scale improved (MESSi) questionnaire. We also administered questionnaires assessing personality (NEO-Five Factor Inventory; NEO-FFI) and reinforcement processing: the Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ), and the Positive and Negative Affect Schedule (PANAS). Moreover, we used functional magnetic resonance imaging (fMRI) during the Monetary Incentive Delay Task, which is a common method of assessing reward- and punishment-motivated behavior. Analyses were conducted using the FSL program and statistical packages in Python. We found a positive correlation between a value of distinctness and a level of neuroticism, sensitivity to punishment, and negative affect. fMRI results showed increased activity during the anticipation phase of 'punishment' trials in the bilateral Superior Frontal Gyrus and Supplementary Motor Cortex (BA 8, 6) for higher values of the distinctness. The results emphasize the negative emotionality aspect of high-distinctness people and suggest the association between a higher value of distinctness and enhanced neural processing of punishment-related information.

Funding: This work was supported by the Ministry of Science and Higher Education (Poland) as a project under the program Excellence Initiative – Research University (2020-2026) no. BOB-IDUB-622-28/2023 (IV.4.1).

ASSOCIATION BETWEEN PSYCHOPATHY AND IMPULSIVITY: A THREE-LEVEL META-ANALYSIS OF SELF-REPORT AND BEHAVIORAL MEASURES

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Psychopathy is a personality disorder that manifests as a syndrome characterized by a constellation of affective, interpersonal, and behavioral features. Every conceptualization of psychopathy considers impulsivity a central feature of the disorder. However, both psychopathy and impulsivity are multifaceted constructs and associations between the different facets of those constructs has never been subjected to a systematical assessment. We conducted a pre-registered meta-analysis to estimate the direction and the strength of association between psychopathy and impulsivity. Moderator analyses included factors of psychopathy, mea-

sures of impulsivity, demographic characteristics of the participants, recruitment sources, as well as measures of the disorder. One-hundred and sixty-eight articles, consisting of 173 independent samples (N=43,944) were included. The overall association between psychopathy and impulsivity was reliable and yielded a moderate effect size (r=.23), with a stronger association for Trait (r=.27) than State (r=.16) measures with no evidence of publication bias. Factor 1 had a weaker association (r=.10; no Trait-State moderation) than Factor 2 (r=.26; Trait-State moderation: Trait: r=.30; State: r=.13). We show that impulsivity is positively associated with psychopathy, but this association varies by psychopathy factors and the type of impulsivity measure.

CLASSICALLY CONDITIONED SPATIAL DIMENSION OF PAIN IN HUMANS

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One of the most challenging health conditions to address is chronic widespread pain, the mechanisms of which are not fully understood. We used classical conditioning procedures to investigate if the expanded area of pain results from classical conditioning between nociceptive stimuli originating from different nociceptive foci. Healthy adult participants were randomly assigned to one of four experimental groups. In the first group, participants underwent classical conditioning by pairing visual cues with the magnitude of the painful area. They were also informed, through verbal instruction, that one of the visual cues would announce pain distributed at a larger area. In the second group, participants were exposed only to classical conditioning, while in the third group, they only received verbal suggestion. The fourth group served as a control (no conditioning, no instruction). Nociceptive stimuli were delivered through electrodes attached to participants' hands, activating two electrodes for a large distribution or one for a small distribution of pain. Classical conditioning combined with instruction was effective at inducing pain at a larger area despite nociceptive stimulation targeting a small area of the body ($p<0.001$). Furthermore, this effect was preserved even if two methods were used separately: Classical conditioning alone ($p<0.05$) or verbal suggestion alone ($p<0.01$) produced conditioned pain distribution. We did not find a statistical effect in the control group ($p>0.05$).

Funding: The study was funded by a OPUS19 grant awarded by the National Science Centre in Poland (no. 2020/37/B/HS6/04196).

CROSS-MODAL CONGRUENCY EFFECT AS A MEASURE OF BODY OWNERSHIP IN VIRTUAL REALITY. INSIGHTS FROM A FULL-BODY ILLUSION STUDY

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The full-body illusion is a well-established experimental paradigm for inducing illusory ownership over fake or virtual bodies. While subjective ratings and proprioceptive drift have been used to measure this phenomenon, our study aimed to explore the potential of the cross-modal congruency effect (CCE) as an alternative measurement of body ownership. In our study, participants wore VR goggles displaying a mannequin's body and felt vibrations on their feet. Red dots appeared on the mannequin's feet simultaneously, congruently or incongruently with the felt vibration, and participants' task was to report immediately which foot they felt the vibration on. Additionally, they received synchronous or delayed stroking on their abdomen and thighs, while observing the same actions in VR. While synchronous trials yielded stronger subjective rating of ownership in synchronous trials and faster CCE task response time during congruent trials, there was no significant main effect of illusion condition or interaction between illusion condition and congruency on CCE task reaction time. These findings suggest successful induction of the illusion through the first-person perspective, yet the lack of correlation with CCE implies a dissociation between body ownership and cross-modal congruency. Further research is needed to explore the relationship between CCE, peripersonal space, and self-location experiences.

TESTOSTERONE AND CORTISOL JOINTLY MODERATE SUBJECTIVE EXPERIENCE OF STRESS IN MALES

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The dual-hormone hypothesis states that testosterone is positively related to status-seeking behaviors only when cortisol level is low. This idea has been validated in the research on status-relevant behaviors. However, there are no studies investigating this hypothesis in the context of social stress perception. Socially stressful situations might be perceived as a status threat. Therefore, joint effects of testosterone and cortisol are plausible. This study aimed to evaluate if the dual-hormone hypothesis applies to the subjective evaluation of perceived social stress. Mild social stress was induced in 36 males by using a short Sing-a-Song Stress Test. An electrocardiogram was recorded to evaluate heart rate variability (HRV) parameters. Participants indicated perceived stress on the visual analog scale. Before the stress manipulation, saliva samples were collected to measure basal levels of testosterone and cortisol. HRV analysis confirmed stress induction. Moderation analysis revealed a negative association between testosterone and perceived stress when cortisol levels were low. Whereas when cortisol levels were high, testosterone was positively associated with perceived stress. Cortisol was negatively related to perceived stress only when testosterone levels were low. These findings support the dual-hormone hypothesis on the perception of social stress.

EFFECTS OF VIRTUAL HEIGHT EXPOSURE ON POSTURAL CONTROL

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To examine how the fear of falling influences balance control independently of aging and pathology, healthy individuals are exposed to various postural threats, representing natural stressors. The most common postural threat is exposure to height by elevating the surface on which individuals stand. The aim of the study was to examine postural and psychophysiological responses to virtual height exposure in 42 young individuals with different intensities of fear of heights. The measurements were carried out during stance on an unstable surface at ground level and at heights of 20 m and 40 m in a virtual reality environment. The height exposure elicited a complex, robust, and reliable psychophysiological response with significant changes in emotional state, sympathetic activity, and postural control, which were enhanced in individuals with a fear of heights. Those with higher fear showed a rigid and more stiffened posture characterized by smaller magnitude and simultaneously increased velocity of body sway. For the assessment of postural stability in stressful environments, such as height exposure (both real and virtual), it is important to take into account the currently experienced fear and anxiety that can significantly contribute to resulting postural stability and may have more significant implications in populations with a fear of falling.

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ASSOCIATION BETWEEN AIR POLLUTION EXPOSURE AND GLOBAL WHITE MATTER BRAIN MEASURES: NEUROSMOG STUDY

Paulina Lewandowska[1,8]*, Claude J. Bajada[2], Mikołaj Compa[1], Aleksandra Domagalik[3], Katarzyna Kaczmarek-Majer[4], Krzysztof Skotak[4], Małgorzata Lipowska[5,6], Clemens Baumbach[1], Yarema Mysak[1], Katarzyna Sitnik-Warchulska[6], James Grellier[1,7], Iana Markevych[1,9,10] and Marcin Szwed[1]

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Air pollution has been proven to have a negative impact on human health. There is evidence that it can cause cardiovascular disease, pulmonary disease, and breathing problems but there is still little known about how air pollution affects the nervous system. Here, we present preliminary results on how early life (0-4 years) and prenatal air pollution exposure affects global brain measures – fractional anisotropy and mean diffusivity – in children aged 10 to 13 from the NeuroSmog project. We found significant associations between early life NO2 exposure and global white matter integrity measures: fractional anisotropy, and mean diffusivity. There were no significant associations between prenatal exposure to NO2 or early life and prenatal exposure to PM10 and any of the global measures. Our result is in line one previous study and suggests that air pollution exposure during the crucial developmental period may have a negative effect on the development of the children's brain. It is a prelude for the main fixel-specific whole brain analysis.

Funding: Supported by "NeuroSmog: Determining the impact of air pollution on the developing brain" (Nr. POIR.04.04.00-00-1763/18) grant to Marcin Szwed implemented as part of the TEAM-NET programme of the Foundation for Polish Science, co-financed from EU resources obtained from the European Regional Development Fund under the Smart Growth Operational Programme.

ASSOCIATION BETWEEN AIR POLLUTION AND FUNCTIONAL BRAIN ACTIVITY IN AN ATTENTION TASK IN 10-13 YEAR OLD CHILDREN FROM THE NEUROSMOG STUDY

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Air pollution is one of the main environmental hazards to human health. Toxic pollutants in the air not only affect lungs and cardiovascular systems, but can also negatively impact attention, and brain structure. In the present study we investigated whether long-live and early life exposure to air pollution – nitrous dioxide (NO2) and particulate matter (PM10) – has impact on functional brain activity during an inhibition control task in 447 10–13-year-old children with and without diagnosis of ADHD from the NeuroSmog study. We

found that exposure to PM10, but not NO2 was related to decreased task-related activity in right anterior cingulate cortex and right pre-supplementary motor area, regions typically related to attention. To our knowledge, this is the first demonstration of a fMRI task-related activity deficit related to air pollution exposure.

Funding: This work was supported by the "NeuroSmog: Determining the impact of air pollution on the developing brain" (Nr. POIR.04.04.00-1763/18-00) grant to Marcin Szwed implemented as part of the TEAM-NET programme of the Foundation for Polish Science, co-financed from EU resources obtained from the European Regional Development Fund under the Smart Growth Operational Programme. Additional funding came from a grant from the Priority Research Area ("Anthropocene") to Marcin Szwed under the Strategic Programme Excellence Initiative at Jagiellonian University, Poland.

RESTING-STATE FUNCTIONAL CONNECTIVITY OF AMYGDALA SUBDIVISIONS AND ITS CORRELATION TO SEVERITY OF COMPULSIVE SEXUAL BEHAVIOR DISORDER

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Compulsive sexual behavior disorder (CSBD) is an impulse control disorder characterized by the inability to resist engaging in various sexual behaviors. It has been suggested that the amygdala could play an important role in the pathogenesis of this disorder. This study aimed to assess whether resting-state functional connectivity of the amygdala subdivisions' is correlated to the severity of CSBD symptoms. An amygdala parcellation based on Recurrence Quantification Analysis was performed on resting-state fMRI data from 45 heterosexual CSBD male patients. The severity of CSBD was assessed by the Sexual Addiction Screening Test-Revised (SAST-R) and its score was used as a covariate in seed-to-voxel connectivity analysis with amygdala subdivisions as regions of interest. The SAST-R score negatively correlated with the resting-state functional connectivity between the right dorsomedial amygdala and left middle & inferior temporal gyri and right angular gyrus. Such a negative correlation was also observed between the left ventrolateral amygdala and left postcentral gyrus. To the best of our knowledge, this is the first attempt to investigate the amygdala of CSBD patients *via* a parcellation pipeline, which provides a new insight into neural mechanisms underlying this disorder.

Funding: Data collection was supported by the Polish National Science Centre OPUS grant (2014/15/B/HS6/03792) to MG, and MD is supported by the Foundation for Polish Science (FNP), scholarship number START 014.2023.

KEEP IT REAL – EMOTION-BASED PREDICTORS OF PHOTOS' AUTHENTICITY PERCEPTION

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In today's digital age, authenticity assessment of media content faces challenges due to the blend of traditional and social media, and the rise of deep fakes. We aimed to uncover cognitive processes engaged in evaluating the authenticity of the photo in a media-centric environment by investigating the impact of the emotional nature of the photograph on its authenticity assessments and examining the correlation with political orientation of participants. We have shown 1000 contemporary press photographs – all of them real – to 300 people from the general population and asked them to classify each as real or fake. In a subsequent online study 600 participants rated those photos on valence and arousal scales, as well as marked emotions they felt while viewing the picture. At the end participants filled the political orientation questionnaire with economic and cultural subscale. Anger, compassion, disgust, excitement, fear, guilt, hope, pain, sadness, and tenderness significantly correlated with image authenticity score. Women reported more sadness, fear, and regret compared to men, while men reported more excitement and disgust. Depending on polarization on the cultural

and economic subscale, individuals also reported feeling different emotions. Nonetheless, our results highlight how emotions, gender, and political beliefs may differently influence media perception.

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HOW DOES APPETITE CHANGE IN A SLEEP DEFICIT STATE?

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Food intake is regulated by two complementary drives: the homeostatic pathway based on energy balance regulation, and hedonic involving the brain reward system. Hedonic regulation can override the homeostatic pathway during energy abundance by increasing the desire to consume foods that are highly palatable. Sleep is bi-directionally linked to energy balance. The mechanisms mediating the relationship between sleep duration and food intake are likely multifactorial and include differences in appetite-related hormones, hedonic pathways, extended hours of food intake. The present study examined the effects of chronic sleep deprivation on appetite regulation by analyzing subjective ratings of visual stimuli presenting food. Thirty healthy volunteers (mean age, 23.4 ± 3.58 years; 57% females) took part in a study that compared their responses in two conditions: chronic sleep deficit (5 nights with sleep restricted to 5 hours) and regular sleep. In both conditions, participants were presented with 64 visual stimuli representing various high-energy and low-energy foods. Based on our findings, we can say that subjective appetizing ratings of foods increase with the levels of subjective sleepiness and not with objective sleep curtailment. It can also be observed that appetite ratings do not correlate with the actual level of hunger – these represent separate mechanisms.

Funding: This research was supported by the grant from the Polish National Science Centre No 2018/29/B/HS6/01934.

POTENTIAL EFFECTS OF RED/GREEN COLOUR-VISION DEFICIENCIES ON THE SELF-ESTEEM IN CHILDREN

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Approximately 3 million people in the UK suffer from the most common red/green colour-vision deficiency (CVD). It affects different aspects of lives, including education, social interactions, and general quality of life. Children with CVD may perform poorly on colour-related tasks in comparison with their peers. This study aimed to investigate differences in self-esteem between school children with CVD and with normal colour vision. Children were tested using battery of colour vision tests (Ishihara Plates, Anomaloscope, Farnsworth-Munsell D15, Medmont C-100). Their self-esteem was measured with MMG, which includes two motives: achievement (hope for success (HS), fear of failure (FF)) and affiliation (hope for affiliation (HA), fear of rejection (FR)). Data from 35 CVD participants and 60 controls was analysed. An independent 2-samples t-test was performed to test for significant differences in their MMG scores. Results of the main analysis did not show a significant difference. Additional analyses revealed a significant difference between CVD students and controls in the FF motive in art scenario ($p<.05$). The main limitation of this study was the small sample size. Further research should consider different types of CVD and its severity independently and account for age.

THE LONG-TERM INFLUENCE OF EXERCISE ON EMOTIONAL RESPONSIVENESS: EVIDENCE FROM NEURAL RESPONSES TO PICTURES

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Physical exercise offers many benefits for both physical and mental health. Recent studies have demonstrated that acute exercise positively affects emotional responsiveness by enhancing neural responses to positive stimuli while decreasing responses to negative stimuli. However, it remains an open question whether long-term exercise exerts a similar influence on emotional responsiveness. To address this gap, we conducted a longitudinal experiment in which 53 participants either engaged in a series of aerobic exercises over a 1.5-month testing period (18 training sessions in total) (n=23, experimental group) or maintained their usual habits (n=30, control group). Before and after intervention participants underwent a passive picture presentation task involving viewing positive, neutral, and negative images. EEG was concurrently recorded to assess a neural marker of emotional responsiveness: LPP component. Findings revealed a significant effect of exercise in one of the subcategories of pictures. Specifically, participants in the experimental group exhibited a lower amplitude of the LPP component in the posttest compared to the pretest in response to erotic images. We speculate that these findings may suggest a decreased sexual drive, possibly resulting from the energy expended during exercise. The evolutionary explanation of the results may be a potential energy-saving mechanism.

Funding: Project funded by NCN: Heart & brain interactions as a new approach to understanding the relationship between exercise and mood, 2021/43/D/HS6/02959.

POSTER SESSION III – LEARNING AND MEMORY

27th April, 2024 (Saturday), 14:00–15:15

EVALUATION OF COCAINE ADDICTION IN MALE OFFSPRING RATS FOLLOWING MATERNAL FRUCTOSE DIET

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Recent preclinical studies report that the maternal fructose diet is a sufficient factor for changes in the emotional status of offspring. As well, individual mental health predispositions such as anxiety and depression have been identified as triggers to cocaine use disorder. Our preclinical study aimed to examine the impact of maternal fructose diet consumption on cocaine-seeking behavior in male offspring Wistar rats. Rats after maternal fructose diet during pregnancy and lactation were used in the intravenous cocaine self-administration models in an increasing fixed ratio (from FR1 to FR5) reinforcement schedule with a stable dose of cocaine (0.5 mg/kg/infusion) or increasing doses of cocaine (from 0.25 to 1 mg/kg/infusion) under a stable FR1. Later, we evaluated the rat's motivation in a progressive ratio test, abstinence in extinction training, and reinstatement of cocaine-seeking induced by conditional or unconditional stimuli. Our results showed that perinatal offspring exposure to fructose changed neither cocaine reinforcement nor cocaine motivation. Finally, we showed that fructose males displayed higher cocaine-induced reinstatement, suggesting that perinatal diet can change offspring sensitivity to the addictive psychostimulant.

Funding: This study was supported by the Department of Drug Addiction Pharmacology Maj Institute of Pharmacology Polish Academy of Sciences statutory funds.

BEHAVIORAL CHARACTERIZATION OF OXYCODONE WITHDRAWAL IN RATS

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Opiod withdrawal during abstinence in opioid-dependent patients is considered one of the major reasons for relapse to opioid-seeking and opioid-taking behaviors. This symptom of opoid use disorder (OUD) is associated with dysphoria and manifests in form of specific motivational/affective signs which can be modeled in animal models of OUD. Here we aimed to demonstrate behavioral responses accompanying oxycodone withdrawal. We used male Sprague-Dawley rats and acute and chronic oxycodone administration to induce opioid physical dependence. To induce opioid withdrawal animals were pretreated with naloxone (1 mg/kg) 3h prior to last oxycodone administration. We used saline treated rats as controls. We used conditioned place aversion as well as measurement of ultra-sonic vocalizations (USV) to measure motivational/affective symptoms of withdrawal. Naloxone administration induced significant place aversion in both acute and chronic oxycodone- (but not saline) treated rats. In addition, several somatic signs of withdrawal were present after naloxone administration. Interestingly, naloxone-induced oxycodone withdrawal was not accompanied by increased aversive/dysphoric (22 kHz) USV. Together, our results demonstrate that naloxone-precipitated oxycodone withdrawal in rats is associated with robust dysphoria which can be readily measured in conditioned place aversion paradigm.

Funding: The National Science Centre grants no: UMO-2020/39/B/NZ7/03537.

SEX-SPECIFIC NEUROBEHAVIORAL CONSEQUENCES OF STRESS SYSTEM MANIPULATIONS IN A RAT MODEL OF NEGLECT

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Neglect, the failure to provide children with physical and emotional needs is known to alter the development of biological stress response systems. The current study examined the neurobehavioral consequences of maternal separation (MS) in rats, a procedure mimicking the environmental conditions of neglect, and investigated whether this paradigm altered the response to acute treatment with stress-related drugs later in life. 64 adult rats (equally divided for group and sex) were assessed for behavioral flexibility and feedback sensitivity, measures linked to psychiatric vulnerability in humans, on a spatial probabilistic reversal learning task. We did not find evidence of cognitive deficits in MS rats, instead only female MS rats had a better task performance than controls and this difference was also present after the acute administration of corticosterone, an unpredictable stressor. Propanolol administration, used to treat task-based anxiety, had positive or negative effects on the key measure for cognitive flexibility in control females and MS rats respectively. Citalopram, a common antidepressant, had the opposite effect, increasing cognitive flexibility only in MS female rats and decreasing task performance in control females. Our results suggest a putative resilient phenotype in MS females that confers them better task performance and better response to unpredictable stress later in life but affects their treatment outcomes differently. Indeed, we bring evidence to suggest that in rats the effects of acute administration of propranolol and citalopram are consistently present only in females and gain different outcomes for control and MS rats. Our findings may have translational relevance to test for personalized care based on sex and maltreated status that could lead to better treatment outcomes.

Funding: Support provided by the Amgen Foundation.

SEX DIFFERENCES IN THE BEHAVIORAL AND MOLECULAR PHENOTYPE OF MICE LACKING K-OPIOID RECEPTORS ON SEROTONERGIC NEURONS

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κ-opioid receptors (KORs) play a major role in the regulation of the activity of the brain's serotonergic system and accordingly have long been investigated as a potential target for the treatment of anxiety or affective disorders. Here we assessed the behavioral phenotype of female and male mice with selective inactivation of KORs on serotonergic (5-HT) neurons (Oprk1Tph2CreERT2 strain). Initial behavioral characterisation revealed no apparent mutation effects, normal activity in the open field, and an intact preference for sweet taste. Thus, we performed the light-dark box test to measure an unconditioned anxiety response. We observed a significant effect of interaction between sex and genotype on latency to enter the light box. Next, we analysed the contents of monoamines in the striatum (STR) and frontal cortex (FC). Considering the 5-HT neuron function, we found a significant effect of sex on 5-HT levels in FC and an interaction between sex and genotype. There was a significant effect of genotype on noradrenaline level in STR and dopamine (DA) level in FC. In terms of sex differences, we observed a significant effect of sex on DA levels (PFC and STR), 5-hydroxyindoleacetic acid (PFC and STR), homovanillic acid (STR), and 3-methoxytyramine (STR). Thus, we find that the loss of KORs on serotonergic neurons causes a sex-dependent change in anxiety-like behaviors.

Funding: The National Science Centre, Poland OPUS 2019/35/B/NZ7/03477.

ESTABLISHMENT OF A MEMORY-EVALUATION ENABLING MODEL IN ADULT *DANIO RERIO*

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Nowadays globally, there is an ongoing rise of neurological disorders such as Alzheimer's disease, which is the leading cause of dementia. Currently, no effective treatment for dementia is known. Therefore, the development of new animal models to evaluate the procognitive effects of new molecules is needed. Zebrafish exhibit anatomical similarities to the mammalian brain, characterized by high homogeneity of hippocampus-like and amygdala-like structures, the primary areas responsible for memory in the human brain. Moreover, zebrafish demonstrate a resemblance in cholinergic, glutamatergic, and monoaminergic signaling, making them an appropriate neurobiological model for designated research. The study aimed to establish a novel model of memory impairments in adult *Danio rerio* induced by scopolamine (50, 100, 150 µM), a cholinolytic agent. Spatial memory and response to novelty in zebrafish were assessed using the Y maze. Study results showed that scopolamine impairs memory processes in zebrafish. These effects were sex-dependent as scopolamine decreased the time spent in the novel arm in males solely in the highest concentration and in females both at 100 µM and 150 µM concentrations. In conclusion, this study provides evidence that the proposed zebrafish behavioral model may be considered an effective platform for developing therapies for neurological disorders.

CHONDROITIN 4-SULPHATE KNOCKOUT EFFECTS ON SHORT-TERM MEMORY

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Perineuronal nets (PNNs) enwrap selected populations of neurons and are involved in the regulation of neuroplasticity. Their composition shifts during the critical period (CP) of brain development and continues to change through ageing, correlating with cognitive decline. Chondroitin sulfates are key components of PNNs, and the ratio of their sulfation patterns changes in favour of C4S over C6S upon maturation, leading to increased inhibitory properties of PNNs. In the current study, we are exploring the function of C4S in cognition, using chondroitin 4-sulfotransferase (Chst11) KOs under parvalbumin (PV) promoter in contrast with WT animals of 3 and 6 months of age. To evaluate short-term memory, we performed Novel Object Recognition (NOR) and the Morris Water Maze (MWM) tasks; sociability was evaluated through the Three Chamber Task (TCT). Chst11 KO mice have shown generally improved short-term memory compared to WT mice. Results from TCT suggest that KOs' general sociability is preserved. In conclusion, Chst11 KOs showed consistent cognitive superiority over wild types and had no decrement in sociability, suggesting C4S's to be a promising target for therapies for disorders causing cognitive decline, such as in Alzheimer's disease.

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HBK-14 MITIGATED MK-801 NEGATIVE EFFECTS ON EMOTIONAL MEMORY IN THE PASSIVE AVOIDANCE TEST IN MICE

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Cognitive deficits, prevalent in affective disorders, significantly decrease the quality of patients' lives. Moreover, the majority of antidepressants fail to address memory impairments associated with depression. Therefore, as a continuation of the study on HBK-14, a dual 5-HT1A and 5-HT7 antagonist with proven antidepressant-like and anxiolytic-like activity in rodents, we now aim to evaluate its potential to mitigate memory impairments. We used a passive avoidance test to examine HBK-14's effects on long-term emotional memory in male mice. Memory deficits were induced by the administration of an NMDA receptor antagonist, MK-801, or a muscarinic receptor antagonist, scopolamine. HBK-14 was tested at doses of 0.625, 1.25, and 2.5 mg/kg, with rivastigmine employed as a reference drug. At a dose of 2.5 mg/kg, HBK-14 significantly increased latency to enter the dark chamber in the retention trial compared to the MK-801-treated control group. However, it did not protect animals from memory impairments induced by scopolamine. In summary, our study indicates that HBK-14 has the potential to mitigate long-term emotional memory deficits associated with glutamatergic system imbalance. This encourages further research to explore mechanisms underlying HBK-14's antiamnestic effect.

TARGETING BUTYRYLCHOLINESTERASE AND P38A MITOGEN-ACTIVATED PROTEIN KINASE AS AN APPROACH TO ATTENUATE LEARNING AND MEMORY DEFICITS – A MOUSE STUDY

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Available drugs for Alzheimer's disease (AD) attenuate memory loss only in the mild to moderate phase of the disease. Therefore, novel procognitive drugs candidates are urgently needed. Two enzymes: butyrylcholinesterase (BuChE) and p38α mitogen-activated protein kinase (p38α MAPK) are involved in neurodegeneration in the course of AD, so they seem to be potential therapeutic targets for anti-AD drugs. This study investigated procognitive properties of compounds GUK-1329 (a selective BuChE inhibitor), KES-19 (a selective p38α MAPK inhibitor) and KES-29 (a dually-acting BuChE/p38α MAPK inhibitor) in mouse models of amnesia induced by scopolamine or lipopolysaccharide. Passive avoidance (PA), novel object recognition (NOR) and the Morris water maze (MWM) tasks were used to assess the activity of compounds administered intraperitoneally. In the scopolamine model KES-29 was the most active compound in the PA and NOR tasks. In the lipopolysaccharide model KES-29 was the most effective compound which improved spatial learning and memory measured in the MWM task. None of the test compounds induced motor deficits in mice. Since KES-29 was the most effective antiamnesic agent, it can be concluded that combining two mechanisms in one molecule (multi-target-directed ligands) is a promising approach to develop effective anti-AD drug candidates.

Funding: Financial support from the National Science Centre (grant No. DEC-2021/43/I/NZ7/00342) is gratefully acknowledged.

POTENTIAL ANTI-AMNESIC ACTIVITY OF NOVEL SALICYLAMIDE DERIVATIVE IN MICE

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In view of the ageing population, the prevalence of dementia or Alzheimer's disease is expected to be rising. Progressive loss of memory, cognitive deficits and behavior impairments affect patient's daily functioning and quality of life. Unfortunately, there are limited therapies available, which also aren't effective enough. For that reason, the investigation for novel potential anti-amnesic drugs still remains one of the major challenge for neuroscientists. The aim of this study was to explore the novel compound SD1, which is a salicylamide derivative, and test its influence on the long-term emotional and recognition memory in mice. First, we performed passive avoidance task, where the latency to enter the dark compartment was measured. Then, we conducted object recognition test and we measured the time of novel object exploration by mice. Finally, we evaluated, if the compound may ameliorate memory deficits induced by MK-801. All tests were performed using male CD1 mice. The tested compound significantly increased the latency time in the passive avoidance task at the doses 0.625-2.5 mg/kg, whereas it reversed MK-801-induced cognitive disturbances only at one dose (1.25 mg/kg) during this test. On the other hand, the compound did not increase the time of novel object exploration in the object recognition test. Results of this study suggest that novel compound SD1 might improve long-term emotional, but no recognition, memory impairments in rodents and it could be a promising structure in developing novel anti-amnesic agents.

HBK-15, A MULTIMODAL COMPOUND SHOWING FUNCTIONAL SELECTIVITY, ATTENUATES MK-801-INDUCED SPATIAL MEMORY DEFICITS

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Biased agonists exhibit a preference for activating specific signalling pathways, offering potential for innovative treatment strategies that demonstrate pharmacological activity without inducing undesired effects. Our investigation, building on previous research confirming the rapid antidepressant-like properties of a 2-methoxyphenylpiperazine derivative named HBK-15 in rodents, focuses on exploring its memory-enhancing activity and potential functional selectivity upon selected serotonin and dopamine receptors. Employing various cell-based functional assays, we assessed the intrinsic activity of HBK-15 at 5-HT1A, D2S, D2L, and D4 receptors, examining its effect on cAMP production, ß-arrestin recruitment, and/or phosphorylation of ERK1/2. To evaluate the potential antiamnesic properties of HBK-15, we induced memory deficits in mice using NMDA receptor antagonist MK-801, followed by Morris water maze test to assess long-term spatial memory. Our findings revealed varying efficacy and potency of HBK-15 across different signalling pathways, showcasing its functional selectivity at the 5-HT1A, D2S, D2L, and D4 receptors. Furthermore, HBK-15 effectively reversed spatial memory impairments induced by the glutamatergic imbalance. Collectively, these results underscore HBK-15 as a promising candidate for mitigating memory impairments through a distinctive mechanism of action.

Funding: This study was conducted as part of a research project funded by the National Science Centre, Poland (grant 2019/34/E/NZ7/00454).

UNCOVERING THE ANTIAMNESIC POTENTIAL OF HBK-14, A NOVEL 2-METHOXYPHENYLPIPERAZINE DERIVATIVE, IN SCOPOLAMINE-INDUCED RECOGNITION MEMORY IMPAIRMENTS IN MICE

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Cognitive deficits in neuropsychiatric disorders, such as depression and anxiety, necessitate novel therapeutic approaches. HBK-14, a dual 5-HT1A and 5-HT7 receptor antagonist, has shown promise in preclinical studies for its antidepressant-like properties. Expanding upon the previous study on HBK-14, we now aim to investigate its antiamnesic properties using the object recognition test in mice. Male CD-1 mice underwent the object recognition test with a time interval of 24-h between the familiarization and test sessions. HBK-14 was tested at doses of 0.625, 1.25, and 2.5 mg/kg. We used scopolamine, a muscarinic receptor antagonist, to induce memory impairments, and rivastigmine as a reference compound. We found that scopolamine at a dose of 1 mg/kg induced long-term recognition memory impairment. HBK-14 at a dose of 2.5 mg/kg showed a tendency to protect animals from cognitive deficits, however, the effect was not statistically significant. Further research is needed to explore the pharmacological potential of HBK-14.

POSTER SESSION III – PSYCHEDELICS

27th April, 2024 (Saturday), 14:00–15:15

ACUTE BEHAVIORAL EFFECTS AND PHARMACOKINETIC PROFILE OF METHOXPHENIDINE IN WISTAR RATS

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Methoxphenidine (MXP) is a synthetic dissociative substance that has gained attention as a designer drug. MXP belongs to the diarylethylamine class and shares structural features with arylcyclohexylamines, such as phencyclidine, ketamine, and methoxketamine. Despite the potential harmful effects of MXP, our knowledge and understanding of the influence of this new synthetic substance on living organism remained limited hence our primary target was to enrich current knowledge of MXP. Our main intention was to describe in detail the effects of MXP (10, 20, and 40 mg/kg subcutaneously, s.c.) in two behavioral behavioral/physiological procedures and in two temporal windows from administration (15 and 60 min) in order to test: locomotor effects in the open field and sensorimotor gating in the test of prepulse inhibition (PPI). To correlate the behavioral data with serum levels of MXP, the samples for pharmacokinetics were measured using liquid chromatography mass spectrometry. 10 and 20 mg/kg MXP induced significant locomotor stimulation, whereas 40 mg/kg reduced locomotion and increased time spent in the centre of the arena, suggesting sedation/anesthesia or stereotypy. The duration of the effects was present for at least 60-90 min. MXP decreased baseline acoustic startle response (ASR) and disrupted PPI, irrespective of testing onset. Maximal brain levels of MXP were observed 30 min after administration, remained high at 60 min and progressively declined to around zero after 24 hours. Our findings indicate that MXP behaves as a typical dissociative anesthetic with stimulant effects at lower doses, sedative/anesthetic effects at higher doses, and as a disruptor of sensorimotor gating. MXP was found to be a mild stimulant, with anxiogenic and psychomimetic properties, which indicates that in acute human intoxication, unpleasant experiences and potentially negative psychological sequelae might result.

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HEXAHYDROCANABIDIOL: PHARMACOKINETICS, SYSTEMIC TOXICITY, AND ACUTE BEHAVIORAL EFFECTS IN WISTAR RATS

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Hexahydrocannabinol (HHC) is a semi-synthetic cannabinoid that has attracted interest due to its potential psychotropic effects similar to those of natural cannabinoids. This substance is frequently abused in several EU and US countries where it serves as a legal and readily available alternative to Δ9-tetrahydrocannabinol (Δ9-THC). Despite its widespread use, only a limited number of studies have addressed its effects and safety profile. In this study, we investigated the pharmacokinetics, systemic toxicity and acute behavioral effects following oral administration of HHC to male Wistar rats. Two hours after administration of 10 mg/kg, HHC concentrations peaked in both blood serum and brain tissue. According to the OECD Toxicity Assay 423, HHC was classified as a Category 4 substance with a lethal dose of 2000 mg/kg. Behavioral effects were evaluated using the open field and Prepulse Inhibition of Acoustic Startle Response tests, with three different doses (1, 5, and 10 mg/kg) co-administered with sunflower oil (placebo). Compared to placebo, the higher dose (10 mg/kg) induced reduced locomotor activity, increased anxiety and impaired sensorimotor gating. In summary, HHC readily crosses the blood-brain barrier, exhibits mild toxicity and produces behavioral effects similar to other cannabinoids.

Funding: This work was supported by a grant from Czech Health Research Council (project NU21-04-00307), Czech Science Foundation (23-07578K), Ministry of the Interior of the Czech Republic (project VK01010212), Long-term conceptual development of research organization (RVO 00023752), and Specific University Research, Czech Ministry of Education, Youth and Sports (project 260648/SVV/2024), ERDF-Project Brain dynamics, No. CZ.02.01.01/00/22_008/0004643, project VVI CZECRIN (LM2023049) and Charles University research program Cooperatio-Neurosciences and private funds obtained *via* PSYRES, Psychedelic Research Foundation (https://psyresfoundation.eu).

ROLE OF 5-HT2A RECEPTORS LOCATED IN THE CLAUSTRUM ON NEUROTRANSMITTER RELEASE

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Classic psychedelics (psychoplastogens) show their main mechanism of action through 5-HT2A receptors. These receptors are located on layer V pyramidal neurons and GABAergic interneurons of the prefrontal cortex. It appears that the highest density of 5-HT2A receptors is found in the subcortical structure, the claustrum, which has both afferent and efferent connections to virtually all areas of the cortex. However, there is currently a paucity of information regarding the effects of psychedelics on 5-HT2A receptors in the claustrum and the transmitters that are released into the synaptic space as a result of their activation. This study examined the effect of activation of 5-HT2A receptors in the claustrum on the levels of neurotransmitters released. The compound 25I-NBOMe, which is their high-potency agonist, was used to activate 5-HT2A receptors. This effect was studied in freely moving rats, and 25I-NBOMe was administered through a microdialysis probe to the claustrum at the concentration of 500 μM. The results examined by chromatographic techniques showed an increase in the release of monoamines (serotonin, dopamine, and norepinephrine) and glutamate, while a decrease in inhibitory GABAergic transmission was observed. The obtained data will allow us to understand better the mechanism of action of psychedelic substances.

Funding: This research was funded by the National Science Centre grant no. 2020/37/B/NZ7/03753 and statutory funds of the Maj Institute of Pharmacology, Polish Academy of Sciences.

BAEOCYSTIN, A SIGNIFICANT COMPONENT OF HALLUCINOGENIC MUSHROOMS: A BEHAVIORAL EVALUATION IN WISTAR RATS

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Baeocystin (4-phosphoryloxy-N-methyltryptamine) is a naturally occurring indole (tryptamine) alkaloid, found in many Psilocybe species among other psychoactive mushrooms. Because of its structural similarity with psilocybin (and psilocin), and since the latter displays beneficial effects in the treatment of various psychiatric disorders, baeocystin has garnered interest regarding whether it shares such effects with psilocybin. Therefore, behavioral aspects of acute administration of baeocystin were investigated in this study, namely prepulse inhibition (PPI), as it reflects the sensorimotor disruption of information that psychedelic substances commonly display, and locomotor activity in the open field test (OFT), as a marker describing the degree of inhibition or activation. Wistar rats were administered with either 1,25 or 5 mg/kg subcutaneously. Analyses report that baeocystin has no potency to disrupt PPI; furthermore, no significant effects were observed in locomotor activity. Thus, our preliminary results suggest no psychedelic activity. Future investigation on the pharmacokinetic/pharmacodynamic characteristics of baeocystin will further delineate the profile of this yet unexplored substance.

Funding: This work was supported by a grant from Czech Health Research Council (project NU21-04-00307), Czech Science Foundation (23-07578K), Ministry of the Interior of the Czech Republic (project VK01010212), Long-term conceptual development of research organization (RVO 00023752), and Specific University Research, Czech Ministry of Education, Youth and Sports (project 260648/SVV/2024), ERDF-Project Brain dynamics, No. CZ.02.01.01/00/22_008/0004643, project VVI CZECRIN (LM2023049) and Charles University research program Cooperatio-Neurosciences and private funds obtained *via* PSYRES, Psychedelic Research Foundation (https://psyresfoundation.eu).

EFFECTS OF NEUROCHEMICAL MODULATION BY PSILOCIN ON THE GENERATION OF 40 HZ AUDITORY STEADY-STATE RESPONSES IN THE RAT BRAIN

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Serotonergic psychedelics are gaining attention for treating neuropsychiatric disorders. Psilocybin mimics psychotic symptoms, serving as a model for serotoninergic psychosis. The 40 Hz auditory steady-state response (ASSR) reflects gamma-range activity, showing decreased inter-trial phase coherence (ITPC) under psilocybin. However, animal data on serotonergic ASSR modulation are limited. Our study examines 40 Hz ASSR changes in rats given 1 mg/kg psilocin. Nine adult male Wistar rats were implanted with EEG electrodes to record neural activity. Auditory stimulation was used to elicit the 40 Hz responses. Results revealed significantly increased ITPC at the A4 electrode (right hemisphere) post-psilocin, compared to saline, with no significant change at A3 (left hemisphere). This suggests an asymmetric pattern of effects induced by psilocin. While functional asymmetry of the auditory cortex is known in rodents, the observed rise in ASSR ITPC values over the right hemisphere is unprecedented, differing from effects seen in humans or rodents previously. Findings highlight the need for further study on psilocin's impact on rodent ASSR generation mechanisms. Insight into these mechanisms could inform therapeutic applications of serotonergic psychedelics for neuropsychiatric disorders. Additionally, understanding differences in ASSR modulation between humans and rodents could enhance the translational validity of animal models.

B-CARYOPHYLLENE AMELIORATES HYPERACTIVITY AND RESTORES FRONTAL DOPAMINE METABOLISM IN RAT MODEL OF SCHIZOPHRENIA

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Schizophrenia is severe mental illness that can be modeled in animals through the administration of NMDA receptor antagonists, e.g., MK-801, leading to alterations related to those observed in the disease. Endocannabinoid system (ECs) is strongly implicated in pathophysiology of neuropsychiatric disorders such as schizophrenia. β-caryophyllene (BCP), an agonist of CB2 receptor, exerts anti-inflammatory and anxiolytic activity, therefore we aimed to verify its effects on schizophrenia-related behaviors and dopamine (DA) frontal metabolism. Male Wistar rats were injected once daily for 5 days with saline, vehicle, MK-801, BCP or BCP and MK-801 combined. Travelled distance, entries into the inner zone (IZ) and % time spent in the IZ were measured in the open field test to assess locomotor activity and anxiety behavior. DA and its metabolites levels in frontal cortex (FCX) were measured using high-performance liquid chromatography. One-way ANOVA and *post hoc* Tukey test were employed for statistical analysis. BCP ameliorated MK-801-induced hyperactivity, however, we observed no changes in anxiety-related behavior. BCP restored DA frontal metabolism to control level. Positive effects of BCP on locomotor activity may be related to regulatory function of ECs on dopamine neurotransmission in FCX.

Funding: The study was financed from NSC Grant no.2022/45/N/NZ7/04059.

INFLUENCE OF PSILOCYBIN ON THE HPA AXIS ACTIVITY IN RATS

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Clinical studies provide evidence that psilocybin could be used as fast-acting antidepressant but its mechanism of action on the HPA axis activity is still not fully understood. The aim of the study was to determine the effect of a single psilocybin dose (0.6 mg/kg) on monoamine levels in the hypothalamus (HT) and adrenal glands (AD) of rats using HPLC. In addition, serum corticosterone (CRT) concentration was determined by ELISA method. Psilocybin significantly increased the level of dopamine (DA) without affecting the levels of noradrenaline (NA), serotonin (5-HT) and their metabolites DOPAC, HVA and 5HIAA as measured 7 days after administration. Any influence of psilocybin was observed on the tissue levels of NA, adrenaline (ADR), DA and 5-HT in the AD. Serum CRT concentration was decreased 7 days after psilocybin administration. The obtained results indicate that psilocybin can modulate HPA axis function with possible involvement of hypothalamic DA pathways. The impact of psilocybin on HT-HPA may underlie the antidepressant effect of psychedelics.

Funding: The National Science Centre grant no. 2020/37/B/NZ7/03753 and statutory funds of the Maj Institute of Pharmacology, Polish Academy of Sciences.

PSILOCYBIN EFFECT ON NEUROTRANSMITTERS RELEASE IN NAIVE AND STRESSED RATS

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Mood and anxiety disorders are one of the most common threats to mental health, while expressing high levels of comorbidity. Psilocybin as selective agonist of 5-HT2A receptor seems to exhibit rapid antidepressant and anxiolytic effect in comparison to currently used antidepressant drugs. The aim of this study was to measure the effect of acute low dose of psilocybin (0,6 mg/kg) in frontal cortex on 35 mM KCl-evoked neurotransmitters release in naive and chronic mild stressed rats. The levels of noradrenaline (NA), dopamine (DA), serotonin (5-HT), glutamate (GLU) and γ-aminobutyric acid (GABA) in the frontal cortex were measured by UHPLC using microdialysis in freely moving rats. Except GABA, psilocybin increased evoked release of NA, DA, 5-HT and GLU in naive rats. In contrast, psilocybin decreased DA, 5-HT and GABA release but did

not affect NA and GLU level in stressed animals. It may be concluded that increased release of neurotransmitters in naive rats seems to be mediated by 5-HT2A receptor that could be dysfunctional in stressed animals. The recruitment of 5-HT1A receptors under stressed conditions may be responsible for inhibitory psilocybin effect on DA, 5-HT and GABA release.

Funding: The National Science Centre grant no. 2020/37/B/NZ7/03753 and Statutory funds of Department of Pharmacology, Unit II, Maj Institute of Pharmacology, Polish Academy of Sciences.

POSTER SESSION III – BILATERAL BRAIN-BODY INTERACTIONS

27th April, 2024 (Saturday), 14:00–15:15

GASOCRINE SIGNALING *VIA* GASORECEPTOR PROTEINS

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I recently proposed gasocrine signaling for gas-gasoreceptor protein interactions-driven cellular signalling. To investigate gasocrine signaling, there is a critical need to identify gasoreceptors for the essential gasotransmitters like O2. Based on existing scientific literature, I propose that heme-based O2 sensors, featuring diverse signaling domains across genera, should be explicitly designated as O2 gasoreceptors. Acknowledging that O2 gasoreceptors are likely to belong to multiple protein classes with diverse signaling domains and pathways will facilitate a comprehensive search for O2 gasoreceptors in all organisms and across every cell type. This approach will broaden the investigation beyond specialized tissues or cells, encompassing a systemic exploration.

ON METABOLIC DETERIORATIONS IN PENTYLENETETRAZOL (PTZ)-KINDLED RATS REVEALED WITH GLUCOSE TOLERANCE TEST AND LIVER HISTOLOGY

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Manifestations of metabolic syndrome (MS) manifestations in chronic epilepsy models were in the scope of the investigation. Kindling was induced by daily injections of PTZ at a dose of 35 mg/kg i.p. for three weeks. Those animals with fully developed generalized seizures were used for investigations. Glucose and insulin levels were not different from control rats, while PTZ-kindled rats demonstrated decreased tolerance to glucose tests. Pentoxiphylline administration(100 mg/kg, i.p., during a week daily) caused partial restoration of glucose tolerance test and the inhibition of kindled seizures. On H&E stained liver of PTZ-kindled rats, the hepatocytes with normal vesicular nuclei were present with a deep acidophilic cytoplasm in some cells. The binucleated hepatocytes were scarcely present. The focal aggregation of mononuclear inflammatory cells between the hepatocytes with deep acidophilic cytoplasm and small, shrunken, deeply stained nuclei was seen. Also, the sparse presence of the hypertrophied intra-sinusoidal von Kupffer cells between the hepatocytes was registered. In the PTZ-treated liver tissues, some central fatty deposits and additional smaller microdeposits around the hepatocytes with increased infiltration of von Kupffer cells encroaching on those fatty lipid deposits were determined. The data favored moderate functional and morphological deteriorations in PTZ-kindled rats corresponding to metabolic syndrome.

Funding: This research was funded by the Ministry of Health Care of Ukraine (Number of research work 0121U114510).

THE LINK BETWEEN BRAIN AND PERIPHERAL IMMUNE SYSTEM IN ALZHEIMER'S DISEASE – A STUDY IN APPNL-F/NL-F KNOCK-IN MICE

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Alzheimer's disease (AD) is a major public health concern, with observed changes in peripheral immune cell behavior potentially shedding light on brain dysfunction mechanisms. Studying primary and secondary immune cell populations may provide valuable insights into these processes. This research aimed to study the cognitive changes and profile of immune cells in the brain and the periphery in the APPNL-F/NL-F mice model of AD (KI). Nine-month-old C57BL/6J WT and KI mice were sacrificed, and their hippocampi and frontal cortices were dissected. Mouse ApoE, Aβ42/Aβ40 ratio, and cytokine levels (IL-1β, IL-6) were measured using ELISA test. Additionally, the proliferative response of splenocytes and metabolic activity of splenocytes and thymocytes (MTT, LDH, NO) after lipopolysaccharide (LPS) and/or concanavalin A (ConA) stimulation were examined. Despite intact spatial memory, KI mice showed elevated Aβ42/Aβ40 ratio, ApoE levels, and pro-inflammatory cytokines. Differential cellular reactivity was observed, particularly in the spleen, with increased LDH and NO release from KI mouse splenocytes upon ConA and LPS stimulation. Thus, we demonstrated that brain immune status and peripheral immune cell reactivity are affected in AD and predict the occurrence of cognitive disturbances.

Funding: Funded by the National Science Centre, Grant No: 2021/43/B/NZ4/01133; Task number 7.

CHANGES IN THE ALLATOTROPIN SIGNALLING DURING ACTIVATION OF THE IMMUNE SYSTEM OF MEALWORM BEETLE, *TENEBRIO MOLITOR L.*

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Cooperation between the nervous and immune systems is one of the essential factors for maintaining homeostasis in animals. A crucial role in this process plays neuropeptides and their receptors. Our study aimed to analyse the dependence between the activation of the immune system and the allatotropin system, which has many functional similarities to the orexins system in vertebrates. Firstly, we identified the presence of transcripts of genes encoding allatotropin precursor and receptor in the nervous system (brain and ventral nerve cord) and immune-related cells (haemocytes and fat body). Secondly, to verify if allatotropin signalling takes part in the regulation of the immune system, we tested whether the application of immune activators affects the expression of genes encoding allatotropin precursor and receptor. The obtained results confirmed this supposition. However, the observed changes in the expression level of gene encoding allatotropin precursor and receptor depend on phase of infection, type of immune activator and tested cells. Additionally, we have shown that cytokines, also in insects, can modulate the neuropeptide signalling. All these results are important steps in understanding the evolutionary basis of hormonal regulation of the immune response.

Funding: This research was partially supported by a research grant from the Initiative of Excellence– Research University (102/13/SNP/0013).

ALLATOTROPIN AFFECTS THE IMMUNE SYSTEM ACTIVITY OF MEALWORM BEETLE, *TENEBRIO MOLITOR L.*

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Despite wide knowledge about the activity of insect immune system, some aspects, such as the hormonal regulation of immune response require further studies. The results of current research suggest that the crucial compounds that link insect neuroendocrine and immune systems are neuropeptides, such as allatotropins (AT). In the presented research, the influence of Tenmo-AT on immune system activity of mealworm beetle,

Tenebrio molitor was analysed. For example, the injection of different concentrations of Tenmo-AT (10-7 M and 10-5 M) increased the number of circulating haemocytes. Moreover, this neuropeptide also affects cellular and humoral mechanisms, such as phagocytic activity of haemocytes and enzymatic activity of haemolymph. Additionally, the injection of Tenmo-AT influences the expression levels of immune-related genes in the fat body and haemocytes of T. molitor. It should be noted that the most of the observed effects were time and dose dependent. The obtained results allow to better understand the role of insect neuropeptides in the regulation of the immune response. Due to partially structural and functional homology of insect AT and vertebrate orexins, our study is also an important step in research concerning the evolution of neuropeptide signalling.

Funding: This research was partially supported by a research grant from the Initiative of Excellence – Research University (102/13/SNP/0013).

EFFECT OF SLEEP DEPRIVATION ON GUT-BRAIN AXIS OF PARKINSON MODEL *DROSOPHILA MELANOGASTER* STRAIN

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Parkinson's disease is a neurodegenerative disorder in which dopaminergic cells located in the brain undergo atrophy primarily causing movement disorders such as the characteristic tremor. Less well-known, but equally important symptoms involve digestive system dysfunction and disturbance of the diurnal clock rhythm. Our study attempts to link sleep deprivation with gut-brain axis dysfunction using *Drosophila melanogaster* model. This model was chosen due to the conservation of many genes, signalling processes, cellular mechanisms and neuronal processes. Organized central nervous system and well-described behavioral phenotypes along others are the reasons why *Drosophila* was already used in numerous studies of the circadian clock or neurodegenerative disorders. In our experiments young wildtype Canton S, white mutant and park mutant male flies were subjected to 17 hours of mechanical sleep deprivation. Next, heads and the middle part of the gut were collected and gene expression analysis was performed. We focused on clock genes per, tim to check whether clock mechanism was affected through sleep deprivation. We investigated also ninaD and npf gene expression levels to check connection between sleep level and gut function. We observed statistically significant differences in the expression of the studied genes after sleep deprivation in all studied lines. Our experiment shows that disruption of the diurnal rhythm has a negative impact on the gut-brain axis, causing irregularities in gut function at the molecular level.

REGULATIONS OF ENERGY METABOLISM AND INFLAMMATORY RESPONSE IN BBB PERMEABILITY DISORDERS IN APOE-/-/LDLR-/- DOUBLE KNOCKOUT MICE IN THE COURSE OF HYPERCHOLESTEROLEMIA

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Hypercholesterolemia can be encountered among the most frequent metabolic disorders coexisting with several cardiovascular and cerebrovascular diseases. The consequences of the development of hypercholesterolemia are both morphological and functional, affecting all constituents of the nervous tissue. In this study we aimed to determine the level of activity of extracellular adenine nucleotide pathway enzymes in the murine brain microvascular endothelial cells, the blood-brain-barrier (BBB) permeability changes, and inflammatory response in brain tissue. 3-month-old ApoE-/-/LDLR-/- double knockout mice developing hypercholesterolemia, as an experimental group, and age-matching C57/BL6 mice, as a control group were

used in the study. The HPLC method, immunofluorescent staining of isothiocyanate-dextran (FD40), and ELISA test were used to assess the expression of e-NTPDase, ecto-5'-NT and eADA enzymes, BBB permeability changes, and concentrations of cytokines IL-1β, IL-6, respectively. The results showed raised activity of eADA, increased FD40 leakage through the BBB and elevated levels of IL-1β and IL-6 in the hypercholesterolemic mice. The consequences of developing hypercholesterolemia are related to the disorders of brain energy metabolism, changes in BBB permeability, and initiation of the inflammatory response. Moreover, hypocholesterolemia shifts the energy metabolism pathway towards the synthesis of inosine with immunomodulatory and neuroprotective effects, which may indicate a strong need to protect brain endothelial cells from damage and even cell death.

THE NEURONAL LOSS IN THE CORTEX AND HIPPOCAMPUS AFTER A TRAUMATIC BRAIN INJURY IS SEX-DEPENDENT

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Traumatic brain injury (TBI) is a risk factor for the development of epilepsy and neurodegeneration, partially mediated by neuronal loss. The aim of this project was to observe the loss of various types of neurons after brain injury and identify potential sex differences. Penetrating cortical brain injury was induced on postnatal day 30 (P30) in male and female rats. On P60 animals were perfused, brain tissue was sectioned and stained for PV (parvalbumin), NPY (neuropeptide Y), and nNOS (neuronal nitric oxide synthase). PV-, NPY-, and nNOS-expressing neurons were counted in the hippocampus, perilesional cortical area, and contralateral hemisphere of injured animals and in non-injured controls. The analysis revealed a significantly lower number of PV-expressing neurons in deeper layers (V–VI) of perilesional cortex of females in comparison to non-injured controls, similar changes in the contralateral hemisphere, and no impact of TBI on the number of PV-expressing cells in males. NPY-expressing neurons decline was observed in medial hippocampus of both hemispheres compared to controls in male rats but not in female rats. On the other hand, more nNOS-expressing neurons were observed in perilesional cortex of injured rats of both sexes compared to controls. To conclude, TBI affects differently various neuronal populations in both hemispheres in a sex-dependent manner.

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TRAUMATIC BRAIN INJURY AFFECTS THE INTRINSIC ACTIVE MEMBRANE PROPERTIES AND EXCITATORY TRANSMISSION OF GRANULE CELLS

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Traumatic brain injury (TBI) can lead to a wide range of physical and cognitive impairments and it is known to impact neuronal excitability and synaptic functions. Although hippocampal impairments have been widely described following TBI, the specific effects on dentate gyrus (DG) remains to be fully understood. Here we investigated the effects of TBI on the excitability of granule cells and excitatory postsynaptic transmission in the DG at three different time periods, 3 days, 15 days and 4 months after the injury. Our results indicate that TBI does not provoke changes in passive membrane properties. By applying dimensionality reduction analysis of action potential (AP) properties, we identified the variables that exhibited significant short- medium and long-term changes. We observed that the AP half-width, AP overshoot and AP amplitude was greater in TBI cells. Moreover, the duration of afterhyperpolarization was reduced when

compared to control cells. Lastly, although amplitude of sEPSC did not show differences, significant changes in frequency of sEPCS were observed in TBI cells, which did not follow the same temporal evolution as control animals. These findings indicate that at the long-term TBI increases the intrinsic excitation of granule cells and excitatory synaptic activity of the DG.

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DEXAMETHASONE CHANGES THE CONTENT OF NON-RESIDENT MESENCHYMAL CELLS IN THE GLIAL SCAR

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The effect of dexamethasone (ICH/DEX) was studied using the intracerebral hemorrhage (ICH) rats' model on the content of non-resident mesenchymal cells in the glial scar (GS). A significant number of CD44+ cells was detected in GS ICH after 3 and 10 days, and decreased up to 60 days after the lesion. In ICH/DEX, the maximum content of these cells was observed after 30 days of the experiment. The content of CD44+ cells in GS depended on the volume of the brain lesion ($p=0.037$). In GS, the number of CD146+ cells was determined to be lower than CD44+ cells. CD68+ cells in GS were rarely detected, and their content did not significantly differ between ICH and ICH/DEX. CD90+ cells were only occasionally found in GS in ICH, whereas in ICH/DEX they were found in greater numbers and more often at 10 and 30 days after damage. CD44+- often, and less often CD90+- CD146+ cells had a blast-like phenotype. Thus, the number of CD44+-cells in GS depends on the brain lesion volume, and CD68+-, CD90+- and CD146+- are independent, but have a certain relationship with each other. DEX promoted persistence of CD44+ and CD146+ cells in GS.

Funding: Ministry of Health of Ukraine, state registration #0123U101051, *Lauréate scientifique du programme PAUSE 2022-2024, France.

NEOVASCULOGENESIS IN THE BRAIN PERIHEMATOMA AREA WITH DEXAMETHASONE ACTION

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The effect of dexamethasone (Dex) on neovasculogenesis in the brain perihematomal region (BPHR) was studied using a model of hemorrhagic stroke in rats. In BPHR (control), after 1-10 days, the number of cells increased rapidly, reaching a maximum on the 30th day of the experiment, and then appeared smaller after 60 days. Among them, CD133+ cells were detected. After 3 days, thin endothelial tubes formed by CD31+ cells appeared, the number of which increased until day 10. After 30 days, they acquired signs of maturity, which was manifested in their complexation with perivascular cells, and their contours often showed immunoreactivity to smooth muscle actin. With Dex action, the accumulation of BPHR cells, including CD133+ cells,

was sharply reduced. The new formation of CD31+-endothelial cells tubes after 3 days of the experiment was sharply suppressed. The number of newly formed vessels in the second month was lower, but the volume of structures with the expression of smooth muscle actin in their wall was larger. Thus, Dex suppresses neovasculogenesis in BPHR, which may act as an additional factor in the development of astrogliosis, in addition to the direct effect of corticosteroids on activated astroglia.

Funding: Ministry of Health of Ukraine, state registration #0123U101051, *Lauréate scientifique du programme PAUSE 2022-2024, France.

CAN KETOGENIC DIET COUNTERACT THE DAMAGE CAUSED BY TRAUMATIC BRAIN INJURY? A TRACTOGRAPHY STUDY OF THE STRUCTURE OF NEURONAL CONNECTIONS IN RAT BRAIN

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The ketogenic diet (KD) is a type of low-carbohydrate diet in which the intake of fats significantly increases while maintaining an adequate amount of proteins, which has been identified as a potential therapy to enhance recovery after traumatic brain injury (TBI). Tractography is a 3D neuromodeling technique used for visualizing nerve tracts based on diffusion tensor imaging (DTI). This study aimed to investigate differences in the structure of neuronal connections between injured and uninjured rat brains treated with ketogenic diet and normal diet (ND). Rats were divided into groups obtaining a normal or ketogenic diet from postnatal day 27 (P27). On P30, penetrating brain injury was induced in the cerebral cortex in half of the animals from each group. The animals were perfused on P60, and the brains were dissected. DTI brain images were obtained and analysed using DSI Studio software. Obtained 3D models showcase a recovery improvement in KD-treated injured rats in the region of injury. Quantitive data, however, has shown overall fewer nerve tracts in KD-treated in comparison to ND-treated brains. These results support evidence that KD may be a therapeutic strategy for treating TBI.

Funding: U1U/W18/NO/02.05 IDUJ.

CELL-SPECIFIC REGULATION OF NEURONAL AND GLIAL GLUCOSE METABOLISM BY NEURODEGENERATION-ASSOCIATED PROTEIN TDP-43

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Amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) are fatal neurodegenerative disorders with significant clinical and molecular overlaps. Cytoplasmic mislocalization and subsequent loss of nuclear functions of TAR-DNA-binding protein 43 (TDP-43) are considered critical events in the pathogenesis of ALS and FTLD. Intriguingly, conventionally unfavorable metabolic conditions, such as diabetes mellitus, are paradoxically associated with a better prognosis in ALS and FTLD, which signifies a potential role for metabolic pathways in TDP-43-associated neurodegeneration. To understand the interplay between TDP-43 and metabolic signaling in neurodegenerative contexts, we simulated TDP-43 loss of function using RNA interference in mouse NSC34 motor neurons, N2A neuroblastoma cells, and BV2 microglia. This was followed by comprehensive metabolic profiling, including metabolic flux analyses, to examine glycolysis and oxidative phosphorylation dynamics. Our findings revealed distinct cell-specific metabolic phenotypes following TDP-43 depletion. NSC34 motor neurons exhibited a hypermetabolic phenotype with accentuation of both glycolysis and oxidative phosphorylation. However, N2A cells displayed a hypometabolic phenotype, whereas BV2 microglia cells only exhibited an increase in glycolysis. These metabolic maladaptations upon TDP-43 depletion underscore the role of TDP-43 in neuronal and glial energy metabolism and provide insight into the selective vulnerability of motor neurons in TDP-43 proteinopathies.

ANALYSIS OF THE SECRETOME IN GLIAL CELLS IN A RAT MODEL OF NEONATAL ASPHYXIA *IN VITRO*

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The problem of neonatal hypoxia-ischemia (HI) leading to neurological dysfunction, still needs to be studied. Therapeutic hypothermia is still the only available treatment. Analysis of the secretome of glial cells subjected to oxygen-glucose deprivation (OGD, mimicking HI) brings us closer to understanding the mechanism(s) initiated by neonatal asphyxia. The mixed glial cultures were prepared from the brains of 1-2 day old Wistar rats. Individual glial cell fractions (microglia, oligodendrocyte precursor cells/OPCs, astrocytes) were isolated and subjected to OGD as monocultures or co-cultures and cultured under serum-free and physiological normoxic conditions (5% oxygen). Supernatants conditioned by glial cells were collected and analysed for cytokine concentrations using the Luminex technique. An approximately 8-fold increase in CXCL1 amounts was detected in supernatants conditioned by OGD-treated OPCs compared to microglial culture supernatants. Significant differences in CXCL10 levels were observed between the control and OGD groups of the glial fractions studied, particularly between those cultured alone or in co-culture. In contrast, IL-4, IL-6 and IL-10 levels showed no significant differences. Examination of cytokine levels suggests that cells cultured as monofractions respond differently from those in co-cultures with other glial cell types, providing valuable information for basic and preclinical research aimed at testing potential drug therapies.

Funding: Supported by ESF, POWR.03.02.00-00-I028/17-00 and Statutory grant no.6 (MMRI PAS).

EFFECT OF HYPOXIC-ISCHEMIC CONDITIONS ON THE MITOCHONDRIA-LOCATED SIRTUIN 3 IN NEONATAL RAT GLIAL CELLS

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Perinatal asphyxia results from impaired tissue oxygenation during labor, leading to hypoxia-ischemia (HI) and brain damage due to neuronal loss and abnormal glial cell function. This is one of the causes of neonatal death and a major cause of neurodevelopmental disorders in childhood. Due to the altered bioenergetics associated with HI, mitochondria are one of the potential targets for clinical intervention aimed at restoring affected neural tissue. To address this issue, a study was undertaken to evaluate mitochondrial DNA (mtDNA) content and mitochondria-located sirtuin 3 (SiRT3). Primary mixed glial cell cultures were obtained from neonatal Wistar rats and used for astrocyte isolation after 12 days. Cells cultured in physiological normoxia were subjected to oxygen-glucose deprivation (OGD) to mimic an *in vitro* HI insult. At 3, 24 and 72 hours after OGD, astrocytes were harvested for immunocytochemical, biochemical and molecular analyses. Determination of SIRT3 amounts in the mitochondrial fraction showed a significant increase at 24 hours after OGD (555. 48 *vs.* 1709.91 pg/mg protein content). These changes are accompanied by an increase in the ratio of mtDNA to nuclear DNA. This suggests that mitochondria are involved in the self-defense mechanisms rather than in development of HI sequelae leading to brain damage.

Funding: Supported by National Science Center in Poland, grant: 2021/03/Y/NZ4/00214.

MICRO-RNA ALTERATIONS IN POST-STROKE BRAIN FOLLOWING PHYSICAL EXERCISE IN MICE

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Stroke causes acute brain injury becoming a leading global cause of morbidity and mortality with limited treatments although it is known that neuroprotective and neurorepair mechanisms are activated spontaneously following the ischemic stroke onset in the affected tissue, including angio-vasculogenesis and neurogenesis. Post-stroke recovery in patients with neurological deficits include neuro-rehabilitative therapies

to improve functional independence, but the molecular basis for rehabilitation-induced recovery remains unknown. Our hypothesis is that micro-RNAs (miRNAs) might play an important role in recovery mechanisms induced by rehabilitation and may serve as biomarkers. To identify specific miRNAs involved in post-stroke recovery we induced permanent distal middle cerebral artery occlusion (pdMCAO) in mice (C57BL/6J, 9-11 weeks males/females) and conducted post-stroke rehabilitation by physical exercise with treadmill. Mice were divided into rehabilitation groups (RHB) of 1 and 3 weeks undergoing daily treadmill running, and corresponding groups without rehabilitation (NO-RHB) (n=12/group). TaqMan Low Density miRNA Arrays (TLDAs) were used to screen the different expression of 641 miRNAs in brain ischemic tissue at the end of the RHB/NO-RHB treatment (n=4/group). RNA extraction, reverse transcription, and preamplification using target miRNA-specific primers preceded real-time qPCR analysis. Normalization and relative expression calculations using the 2^- ΔΔCq method revealed diverse miRNA expression patterns over time and/or rehabilitation. Selected miRNAs underwent validation in the larger animal group. Given miRNAs' pivotal role in ischemic stroke physiopathology and reparative processes, this study shows for the first time the post-stroke rehabilitation's impact on brain miRNA expression. Findings could serve as prognostic biomarkers or targets for novel ischemic stroke treatments.

Funding: STROKE-RICORS network (RD21/0006/0007) from Instituto Carlos III AGAUR supports the Neurovascular Research Laboratory (SGR2021/0656).

SELECTIVE TARGETING OF NON-NUCLEAR ESTROGEN RECEPTORS WITH PAPE-1 AS A NOVEL THERAPY AGAINST STROKE THROUGH INHIBITION OF NECROSIS AND EXCITOTOXICITY

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The aim of our study was to address the urgent global need for an effective strategy against acute stroke, proposing the newly designed PaPE-1 as a promising answer to limitations of existing therapeutic solutions, mainly associated with narrow therapeutic window. PaPE-1 is able to activate non-nuclear estrogen signaling, minimizing adverse hormonal effects associated with nuclear estrogen receptors signaling. Our goal was to provide evidence for PaPE-1 neuroprotective potential, including the ability to reduce necrosis and control the excitotoxicity by regulating Ca2+ flux and expression of NMDA receptors subunits – key players in stroke pathogenesis. In our study we employed a cellular model of stroke, constituted by subjecting primary neocortical cultures to 6 h of hypoxia followed by 18 h of reoxygenation. The effectiveness of the treatment was validated by a variety of biochemical and molecular assays, e.g.: AlamarBlue viability assay, LDH release, Fluoro-Jade C staining, neutral red uptake and quantifying the expression of NMDA – related genes and proteins using qPCR and ELISAs. Our research proved that post-treatment with PaPE-1 protects brain neurons against hypoxia/ischemia by inhibiting excitotoxicity and necrosis, serving as an effective therapeutic intervention against stroke.

Funding: The National Science Centre of Poland, No. 2021/43/D/NZ7/00633.

THE HDAC INHIBITOR, SODIUM BUTYRATE, PREVENTS SYNAPSE DEGRADATION IN RAT BRAINS SUBJECTED TO NEONATAL HYPOXIA-ISCHEMIA

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Neonatal hypoxia-ischemia (HI) triggers a cascade of biochemical events including excitotoxicity, oxidative stress, and inflammation that leads to extensive brain damage manifested, among others, by the elimination of synaptic connections. Our previous studies have shown that the histone deacetylase inhibitor (HDACi)-sodium butyrate (SB) diminished inflammatory processes and reduced brain damage. The main purpose of this study was to examine the effect of SB treatment on synapse elimination after HI. Research included two models of neonatal hypoxic-ischemic brain injury: an *in vivo* study in 7 days old rats pups and an *in vitro* study in rats neural cells. We observed a reduction in synaptic protein expression in rat brains after HI, which returned to control levels after SB administration. HI caused brain damage and disruption of synaptic mor-

phology. SB treatment in HI animals decreased damage and improved tissue morphology. Furthermore, we noted a reduced number of neuronal processes in the *in vitro* HI model, which increased after sodium butyrate treatment. These results suggested the neuroprotective effect of SB, as well as the protection of synaptic connections. Therefore, pharmacological modifications of complement activation could create new therapeutic approaches to reduce brain damage.

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ROLE OF KETOGENIC DIET IN MODULATING NEUROSTEROID CONCENTRATION IN TBI – AN *IN VITRO* APPROACH

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Traumatic brain injury (TBI) is one of the most common causes of disability, with an annual incidence of more than 50 million cases. It is caused by a sudden injury to the brain by an external force. Research suggests that ketogenic diet (KD) may have a neuroprotective effect in this disease, although the exact mechanism is not yet understood. Produced in KD ketone bodies can be used as a substrate for cholesterol production, which then can be converted to steroids, including neurosteroids. Neurosteroids have an ability to modulate function of GABA A and NMDA receptors, making them promising candidates as potential therapeutic agents. In this study primary rat cerebral cell cultures of hippocampus and cortex were used. KD was induced by administration of beta-hydroxybutyrate and TBI was modelled by wound healing assay. Concentrations of neurosteroids pregnenolone, allopregnanolone and tetrahydrodeoxycorticosterone were measured using ELISA. The results show increased production of tetrahydrodeoxycorticosterone in cortical cells during KD treatment in TBI model compared to the uninjured group. In conclusion, this study opens up new perspectives for research into the effects of the ketogenic diet on neurosteroid production and its potential role in TBI handling.

POSTER SESSION III – BRAIN CANCER

27th April, 2024 (Saturday), 14:00–15:15

EFFECT OF DOXORUBICIN ON THE INVASIVENESS OF GLIOBLASTOMA MULTIFORME CELLS

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Glioblastoma multiforme (GBM) is a highly malignant tumour of the central nervous system characterized by aggressive nature and frequent emergence of drug resistance therefore making traditional treatments insufficient. Doxorubicin (DOX) as an effective and widely used chemotherapeutic agent in other types of cancer may be a candidate for the treatment of GBM. The study aims to assess the effect of doxorubicin on the invasive potential of GBM cells using animal model. For this purpose, human T98G cells were exposed to DOX for 48h followed by 7 or 14 days of recovery after drug removal and next administered into the striatum of male Wistar rats. Blood analysis showed a significant decrease in platelet count and blood urea nitrogen in the group of animals injected with T98G cells after 14 days of recovery. Distribution of tumour cells was assessed based on immunocytochemical staining of brain slices for glial fibrillary acid protein (GFAP) and human nuclear antigen (HuN) analysed with the fluorescence microscope. For precise visualisation of the cells at the injection site, 3D scans were obtained using an image deconvolution processing. Research explores the impact of doxorubicin on GBM invasiveness, providing insights into drug-resistance mechanisms and potential new treatment strategies.

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DYNAMIC CHANGES IN CELLULAR MORPHOLOGY

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The cytoskeleton plays a crucial role in the development and physiological functioning of neurons. Many pathological conditions (i.e., neuroinflammation) that disrupt the cytoskeleton seriously affect neuron morphology. Our research aim is to gain further insights into the impact of cytochalasin D on cellular morphology. The main purpose of our study is to examine the alterations in the morphology of neuroblastoma cells when exposed to various substances. We established our methodology with stromal cells with fluorescence microscopy imaging following ImageJ analysis. We acquired stromal cell morphology data from the control sample cell spread area was decreased control cell 192.651 µm2 to CytoD treated 129.703 µm2. The nucleus projecting area was decreased in control cells 1714.994 µm2 and the CytoD treated cells 765.4412µm2. We observed that Cyto D has a considerable effect on stromal cells' cytoskeleton development. We are applying the same methodology SH-SY5Y cell line with neuronal characteristics to address our research aim. Thanks to our research we gain important information about the contribution of cytoskeleton neuronal characteristics.

Funding: This work was financially supported by the "Student Research Project" sponsored by the Faculty of Biochemistry, Biophysics, and Biotechnology of Jagiellonian University (to M. Eren).

THE ROLE OF VLCFA ON PROGRAMMED CELL DEATH AND MIGRATION OF GLIOMA CELLS

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Gliomas are the most malignant tumours of CNS. Due to their infiltrative nature, complete surgical resection is practically impossible, and in the course of radio- and chemotherapy, treatment resistance is very often acquired. Recent studies indicate that this process involves an increased level of very long chain fatty acids (VLCFA), which reduce the permeability of cell membranes and hinder the penetration of chemotherapy drugs into cells. The crucial role in these processes plays ELOVL1 elongase, responsible for elongation of VLCFA. Therefore, the aim of study was to investigate the effect of a specific inhibitor of ELOVL1 enzyme on the induction of programmed cell death and migration potential of gliomas. Human glioma cells (MOGG-CCM and T98G) were incubated with inhibitor for 24h. Staining with specific fluorochromes: Hoechst 33342, propidium iodide and acridine orange was used to visualize apoptosis, necrosis and autophagy. The levels of ELOVL1, ABCD1 and SCD1 proteins were determined by using Western Blot method. To determine cell viability and mobility, MTT Assay and Wound Assay were used. The obtained results showed that the specific inhibitor of ELOVL1 enzyme effectively induced apoptosis, reduced cell viability and migration potential of both the MOGGCCM and T98G cell lines.

CHANGES IN GLIOBLASTOMA-NEURON CROSS-TALK IN THE TUMOR MICROENVIRONMENT UPON ACCIDENTAL OVEREXPOSURE TO EXTREMELY LOW-FREQUENCY ELECTROMAGNETIC FIELD

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Though the factors causing gliomas, the aggressive and fatal cancer, have not yet been identified, progress has been made in the field of understanding the glioma development. The microvesicles release is the extracellular way for cells to interact with their surroundings by paracrine regulating the rate of proliferation, mi-

gration and apoptosis. Thus, any changes in the cancer microenvironment may affect the content of microvesicles and, as a result, the rate of tumor development. While occupational exposure to extremely low-frequency electromagnetic fields (ELF-EMF) has been suspected as a brain tumor risk factor, literature reports lack consensus, and the interaction between ELF-EMF exposure and glioma-derived microvesicle release remains poorly understood. Therefore, our study focuses on changes in the microvesicles released by neurons and glioma cells exposed to ELF-EMF (50 Hz, 7 mT, 60 min). Subsequently, untreated cells were exposed to these microvesicles. Our results show that ELF-EMF exposure increases microvesicles release. Administration of EMF-treated microvesicles decreases neuronal viability, causes changes in apoptosis rate and migration rate of gliomas. The collected data suggest that ELF-EMF exposure can potentially contribute to glioma progression by modulating microvesicle quantity and content.

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POSTER SESSION III – EPILEPSY

27th April, 2024 (Saturday), 14:00–15:15

EPILEPTIC SEIZURES AND GASOTRANSMISSION. IMMUNOHISTOCHEMICAL EXAMINATION OF THE SPATIOTEMPORAL PATTERN OF EXPRESSION OF GASOTRANSMITTER-SYNTHESIZING ENZYMES IN A RAT MODEL OF EPILEPTIC SEIZURES

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Epilepsy is a prevalent neurological disorder characterized by seizures originating from bioelectrical dysfunctions in hyperexcited neurons. Nitric oxide (NO), carbon monoxide (CO), and hydrogen sulfide (H_2S) act as nonclassical gaseous neurotransmitters involved in various physiological and pathophysiological processes within the central nervous system. Little is currently known regarding their role in epileptogenesis and the progression of epilepsy. Given the complexity of epilepsy and the diverse functions of gasotransmitters, we suggest a significant interplay between these phenomena. We aim to identify the spatiotemporal activation profiles of gasotransmitter systems following pilocarpine-induced seizures in adult male Wistar rats. Our preliminary studies indicate the involvement of the brain's nitrergic system in response to seizures during the early stage of epileptic activity (up to 12 hours from onset), with rapid attenuation. Utilizing immunohistochemical labelling, our research will assess the expression levels and localization of key enzymes involved in gasotransmitter synthesis, including nNOS, iNOS, CBS, MPST, HO1, and HO2. Reactive changes in the tissue resulting from pilocarpine-induced status epilepticus encompass widespread and time-dependent alterations originating from the piriform cortex, amygdala, and hippocampal formation, spreading to broader cortical and subcortical areas. Immunohistochemical examinations indicate the spatiotemporal changes in the expression of gasotransmitter-synthesizing enzymes during epilepsy.

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EFFECT OF REPEATED TREATMENT WITH SSR504734, A SELECTIVE GLYCINE TRANSPORTER TYPE 1 INHIBITOR, ON SEIZURE THRESHOLDS AND AMINO ACID LEVELS IN BRAIN STRUCTURES OF MICE

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Glycine transporter type 1 (GlyT1) is involved in regulation of both excitatory glutamatergic and inhibitory glycinergic neurotransmission by controlling the reuptake of glycine. By changing extracellular glycine concentrations, GlyT1 inhibitors can influence the excitation/inhibition balance and thereby affect seizure susceptibility. The aim of the study was to investigate the effect of a 2-week treatment with SSR504734, a selective GlyT1 inhibitor, on seizure thresholds in three seizure tests in mice: the 6 Hz-inducted psychomotor seizure test, maximal electroshock seizure test (MEST) and intravenous (i.v) pentylenetetrazole (PTZ) infusion test in adult male CD-1 mice. In addition, the changes in the amino acid levels in different brain structures were analyzed using the HPLC-ESI-MS technique. We found that SSR504734 (30 mg/kg) significantly increased the threshold for the tonic hindlimb extension in the MEST but it was ineffective in the 6 Hz and i.v. PTZ-induced seizure thresholds tests. Analysis of amino acids content in brain structures showed significant increase in glycine concentration in the brainstem and increase in serine concentration in the cerebral cortex. The obtained results suggest that inhibition of GlyT1 can suppress tonic seizures.

Funding: Research project financed by the National Science Center UMO-2021/41/B/NZ7/00328.

CEREBELLAR TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) AND PITOLISANT PREVENTED BEHAVIORAL AND NEUROINFLAMMATORY DISTURBANCES IN PENTYLENETETRAZOL (PTZ)-KIDNLING

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The work aimed to investigate behavioral manifestations in PTZ-kindled rats under combined treatment with the histamine H3 receptor inverse agonist pitolisant and mTOR blocker rapamycin. Kindling was produced in Wistar male rats by administering three weeks of pentylenetetrazole (PTZ, 35.0 mg/kg, i.p.). tDCS of the cerebellum (500 mcA, anode, 5.0 min) and pitolisant (Selleck, 5.0 mg/kg) were treated for ten days in fully kindled rats. Behavior was investigated in the open field test. Immunohistological data – Ki67, collagen IV type, and CD34 in brain slices was quantified using the object colocalization module available in the HALO software (Indica Labs, USA). The number of crossed central squares of the kindled animals in the open field was 4.1 times less than in control rats ($P<0.01$). Under conditions of combined treatment with tDCS and pitolizant, the reduction of central squares crossing was 18.5% ($P>0.05$), while differences remained after separate drug administration. The density of Ki67, collagen IV type, and CD34 in cortical slices of kindled rats was higher by 1.75-3.5 times ($P<0.01$) than in the sham-stimulated control and reduced by 1.5-2.3 times after combined treatment ($P<0.01$). A conclusion was made that the developed treatment effectively controls neuroinflammation, which underlays chronic brain epileptization.

Funding: Research was supported by the Ministry of Health Care of Ukraine (grant N0121U114510).

ANTISEIZURE EFFECTIVENESS OF NICOTINAMIDE AND DIAZEPAM INCREASED AFTER BRAIN TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS)

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tDCS of the cerebellum prevented PTZ-kindled seizures, and such an effect was strengthened after diazepam administration. The work aimed to investigate the pronouncement of antiseizure effects of nicotinamide and diazepam performed after preliminarily applying tDCS to the cerebellar or forebrain of PTZ-kindled rats. Kindling was induced with three weeks of PTZ (35.0 mg/kg, i.p.) administrations. Rats with generalized tonic-clonic seizures were used for the observation. Nicotinamide (100.0 mg/kg, i.p.) and diazepam (0.5 mg/kg, i.p.) did not significantly reduce seizure severity. Being administered after three trials of tDCS of the cerebellum (500 mcA, anode, 5.0 min), the severity of seizures was reduced in both nicotinamide and diazepam-treated rats by 35.0% and 45.0% correspondently ($P<0.01$). Generalized tonic-clonic fits were prevented, and rats demonstrated myoclonuses of forelimbs and rearings. In rats with forebrain tDCS, nicotinamide administration resulted in the development of generalized seizure fits in 6 out of 9 rats ($P>0.05$), while the latency of seizures increased by 1.57 times ($P<0.05$). Diazepam (0.5 mg/kg) prevented generalized seizures in 6 out of 9 rats and reduced seizure severity by 26.5% ($P<0.05$). Gained data favored the heightening of sensitivity to antiseizure effects of nicotinamide and diazepam caused by anode tDCS of the cerebellum and forebrain.

Funding: Research was supported by the Ministry of Health Care of Ukraine (grant N0121U114510).

NEURONAL LOSS AND NEOANGIGENESIS ARE SUPPRESSED WITH CEREBELLAR TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) IN PENTYLENETETRAZOL (PTZ) KINDLING

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The work aimed to investigate the effects of cerebellar tDCS on neurons' degeneration and microvessels' density in the brain structures of PTZ-kindled rats. Kindling was produced in Wistar male rats by administration of three-week PTZ (35.0 mg/kg, i.p.). tDCS of the cerebellum (500 mcA, anode, 15.0 min) was performed before each PTZ injection. Neurons were counted with light microscopy using the object colocalization module available in the HALO software (Indica Labs, USA). The number of degenerative neurons in the frontal cortex and hippocampus (CA3) of PTZ-kindled rats by 3.4 and by 4.9 times correspondently exceeded those in the intact control group ($P<0.001$). The number of microvessels in the frontal cortex and the ventral hippocampus exceeded such ones in the control by 44.5% and 49.2% ($P<0.05$). In tDCS-treated rats, the number of degenerative neurons in the frontal cortex and ventral hippocampus was less by 1.85 and 2.30 ($P<0.05$) times, and the number of microvessels was less by 1.52 and 1.76 times when compared with data in kindled rats ($P<0.05$). Hence, data favors the pathogenic significance of neuronal loss and angiogenesis as a mechanism of chronic epileptic activity development and the effectiveness of prevention, such deteriorations with cerebellar tDCS.

Funding: Research was supported by the Ministry of Health Care of Ukraine (grant N0121U114510).

OXIDATIVE STRESS CONTROL IN PENTYLENETETRAZOL (PTZ) KINDLING WITH CEREBELLAR TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS)

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This work aimed to investigate the level of oxidative stress markers in pentylenetetrazol (PTZ)-kindled animals and the effects of cerebellar tDCS. Kindling was produced in Wistar male rats by administration of three-week PTZ (35.0 mg/kg, i.p.). tDCS (500 mcA, 15 min) of the zone of cerebellar surface was delivered in 30 min five days before testing PTZ administration. The tissue of hemispheres was gained in two hours from the last tDCS. Spectrophotometric measurements of thiobarbituric acid reactive substances (TBARS), the activity of superoxide dismutase (SOD), and catalase were performed. tDCS prevented generalized seizures in 7 out of 8 animals ($P<0.05$). The level of TBARS in kindled rats with tDCS was 6.87+0.74 nmol/mg of tissue and exceeded the control value by 2.47 times ($P<0.01$). In kindled rats, SOD (6.53+0.72 U/mg tissue) and catalase (2.37+0.23 nM) activity were less than in the control animals by 49.6% ($P<0.05$) and 16.2% ($P>0.05$) correspondently. tDCS reduced TBARS content by 45.0% ($P<0.01$) and elevated SOD activity by 35.6% ($P<0.05$) when compared with the kindled rats. Catalase activity increased after cerebellar tDCS – up to 2.15+0.33 nM ($P>0.05$). Hence, the obtained data revealed the significant contribution of oxidative stress suppression to the antiseizure effects of cerebellar tDCS.

Funding: Research was supported by the Ministry of Health Care of Ukraine (grant N0121U114510).

6-HZ REPEATED TRANSCORNEAL STIMULATIONS IN RATS FAILED TO INDUCE KINDLING SEIZURES

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Our work aimed to produce kindled seizures with transcorneal 6-Hz electrical stimulation (ES) (32 mA 6 Hz for 3 seconds (GRASS stimulator, Astro.Med.Inc., USA) that was performed daily 5 times per week. Altogether 25 stimulations were delivered to each rat. During ES, clonic seizures of body muscles were seen with trouble tails that were stopped immediately after ES cessation. During ES, all body's tail tonic tension and myoclonus were seen in response to each stimulus delivered. After stopping ES, no seizures were seen, and rats demonstrated intensive exploratory behavior during the first 1-5 min with sniffing, head nodding, horizontal and vertical locomotion, and maintenance of high tail tonus. During this period, decreased pain sensitivity was seen (one scored severity out of four score scales). Grooming was a prediction for the normalization of animal behavior. EEG registration revealed spike–wave bursts registered in the ventral hippocampus and frontal cortex from 5-10 sec up to 1.0-1.5 min after stimulation. Duration of epileptiform activity was stable in the course of the delivery of stimulations. Hence, daily performed repeated ES, no post stimulative seizures were seen, and electrographic post stimulative deteriorations were slight and did not increase with their length in the course of ES delivery.

Funding: Research was supported by the Ministry of Health Care of Ukraine (grant N0121U114510).

RAPAMYCIN COMBINED WITH PITOLISANT ALLEVIATES ANXIETY AND DEPRESSION IN PENTYLENETETRAZOL (PTZ)-KINDLED RATS

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The work aimed to investigate the anxiety and depression manifestations in PTZ-kindled rats under combined treatment with the rapamycin and histamine H3 receptor inverse agonist pitolisant. Kindling was produced in Wistar male rats by administration of three-week PTZ (35.0 mg/kg, i.p.). Treatment with rapamycin (Pfizer, 0.5 mg/kg) and pitolisant (Selleck, 5.0 mg/kg) was performed for ten days in fully kindled rats. Control rats were treated with DMSO. Kindled animals spent less time (2.7 times) in the open area of the elevated plus maze (EPM) in comparison to the control ($P<0.001$). Following the combined administration of drugs, the period that kindled rats spent on the open arms of EPM was increased by 2.2 times compared to the control kindled rats. In the Porsolt forced swimming test, immobility response in kindled rats was higher by 37.5% ($P<0.01$) than in control. The immobility duration in rapamycin-treated rats remained higher by 29.0% ($P<0.01$) and by 23.7% ($P<0.05$) in rats treated with pitolisant. After combined treatment, the immobility duration in kindled rats was shorter by 33.5% ($P<0.001$) compared to the control. The synergy of rapamycin and pitolisant combined treatment was observed concerning abolishing in PTZ-kindled rats behavioral comorbidities such as anxiety and depression.

Funding: Research were supported by the Ministry of Health Care of Ukraine (grant N0121U114510).

POSTER SESSION III – COGNITION

27th April, 2024 (Saturday), 14:00–15:15

THE MORE DOGMATIC YOU ARE, THE LESS YOU CARE ABOUT EVIDENCE OF ERRORS: AN EVENT-RELATED POTENTIAL STUDY

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Dogmatism is commonly defined as a measure of inflexibility of thinking, unwillingness to change one's beliefs, even when presented with contradictory evidence and rejecting evidence that does not align with preconceived notions. Higher levels of dogmatism have been linked to decreased speed of evidence accumulation. In this study, we aimed to evaluate the association between self-reported dogmatism and evidence accumulation during performance monitoring. We investigated the relationship between dogmatism and three event-related potential components: early and late error positivity (Pe), well-validated indexes of evidence accumulation, and, on an exploratory basis, error-related negativity (ERN). 225 participants (113 females, one non-binary, mean age 23.6 years) fulfilled Altemeyer's DOG Scale and performed a modified Flanker task, while electroencephalography signal was recorded. 20 participants were excluded from the analysis. The results of the linear regression model revealed that the more increased the level of dogmatism, the less pronounced the late Pe. No significant associations were found between questionnaire data and other components. Our results indicate a negative association between dogmatism and the efficiency of evidence accumulation during error monitoring. They suggest that the mental inflexibility of highly dogmatic individuals is accompanied by diminished awareness of committed errors and an underestimation of their motivational value.

Funding: The study was funded by a Sonata Bis grant (2020/38/E/HS6/00490) from the National Science Centre of Poland.

E-SPORTS BEYOND GAMING: A DEEP DIVE INTO INTERCONNECTIONS AND CORRELATIONS OF CHOSEN COGNITIVE FUNCTIONS IN E-ATHLETES POST VIRTUAL REALITY TRAINING

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The realm of electronic sports (e-sports) represents a booming sector within the digital competition landscape. Investigating cognitive function enhancements in e-sports, this study analyzed 128 amateur e-athletes (80 males, 48 females, mean age 22.7±4.02) to understand the impact of VR training on key cognitive functions: reaction time, eye-hand coordination, concentration, alternating attention, and visuospatial memory. Participants were randomly assigned into experimental (E28) and control group (C28), with training spanning twenty-eight consecutive weekdays using the VR game 'Beat Saber.' Preliminary analysis confirmed that differences in daily gaming duration, prior e-sports experience, age, and baseline measures of cognitive functions were statistically non-significant. Statistical analysis, using Spearman Correlation, was focused on evaluating correlations between measured cognitive functions. Correlations were calculated at three stages: pre-training, post-training, and during a follow-up session to gauge both immediate and sustained cognitive impacts. Study aimed to identify which cognitive functions have the highest correlations with others, suggesting their greater importance. While the study did reveal the presence of some correlations between the cognitive functions measured, the results were unexpected. Contrary to our initial hypotheses, there were no significant correlations between concentration and reaction time, or between concentration and eye-hand coordination. These findings challenge our initial assumptions and suggest a more complex relationship between cognitive functions than previously understood, indicating the need for further research to unravel these intricate dynamics.

Funding: The study was funded by Wroclaw University of Health and Sport Sciences.

WHO GAINS AND WHO LOSES? DIVERSE EFFECTS OF HOME-USE BINAURAL BEATS BRAIN STIMULATION

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Neurotechnology-enhanced home learning has recently gained popularity, mainly using binaural beats brain stimulation (BB). However, the impact of BB has yet to be studied in conditions other than laboratory. Thus, urgent questions are raised about what effects home-use BB (hBB) causes. Positive? Neutral? Or even negative? And if it is positive, is it not a placebo effect? Here, we conducted the world's first series of hBB experiments involving 1,500 individuals. They completed a two-part fluid intelligence test at home. While taking the second part, there were several acoustic conditions, such as listening to binaural beats or other sounds and just silence. In the first study, we investigated whether the postulated results of hBB were not due to the placebo effect. The second investigation allowed us to compare hBB effects with cognitive responses to the remaining acoustic stimulation. Both showed that hBB can dramatically deteriorate cognitive effectiveness. However, in the third, we found that hBB may increase fluid intelligence, but only in particular groups of people with specified personality traits. In other words, we have found that most people generally lose by using hBB. Still, there is a small group of people, which we characterize here, who gain from it.

Funding: During this project A.R. and M.K. were supported by European Cooperation in Science and Technology grant: European Network on Brain Malformations (Neuro-MIG) (COST Action CA16118). COST is supported by the EU Framework Programme for Research and Innovation Horizon 2020. A.R. was also a scholarship holder granted by the Foundation of the Adam Mickiewicz University, Poznan, for the academic year 2022/2023.

NEURAL DYNAMICS DURING THE ERIKSEN FLANKER TASK UNDER TIME PRESSURE

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When sensory-guided actions must be performed under time pressure (TP), a trade-off arises between the accuracy of the choice and the time required to make the decision. This trade-off is evident in behavioral studies, where prioritizing speed often leads to more impulsive responses and a higher likelihood of errors. Traditional decision models explain effects of TP through the lowering of a fixed threshold, which terminates the decision process. However, these models leave an open question: At which stage of processing does TP affect neural activity, particularly in tasks that require target selection? To address this issue, we measured the electroencephalogram (EEG) and the electromyogram (EMG) during the flanker task, which required selecting a target among distracting flankers under different TP conditions. The results revealed, that both time pressure (TP) and flanker congruency influenced theta (4-8 Hz) activity in sensorimotor (SMC) and midfrontal (MFC) cortex. In contrast, theta power over occipital cortex (OCC) was only modulated by congruency. With regard to phase connectivity, TP increased theta coherence between the SMC and MFC, whereas congruency modulated ipsilateral connections between the SMC and OCC. Our findings challenge the fixed-threshold perspective, favoring a more nuanced view where TP impacts the neural activity at multiple levels and stages.

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RELIGIOUS FUNDAMENTALISM AND ERROR MONITORING – THE MODERATING ROLE OF THE NEED FOR COGNITIVE CLOSURE

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Previous research has indicated a significant relationship between religious fundamentalism and error monitoring. The aim of this study was to validate these findings and to examine whether this association is influenced by the need for cognitive closure (NFC). Electroencephalography recordings were obtained from 378 healthy participants from different religious backgrounds during a Go/NoGo task. The analysis focused on the well-established biomarker of error monitoring, error-related negativity (ERN), along with self-reported NFC and fundamentalism. Correlation analysis confirmed a significant relationship between fundamentalism and ERN ($r=-.12$, $p<.05$), and revealed a significant association between NFC and fundamentalism ($r=.10$, $p<.05$); the correlation between NFC and ERN was not significant. While the moderation effect of NFC on the association between fundamentalism and ERN was not significant overall ($p=.09$), it became significant when only Christians ($n=234$) were considered. Specifically, the relationship between fundamentalism and ERN was moderated by both general NFC ($\beta=-1.36$, $p<.05$) and two of its subconstructs: preference for predictability ($\beta=-.99$, $p<.05$) and intolerance of ambiguity ($\beta=-1.14$, $p<.01$). Our study confirmed that the higher religious fundamentalism, the more intense error monitoring. Furthermore, the moderation effect of NFC was limited only to Christian group, where a higher level of NFC strengthens the association between fundamentalism and error monitoring.

Funding: This study was supported by the National Science Centre of Poland, grant 2020/38/E/HS6/00490.

BRAINS DO CARE ABOUT OUR BELIEFS. BELIEVING IN FREE WILL AND DETERMINISM IS REFLECTED IN NEURAL CORRELATES OF RESPONSE MONITORING

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There is ongoing debate on whether believing in free will or thinking of the world as deterministic influence our behavior. Various studies have shown that deterministic beliefs impact not only our actions, but also basic neurocognitive processes such as response monitoring. Well established biomarkers of response monitoring are correct-related negativity (CRN), error-related negativity (ERN) and error positivity (Pe). The aim of our study was to investigate associations between these components and believing in free will and determinism. Two hundred twenty three volunteers (112 females, one non-binary, mean age 23.7 years) filled the Nadelhoffer's Free Will Inventory and performed a modified version of Flanker task while their electroencephalographic signal was recorded. Using multiple linear regression models, we found that the stronger the belief in free will, the higher the magnitude of CRN. Moreover, we observed that the higher the level of determinism, the lower the amplitude of Pe. There were no significant associations between beliefs and ERN. Our results indicate that individuals with a strong belief in free will are less certain about correctness of their actions, whereas individuals with a strong belief in determinism are less emotionally concerned about their errors. They also suggest that basic neurocognitive processes related to response monitoring are influenced by whether people believe they can exert intentional control over their actions.

Funding: The study was funded by a Sonata Bis grant (2020/38/E/HS6/00490) from the National Science Centre of Poland.

MICROSTATE ANALYSIS OF REST-STATE EEG UNDER CONDITIONS OF MORAL INJURY

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The neural manifestations of moral injury (MI) remain poorly studied and not well separated from the effects of posttraumatic stress disorder (PTSD). If the differences between MI and PTSD conditions exist, they plausibly can be revealed in the analysis of brain states. The method of brain microstates (MS) looks promising for detecting brain states, specific for MI. In our study, 36 subjects, who lived in Ukraine during the first year of the Russian-Ukrainian war, non-combatants, took part. To assess the level of psychological stress, the following psychological tests were used: PCL-5 (PTSD), GAD-7 (general anxiety), PHQ-9 (depression), MISS-M-SF (moral injury). EEG was recorded during eyes closed rest state using a 21-channel EEG system. EEG data were processed with LORETA software, and MS maps were calculated for 4 microstates. Obtained MS indices (transition rates, transition probabilities, MS durations) were analyzed using generalized linear models approach. It was found that transition rates of the microstate B correlate with MISS-M-SF results, while there were no correlations between MS data and responses to other questionnaires. Microstate B is associated with the visual networks activity, and may reflect different levels of activation of visual imagination depending on MI severity.

REACTING TO TEMPORALLY UNCERTAIN EVENTS INCREASES ERROR DETECTION AND EVALUATION: INSIGHTS FROM AN EEG–EMG STUDY

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In unpredictable contexts, error monitoring typically increases, suggesting a greater subjective cost for maladaptive responses to uncertain events. We explored whether temporal unpredictability amplifies error monitoring using a temporally cued stop-signal task. Symbolic cues predicted (temporally predictable) or not (temporally unpredictable) the target onset. Participants had to inhibit responses in 25% of trials signaled by an auditory tone presented shortly after target onset. Enhanced detection of inhibitory errors was evident, reflected in prolonged motor time (MT), the interval between the onset of the muscle activity and mechanical response that indexes an online detection and an attempt to stop erroneous actions. Likewise, the error-related negativity (ERN), an electrophysiological marker of response outcome evaluation, increased following inhibitory errors in temporally unpredictable conditions. In conclusion, our EMG and EEG findings underscore that the cost of failing to inhibit actions in a temporally unpredictable environment is significantly higher.

Funding: This work was supported by the National Science Centre of Poland grant (2018/31/N/HS6/00633) awarded to Inga Korolczuk.

FUNCTIONAL CHARACTERISTICS OF ATTENTIONAL NETWORKS IN MEDIA MULTITASKERS. NEURAL MECHANISMS UNDERLYING THE ATTENTIONAL FUNCTIONING

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Nowadays, the abundance of technological devices has established an enormous utilization of multimedia sources of stimulation, resulting, especially in young individuals, in the well-known trend of media multitasking (MM). This attitude is reflected in a compulsive consumption of more than one media stream simultaneously or in their usage during the involvement in non-media activities. Findings so far seem to point out a somewhat mixed scenario, documenting various associations, binding the MM with attentional performance. The research project here presented is aimed to comprehensively characterize the attentional functioning of media multitaskers (MMs) brain, by availing of the effective connectivity analysis based on electroencephalography (EEG). 69 participants were recruited on purpose to record brain EEG signal, while performing tasks in selective and divided attention condition. The final scope was to asses their performance in each task condition and merge them with the interplay among neural substrates related to attention, namely: the dorsal attentional (DAN) and the ventral attentional networks (VAN) – connected respectively with the voluntary and the stimulus-driven attentional control – and the fronto-parietal (FPN) and the cingulo-opercular networks (CON), sustaining the DAN and VAN functioning, monitoring and modulating attentional processes.

COGNITIVE LOAD AND STIMULATION OF THE AUTONOMIC NERVOUS SYSTEM

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The magnitude of cognitive load is defined by the current capacity of working memory, i.e., the size of cognitive resources in relation to the stimulating value of the task and the environment in which it is performed. Measurements of the cardiovascular system are considered particularly effective indicators of cognitive load due to their reliability and the possibility of continuous recording. The aim of the study was to

assess the relationship between the magnitude of cognitive load and the activation of the autonomic nervous system. The participants were male and female psychology students (n=20, age M=23). The participants were asked to perform a modified Sternberg task. They were asked to memorize a sequence of two or six digits. After some time, a single digit appeared on the screen. Participants judged whether it had been shown in the preceding sequence. The research tools consisted of: PsychoPy Program, Electrocardiograph, and Svarog. The data were analysed using the t-Student test. Based on the results obtained, it can be concluded that the task involving memorizing a longer sequence of digits was associated with greater cognitive load and greater activity of the autonomic nervous system – with a faster heart rate ($t_{(19)}$=3.858; p<0.001; d=0.865). The results of the study confirm the hypothesis. Cognitive load is associated with an increase in arousal (an increase in the activity of the autonomic nervous system).

Funding: SWPS University.

INDIVIDUAL DIFFERENCES IN PROCRASTINATION: NEUROPHYSIOLOGICAL AND BEHAVIORAL CORRELATES OF STIMULUS PROCESSING, RESPONSE INHIBITION AND ERROR MONITORING

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Procrastination involves delaying necessary tasks, often engaging in substitute activities that are not essential. Research indicates that procrastination is associated with dysfunctions in emotional regulation and cognitive control, including attentional processes, response inhibition, and error monitoring. The aim of our research was to validate these associations using the stop signal task. We collected electroencephalographic recordings from 225 participants (113 women, 1 non-binary, mean age 24 ± 4.18 years) and assessed self-reported procrastination using the 40-item Procrastination Assessment Questionnaire. The analysis revealed that procrastination is associated with amplitudes of sensory P1 (r=0.134, p=.045) and attentional P2 (r=0.146, p=.028) components, time-locked to the go stimulus, as well as with mean go response time (RT) (r=-0.141, p=.035). Additionally, it is correlated with mean RT in failed inhibition trials (r=-0.160, p=.016) and inhibition rate (r=-0.126, p=0.059). However, procrastination is not associated with stop-signal- and response-related components. These results suggest that increased levels of procrastination are linked to stronger perceptual processing and attentional binding to the go stimulus; resulting in shorter RTs but a lower inhibition rate. Although individuals higher in procrastination do not exhibit weakened processing of stop signals and monitoring responses on the neural level, their increased orientation towards go stimuli leads to more inhibitory errors.

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THE ROLE OF PRESUPPLEMENTARY MOTOR AREA IN DECISION-MAKING STRATEGIES – A TMS STUDY

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Complex decision-making requires strategic processing of information. Two strategies have been established: Take The Best (TTB) and Weighted Additive Rule (WADD). TTB relies on the most significant information, while WADD is based on the consideration of all available information. We hypothesize that WADD is strongly associated with inhibitory control, which, according to the literature, is embedded in the functioning of the right inferior frontal gyrus (rIFG) and presupplementary motor area (preSMA). In order to investigate the involvement of those areas in decision-making strategies utilizing, we conducted a study with 34 healthy participants (m age=25) who completed decision-making tasks in three transcranial magnetic stimulation (TMS) sessions targeting preSMA, rIFG, or parietal cortex as sham stimulation. We found that TMS stimulation of preSMA, but not rIFG, impacts strategy preference in this task, such that under preSMA stim-

ulation, participants adapted better to the conditions of the task. Additionally, the need for cognitive closure moderated this effect, so that it was noticeable only in participants with low values on the need for cognitive closure scale. We discuss these results in light of theories of the functional role of preSMA which might be crucial for processing complex information during decision-making.

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THE INFLUENCE OF NORM-REFERENCED FEEDBACK ON NEUROPHYSIOLOGICAL AND BEHAVIORAL INDICES OF ATTENTION

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Procrastination is the irrational delay of task completion. Previous studies have demonstrated that procrastinating students present difficulties in attentional control and performance monitoring, which could be observed in both behavioral and neurophysiological indices. Moreover, our recent research showed that these dysfunctions might be modulated by norm-referenced feedback received in the task. In the present study we wanted to replicate these findings as well as investigate the influence of positive and negative norm-referenced feedback on the frequency and emotional valence of mind-wandering episodes experienced during task completion. To achieve this goal, we recruited high (HP) and low procrastinating (LP) students (N=143), who completed the go/no-go task with thought probes. Obtained results indicated that HP (*vs.* LP) participants more frequently reported negatively valenced task-unrelated thoughts, regardless of received feedback. Moreover, in the HP group, negative (but not positive) feedback resulted in decreased reaction time variability, which is the behavioral index of attentional control. This effect was not observed among LP students. What is interesting, previously found differences between HP and LP individuals in neurophysiological indices of attention and performance monitoring were not apparent in the current study. This suggests that procrastination-related cognitive dysfunctions might depend on the motivational factors.

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FUNCTIONAL CONNECTIVITY IN CHRONIC WORK-RELATED STRESS: A RESTING-STATE EEG STUDY

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The chronic occupational stress is associated with pronounced decline in emotional and cognitive functioning. The studies on neural mechanisms indicate significant changes in brain activity and altered patterns of event-related potentials among burnout participants. This study presents the analysis of resting-state brain functional connectivity. Data were collected from a 256-channel EEG system. The sample consisted of 50 burnout employees and 50 controls matched on age, gender and occupation (Mean age=36.03, SD=8.07; 60 women). The functional connectivity between burnout and control participants was tested in eyes-closed (EC) and eyes-open (EO) conditions using resting state paradigm. The results indicate significant differences in brain activity between burnout and control group. Resting-state network of the burnout group is characterized by decreased functional connectivity in right frontal areas, consistently in all analyzed bands (1-35 Hz) and consistent tendency of increased connectivity in fronto-parieto-occipital and temporal areas in theta1, theta2 and lower alpha (alpha1) bands. Moreover, our analyses for the first time point to distinc-

tive aspects of functional connectivity within alpha3, beta1, and beta2 subbands in the burnout syndrome. These findings provide insights into the neurobiological underpinnings of burnout and its associations with altered resting-state networks.

LATERALIZED STIMULI PROCESSING IN SELECTIVE AND NON-SELECTIVE COVERT AND OVERT ATTENTION

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Slower responses to targets presented in the left visual field can be a result of fatigue. More evidence for this comes from research on covert attention (without eye movements). We tested whether attentional asymmetry differs between selective and non-selective covert and overt attention. We used the eye fixation-related potentials (EFRP) paradigm. The task of 23 right-handed subjects (aged 20-30 years) was to indicate whether the target T is rotated to the left or right side. The letter was displayed alone (non-selective attention) or appeared surrounded by distractors (Ls) (selective attention). The stimuli appeared 4 degrees from the center of the screen and could be perceived without saccades (covert attention, n=256 trials) or 11 degrees from the center of the screen, forcing the participant to make saccades to notice them (overt attention, n=256 trials). Reactions were faster to the right targets only in covert attention, regardless of the selectivity conditions. In overt attention, we found shorter saccades to the left side and the posterior P1 larger from the right than from the left electrodes for the right targets. We relate these results to the functions of inhibiting and enhancing processing by the left and right hemispheres in different attentional conditions.

INTRODUCING A NOVEL QUANTITATIVE MEASURE OF CONSCIOUS PERCEPTION – THE LAG OF CONSCIOUSNESS

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One of the challenges of studying conscious perception stems from the lack of a widely recognized measure for comparing subjective experiences with objective task processing within the same performance dimension. Past research has primarily relied on objective task outcomes (such as accuracy or reaction times) contrasted with subjective judgments (like confidence ratings or the Perceptual Awareness Scale). However, those measures capture entirely different aspects of the task. Here we use a novel behavioral measure of conscious perception to demonstrate how a specific stimulus presentation enables both objective and subjective comparisons within a single task dimension, namely time. In this new type of task, participants are presented with a stimulus whose state is continuously changing. Their goal is to report the state of the stimulus when they first saw it appearing on the screen. Behavioral findings reveal a consistent tendency among participants to overestimate the starting point of the stimulus. After testing the primary form of the procedure with nearly 250 participants, we proceeded to gather additional data employing various experimental setups. The results confirm that, across all of those tasks, there is a systematic disparity in the reported (subjective) and actual (objective) initial state of the continuously changing stimulus, revealing an average delay of 136 ms in participants' perception of stimulus onset. A subsequent follow-up experiment, evaluating participants' capacity to recall the stimulus state from memory, clarifies that this observed effect cannot solely be attributed to an inability to provide accurate responses. Importantly, the LAG exhibits a surprisingly strong dissociation from objective task performance indices such as reaction times. Thus, we conclude that this discrepancy in estimation may signify a delay in becoming aware of the stimulus, which we term the "LAG of consciousness".

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