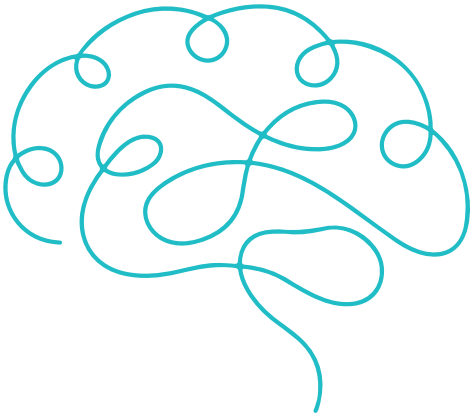
9th CROATIAN NEUROSCIENCE CONGRESS

17th to 19th November 2023

E-BOOK OF ABSTRACTS



9th CROATIAN NEUROSCIENCE CONGRESS

with international participation

17th to 19th November 2023

hybrid congress

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Croatian Society for Neuroscience (CSfN)
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University of Osijek, Rectorate building,
Trg Sv. Trojstva 3/Holy Trinity Square 3, 31000 Osijek

Online over the ZOOM platform

Osijek, 2023.

ORGANIZERS

Croatian Society for Neuroscience (CSfN)
Croatian Institute for Brain Research (CIBR)
Faculty of Medicine, Josip Juraj Strossmayer University of Osijek
Scientific Centre of Excellence for Basic, Clinical and Translational Neuroscience
Croatian Academy of Sciences and Arts

ORGANIZING COMMITTEE

Miloš Judaš (President of the organizing committee), Marija Heffer, Goran Sedmak, Kristina Mlinac Jerković, Senka Blažetić, Maja Valić, Nikola Habek, Rozi Andretić Waldowski, Marta Balog

SCIENTIFIC COMMITTEE

Zoran Đogaš, Marijan Klarica, Zdravko Petanjek, Goran Šimić, Ivana Munitić, Neven Henigsberg, Mario Vukšić, Nicholas James Bradshaw, Svjetlana Kalanj Bognar, Dinko Mitrečić, Darko Chudy, Nataša Jovanov Milošević, Željka Krsnik

ADDRESS OF THE ORGANIZER

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GENERAL INFORMATION

Congress venue

9th Croatian Neuroscience Congress will be held in hybrid form:

- on-line *via* ZOOM platform
- University of Osijek, Rectorate building, Trg Sv. Trojstva 3/Holy Trinity Square 3, 31000 Osijek

Congress language

The official language of the meeting is English and Croatian.

Main topics

- Basic neuroscience
- Clinical neuroscience
- Cognitive neuroscience
- Hypoxic-ischemic damage
- Molecular neuroscience
- Neurodegenerative disorders
- Neurodevelopmental basis of cognitive, mental, and neurological disorders
- Neuropharmacology
- Sleep

Registration fees

	Early bird registration until October 1st 2023	Late registration until the congress
CSfN member	60	100
Non-member of CSfN	100	150
PhD student	30	50
Single-day participation	30	50
Student	0	0

*Fee prices are given in euros

Registration fee includes:

- Unlimited access to all sessions and events during the the meeting
- access to all poster sessions
- certificate of attendance

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Osijek-Baranja County

The city of Osijek

Municipality Bilje

AnimaLab

Frontiers in Molecular Neuroscience

SCIENTIFIC PROGRAMME OVERVIEW

Plenary lecture

Speakers:
Karoly Mirnics (Munroe-Meyer Institute, University of Nebraska Medical Center, Omaha, NE, USA), Željka Korade (Pediatrics and Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE, USA)

CoreNEURO Final Symposium

Centre of Excellence for Basic, Clinical and Translational Neuroscience, University of Zagreb School of Medicine
Speakers:
Miloš Judaš, Ivica Kostović, Željka Krsnik, Milan Radoš, Ana Katušić, Zdravko Petanjek, Goran Sedmak, Nataša Jovanov Milošević, Mario Vukšić, Dinko Smilović, Aleksandra Dugandžić, Nikola Habek, Andrija Štajduhar, Marijan Klarica, Marko Radoš, Neven Henigsberg, Maja Cepanec, Ida Raffaelli, Goran Šimić, Mirta Boban, Marija Heffer, Svjetlana Kalanj Bognar, Nives Pećina Šlaus, Dora Višnjić, Melita Šalković Petrišić, Srećko Gajović, Siniša Škokić, Dinko Mitrečić, Marina Radmilović, Martina Rinčić

Hungarian Neuroscience Symposium

Centre for Neuroscience, University Pecs, Hungary
Speakers:
István Hernádi, Gergely Szarka, Zsuzsanna Helyes, Dóra Zelena, Andrea Tamas, Árpád Dobolyi, Istvan Adorjan, Marianna Pap

Poster sessions

Posters will be presented in 3min talk/oral presentation on Sunday 19th September 2023 according to a schedule. Presenting authors of posters are obliged to present the main findings of their work in 3 minutes talk/on-line presentation, according to a schedule.

Poster presentation award
Poster presentations are important scientific contributions, therefore a prize for the best poster presentations is established. The selection will be done based on scientific merit and clarity of presentation as judged by high-ranking board made up from three members of the Croatian Society for Neuroscience. The awards will be announced during the closing ceremony.

Clinical perspectives symposium

Speakers:
Ivana Rosenzweig, Zoran Đogaš, Rodrigo Herrera-Molina, Ivana Munitić

Exhibition

Traditional Easter eggs - a unique method to develop motoric skills of medical and dentistry students (Joe Petersburger)

Satellite Event and cocktails

From project to knowledge: SineMozak

Presentation of the project Synergy of molecular markers and multimodal in vivo imaging in preclinical assessment of ischemic stroke consequences (Srećko Gajović and collaborators)

Publication following the congress

Frontiers in Molecular Neuroscience

Congress participants and speakers will be invited to publish a paper in a special issue of Frontiers in Molecular Neuroscience, under a Research Topic entitled **Latest Advances in Neuroscience at the 9th Croatian Neuroscience Congress**. Articles of all types will be accepted, including but not limited to original research, short reports, review articles and perspective articles. It is our hope that this special issue will provide an overview of the current hot topics in neuroscience, expert opinions, and most recent original research, representing a go-to collection to consult on latest trends in neuroscience.

Deadlines: Manuscript Summary Submission Deadline 15 January 2024
Manuscript Submission Deadline 04 May 2024

Link to research topic: Latest Advances in Neuroscience at the 9th Croatian Neuroscience Congress | Frontiers Research Topic (frontiersin.org)

PROGRAMME

Friday, November 17th 2023

15.00-16.00 Registration of the participants

16.00-16.30 **OPENING CEREMONY**

Introductory words – Marija Heffer
Short greetings from the President of the Croatian Society for Neuroscience Miloš Judaš, representative of the Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, representative of the Municipality Bilje, representative of the city of Osijek, representative of the Osijek-Baranja county

Choir of the Faculty of Medicine, Josip Juraj Strossmayer University of Osijek

16.30-17.00 **PLENARY LECTURE**

Karoly Mirnics: Neuroimmune changes in schizophrenia

17.00-17.30 **PLENARY LECTURE**

Željka Korade: Cholesterol in brain development

17.30-18:00 **SPONSOR PRESENTATION**

Nataliya Sindeeva, Animalab Croatia / TSE Systems

18.00-18.15 **EXHIBITION OPENING**

Joe Petersburger: Traditional Easter eggs - a unique method to develop motoric skills of medical and dentistry students

18.15-20.00 **SATELLITE EVENT WITH COCTAILS**

Srećko Gajović and collaborators: presentation of the project Synergy of molecular markers and multimodal *in vivo* imaging in preclinical assessment of ischemic stroke consequences From project to knowledge: SineMozak

SATURDAY, November 18th 2023

9.00-14.10	**CORENEURO FINAL SYMPOSIUM, CENTRE OF EXCELLENCE FOR BASIC, CLINICAL AND TRANSLATIONAL NEUROSCIENCE, UNIVERSITY OF ZAGREB SCHOOL OF MEDICINE**
	INTRODUCTORY WORDS
9.00-9.15	Miloš Judaš
09.15-09.25	Ivica Kostović, Željka Krsnik
09.25-09.35	Ivica Kostović, Milan Radoš, Ana Katušić
09.35-09.45	Zdravko Petanjek
09.45-09.55	Goran Sedmak
09.55-10.05	Nataša Jovanov Milošević
10.05-10.15	Mario Vukšić, Dinko Smilović
10.15-10.25	Aleksandra Dugandžić, Nikola Habek
10.25-10.35	Andrija Štajduhar
10.35-10.50	**Coffee and refreshments**
10.50-11.00	Marijan Klarica
11.00-11.10	Marko Radoš
11.10-11.20	Neven Henigsberg
11.20-11.30	Maja Cepanec
11.30-11.40	Ida Raffaelli
11.40-11.55	**Break**
11.55-12.05	Goran Šimić
12.05-12.15	Mirta Boban
12.15-12.25	Marija Heffer
12.25-12.35	Svjetlana Kalanj Bognar
12.35-12.45	Nives Pećina Šlaus
12.45-12.55	Dora Višnjić
12.55-13.05	Melita Šalković Petrišić
13.05-13.15	**Break**
13.15-13.25	Srećko Gajović, Siniša Škokić
13.25-13.35	Dinko Mitrečić
13.35-13.45	Marina Radmilović
13.45-13.55	Martina Rinčić
13.55-14.10	**DISCUSSION AND CLOSING REMARKS -** Miloš Judaš
14.10-15.15	**Lunch break (lunch is provided for congress participants)**

15.15-18.30 **HUNGARIAN NEUROSCIENCE SYMPOSIUM, CENTRE FOR NEUROSCIENCE, UNIVERSITY PECS, HUNGARY**
Chair: Zdravko Petanjek

15.15-15.35 **István Hernádi:** Translational models of human cognitive behavior

15.35-15.55 **Gergely Szarka:** Ganglion cell gap junctions subserve the detection of approach motion in the retina

15.55-16.15 **Zsuzsanna Helyes:** Fractalkine receptor (CX3CR1) mediates neuroinflammation and related hypersensitivity in mouse models of chronic primary pain

16.15-16.35 **Dóra Zelena:** Posttraumatic stress disorder upside down

16.35-16.55 **Coffee and refreshments**

16.55-17.15 **Andrea Tamas:** Examination of pituitary adenylate cyclase-activating polypeptide in Parkinson's disease focusing on correlations with motor symptoms

17.15-17.35 **Árpád Dobolyi:** Social touch affects forebrain centers via direct thalamic projections

17.35-17.55 **Istvan Adorjan:** Cellular biomarkers of autism spectrum disorder and schizophrenia

17.55-18.15 **Marianna Pap:** Investigating the possible role of a novel non-coding RNA in the pathogenesis of glioblastoma multiforme

18.15-18.30 **DISCUSSION AND CLOSING REMARKS**

SUNDAY, November 19th 2023

	POSTER PRESENTATIONS I (3-min oral presentations)
9.00-10.30	Poster presentations according to schedule Chairs: Svjetlana Kalanj Bognar, Kristina Mlinac Jerković, Senka Blažetić
10.30-10.45	**Coffee and refreshments**
	POSTER PRESENTATIONS II (3-min oral presentations)
10.45-13.00	Poster presentations according to schedule Chairs: Svjetlana Kalanj Bognar, Kristina Mlinac Jerković, Senka Blažetić
13.00-13.30	**Pizza break (pizza is provided for congress participants)**
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13.50-14.10	**Zoran Đogaš:** New breakthroughs in research of breathing disorders during sleep
14.30-14.45	**Break**
14.45-15.05	**Rodrigo Herrera-Molina:** Neuroplastin-controlled mechanisms are essential for brain development and adult plasticity: Preclinical and clinical evidence
15.05-15.25	**Ivana Munitić:** Neuroimmune characterization of optineurin insufficiency mouse model
	CLOSING CEREMONY
15.25-16.00	**DISCUSSION, CLOSING REMARKS, BEST POSTER PRESENTATION AWARD** Marija Heffer

POSTER PRESENTATION PROGRAMME

SUNDAY, November 19th 2023

POSTER PRESENTATIONS I (3-min oral presentations)
9.00-10.30 Poster presentations according to schedule
Chairs: Svjetlana Kalanj Bognar, Kristina Mlinac Jerković, Senka Blažetić

PP1. MOLECULAR BACKGROUND OF SOMATOSENSORY ALTERATIONS IN ADOLESCENT RATS AFTER MILD PERINATAL HYPOXIA
Ana Spajić, Barbara Nikolić, *Sara Trnski, Matea Drlje, Mihaela Bobić-Rasonja, Ivan Banovac, Dubravka Hranilović, Zdravko Petanjek, Nenad Šestan, Miloš Judaš, Nataša Jovanov-Milošević*

PP2. DENERVATION-INDUCED CHANGES OF SYNAPTOPODIN, ARC AND GEPHYRIN IN DENTATE GRANULE CELLS FOLLOWING TRANSECTION OF THE PERFORANT PATHWAY
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PP4. CAN HUMAN ORAL MUCOSA STEM CELLS IMPROVE SURVIVAL OF NEURONS AFFECTED BY IN VITRO ANOXIA?
Paula Stančin, *Min Suk Song, Jasmina Isaković, Ivan Alajbeg, Dinko Mitrečić*

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PP8. SEX-SPECIFIC RESPONSE TO KETOGENIC DIET IN C57BL/6N MICE
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10.30-10.45	**Coffee and refreshments**

POSTER PRESENTATIONS II (3-min oral presentations)

10.45-13.00 Poster presentations according to schedule
Chairs: Svjetlana Kalanj Bognar, Kristina Mlinac Jerković, Senka Blažetić

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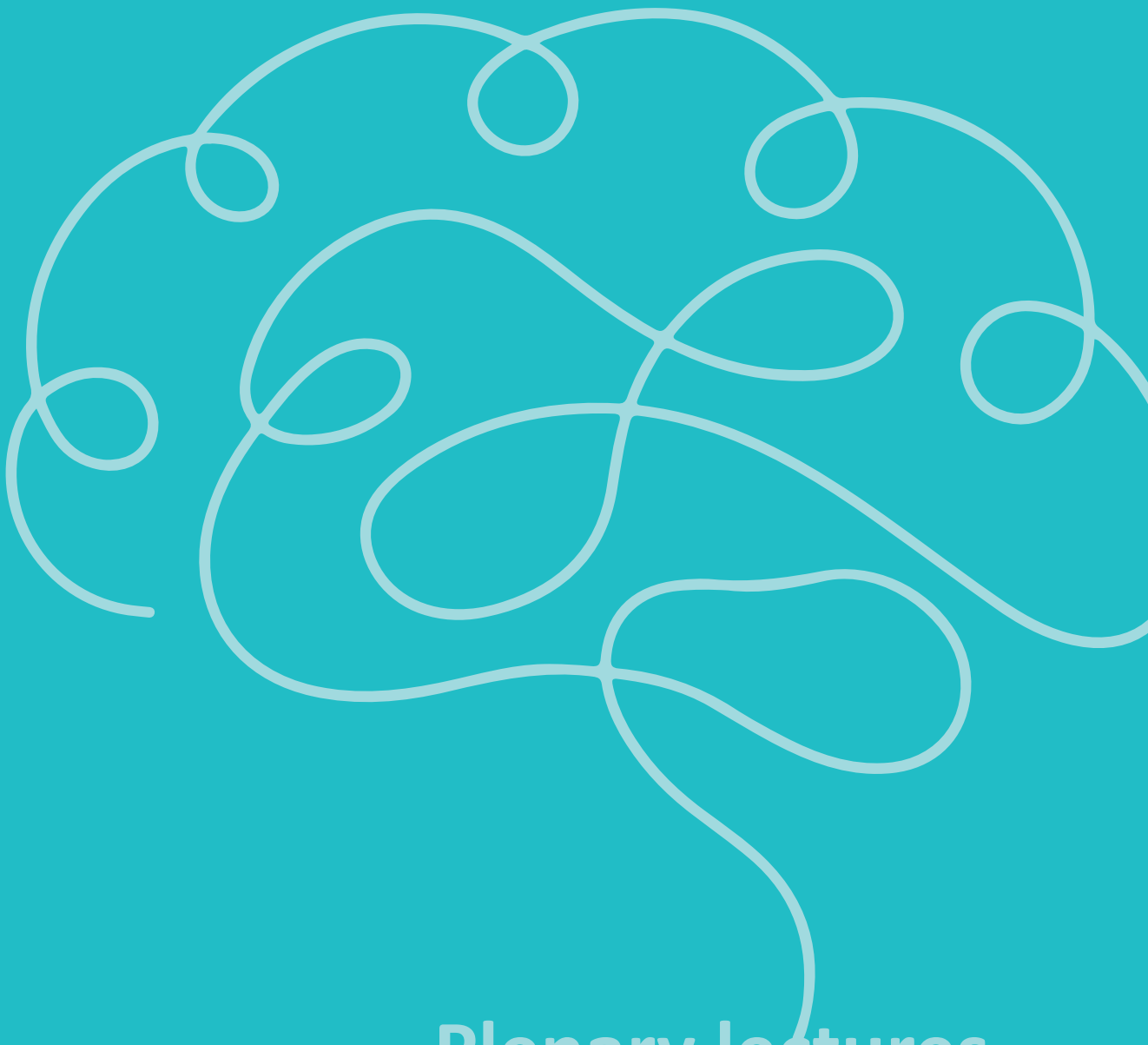
ABSTRACTS



Plenary lectures

NEUROIMMUNE CHANGES IN SCHIZOPHRENIA

Karoly Mirnics

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Epidemiological, genetic, transcriptome, postmortem, peripheral biomarker, and therapeutic studies of schizophrenia all point to a dysregulation of both innate and adaptive immune systems in the disease, and it is likely that these immune changes actively contribute to disease symptoms. Gene*environment interactions play critical roles in emergence and pathophysiology. In both disorders, recent genetic association studies have provided evidence for disease-linked variation in immune system genes and postmortem gene expression studies have shown extensive chronic immune abnormalities in brains of diseased subjects. Furthermore, peripheral biomarker studies revealed that both innate and adaptive immune systems are dysregulated. In both disorders symptoms of the disease correlate with the immune system dysfunction; yet, in autism this process appears to be chronic and sustained, while in schizophrenia it is exacerbated during acute episodes. Furthermore, since immune abnormalities endure into adulthood and anti-inflammatory agents appear to be beneficial, it is likely that these immune changes actively contribute to disease symptoms. Modeling these changes in animals provided further evidence that prenatal maternal immune activation alters neurodevelopment and leads to behavioral changes that are relevant for autism and schizophrenia. The converging evidence strongly argues that neurodevelopmental immune insults and genetic background critically interact and result in increased risk for either autism or schizophrenia.

CHOLESTEROL IN BRAIN DEVELOPMENT

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Cholesterol is an essential precursor for various biologically important molecules and plays an integral role in maintaining cell membrane structure and function. The metabolism of brain cholesterol differs markedly from that of other tissues, and it fully relies on *de novo* synthesis, as the blood-brain barrier prevents the uptake of cholesterol from the circulation. Cholesterol is synthesized and accumulated at the highest rate in the developing brain to meet the needs of rapid growth where it is required for synapse and dendrite formation, axonal guidance, myelination, and serves as a precursor for various biosynthetic pathways. Cholesterol biosynthesis is a complex, multi-step process involving over thirty enzymes. Mutations in sterol enzymes lead to several neurodevelopmental disorders. Examples include Smith-Lemli-Opitz Syndrome, desmosterolosis and lathosterolosis. Several other disorders, including Fragile X syndrome and Rett syndrome have altered cholesterol biosynthesis pathway. Studying transgenic mouse models with mutations in cholesterol synthesis enzymes provides insights into complex cholesterol homeostasis in the brain.

Invited lectures

TRANSLATIONAL MODELS OF HUMAN COGNITIVE BEHAVIOUR

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Detection and effective intervention in progressive neurocognitive disorders are unmet medical needs posing several challenges for translational behavioural neuroscience. Although the generally accepted use of rodent models greatly helps to explore the effects of pharmacological and/or behavioural interventions and provides the foundations for later clinical trials in humans, only non-human primates exhibit those unique complex cognitive abilities that are particularly valuable for studying higher order brain function, connectivity, and the effects of various interventions or treatments in diseased states. Here we aimed to develop and evaluate inter-species preclinical test batteries common between rats, laboratory macaque monkeys and humans for testing various aspects of cognition from basic attention to complex executive functions based on non-verbal psychological tests originally designed for human clinical use. We validated our behavioural paradigms using pharmacologically induced transient and reversible amnesia or increased task complexity. Results indicate that especially response speed, within-trial delay length or stimulus interference prove valuable tools in testing the behavioural manifestations of temporal expectation and working memory maintenance and can foster further research on age-related cognitive impairments. In addition, reversible pharmacological interventions make a valid contribution for modelling certain symptoms of diseased cognitive states. Task performance under various challenge conditions also allows the investigation of new VWM hallmarks in non-pharmacological behavioural models offering effective new test strategies for preclinical research. The present results may also contribute to the development of new, more complex behavioural diagnostic tools that allow for earlier detection and better evaluation of treatment options of cognitive deficits in humans.

GANGLION CELL GAP JUNCTIONS SUBSERVE THE DETECTION OF APPROACH MOTION IN THE RETINA

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In mammals visual information is detected and partially processed by the retina, which receives all visual input and through parallel channels formed by retinal microcircuits processes the information in a visual-feature (color, movement-types, etc.) specific manner, end of these pathways the retinal ganglion cells (RGCs) encode this information. Reconstructing these micro-circuits is essential for understanding how visual elements are encoded and transmiled to image forming brain centers. Following the signal decoding, the brain then provides a motor command to best react to the specific stimulus. One such motor program is the escape behavior initiated by TOFFAlpha RGCs in the retina and processed in the Superior Colliculus as a response to an approaching object. By using in-vitro Ca++- imaging, electrophysiology, and cell injections we show that gap junctions (GJs) serve to synchronize light-response kinetics. In addition, we also prove that TOFFAlpha cells utilize GJs to perform a priming excitation to neighbors. This priming is robust from cells in the epicenter of the approach stimulus towards alpha cell neighbors. Without such priming signal, neighboring cells do not differentiate between lateral moving and expanding objects, with it a single approach stimulus evokes response from an entire TOFFAlpha population and not only from a single cell in the stimulus epicentrum. Finally, we used conditional Cx36-KO mice and GJ blockers in behavioral tests and demonstrated that disruption of GJs blocks the approach stimulus evoked escape behavior. Thus, we conclude that GJs are essential to form a population code to detect approaching objects.

FRACTALKINE RECEPTOR (CX3CR1) MEDIATES NEUROINFLAMMATION AND RELATED HYPERSENSITIVITY IN MOUSE MODELS OF CHRONIC PRIMARY PAIN

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Complex Regional Pain Syndrome (CRPS) developing after a small injury and fibromyalgia being widespread musculoskeletal pain without tissue trauma are chronic primary pain conditions. Psychosocial distress, autoimmunity and complex sensory-immune-vascular interactions are involved in their pathophysiological mechanisms. Since their therapy is unsatisfactory, there is a great need to explore key mediators and identify novel drug targets. We investigated the role of the fractalkine chemokine receptor (CX3CR1) expressed predominantly on microglia in mouse models of CRPS and stress-induced pain.

Plantar skin-muscle incision mimicked micro injury and purified plasma IgG of CRPS patients was injected i.p. daily for 7 days (passive transfer-trauma). Chronic stress was induced by immobilization for 6h/day for 2 weeks. The role of CX3CR1 was investigated by gene-deficient mice and the antagonist AZD8797 (80 µg/kg i.p/day). Paw mechanonociceptive threshold was measured by aesthesiometry, astrocyte and microglia markers in pain-related central nervous system regions by glial fibrillary acidic protein and Iba1 immunohistochemistry.

CRPS IgG significantly enhanced plantar incision-induced mechanonociceptive threshold decrease (hyperalgesia) by 40-50%. Chronic restraint stress induced 20-25% hypersensitivity without any other behavioral alterations. Microglia and astrocyte number/density in the spinal dorsal horn, periaqueductal gray and somatosensory cortex increased in both models demonstrating neuroinflammation. Genetic deletion of CX3CR1 and its blockade by the antagonist reduced pain behavior, as well as micro- and astrogliosis in both cases.

CX3CR1 is involved in CRPS- and stress-related neuroinflammation leading to central sensitization and chronic pain, which provides novel analgesic perspectives for CX3CR1 antagonists.

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POSTTRAUMATIC STRESS DISORDER UPSIDE DOWN

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Posttraumatic stress disorder (PTSD) is a highly prevalent, devastating brain disorder. As only vulnerable subjects develop symptoms identifying markers of resilience maybe helpful for prevention. We try to approach the disease from the intestines.
Male Long Evans rats were traumatized using electric footshock and - based on an array of behavioral parameters – control, vulnerable and resilient subgroups were determined. After sacrifice ileal parameters (histology, rtPCR), caecal microbiota content, small chain fatty acid (SCFA) levels as well as prefrontal cortex (PFC) samples were studied.
The thickness of the intestinal villi was the smallest in the vulnerable subjects withouth changes in the expression of connective markers (zonula occludens-1, occluding, claudin-1,-8,-12). Althought there were no changes in the inflammatory parameters (TNFalfa, IL-1beta, IL-10, TLR-4) either, but the microbiom regulating markers differed between groups. The vulnerable group had the highest mucin producing Muc2 mRNA level and the lowest integrity marker Reg3b mRNA. In accordance with Muc2 changes the most prominent difference in the intestinal microbiota composition was in the relative abundance of the bacterium Akkermansia muciniphila. The lack of alteration in the plasma and faecal SCFA content suggest other mediators. Nevertheless, in PFC the expression of zonula occludens-1 and claudin-11 correlated positively both with the behaviour and the amount of Accermansia municiphila.
Our findings suggest an suggesting an upside down control of the behaviour as alteration in microbial composition and intestinal integrity might influence the development of PTSD-like symptoms possibly through altering the brain integrity. Therefore probiotics might be beneficial in prevention.

EXAMINATION OF PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE IN PARKINSON'S DISEASE FOCUSING ON CORRELATIONS WITH MOTOR SYMPTOMS

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The neuroprotective effects of pituitary adenylate cyclase-activating polypeptide (PACAP) have been shown in numerous in vitro and in vivo models of Parkinson's disease (PD) supporting the theory that PACAP could have an important role in the pathomechanism of the disorder affecting mostly older patients. Earlier studies found changes in PACAP levels in neurological disorders, therefore, the aim of our study was to examine PACAP in plasma samples of PD patients. Peptide levels were measured with ELISA and correlated with clinical parameters e.g. age, stage of the disorder based on the Hoehn and Yahr (HY) scale, subtype of the disease, treatment and specific scores measuring motor and non-motor symptoms, such as Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Epworth sleepiness scale (ESS), Parkinson's disease sleep scale(PDSS-2) and Beck-Depression Inventory(BDI). Our results showed significantly decreased PACAP levels in PD patients without deep brain stimulation(DBS) therapy and in akinetic-rigid subtype, additionally we also described further decrease in the HY stage 3 and 4. Elevated PACAP levels were found in patients with DBS. There were no significant correlations in PACAP level with MDS-UPDRS, type of pharmacological treatment, PDSS-2 sleepiness and depression(BDI) scales, but we found increased PACAP level in patients with more severe sleepiness problems based on the ESS scale. Based on these results we suggest that following the alterations of PACAP with other frequently used clinical biomarkers in PD patients might improve strategic planning of further therapeutic interventions and help to provide a clearer prognosis regarding the future perspective of the disease.

SOCIAL TOUCH AFFECTS FOREBRAIN CENTERS VIA DIRECT THALAMIC PROJECTIONS

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Social touch originates from a conspecific individual. While modern psychology recognized its significance, the underlying neurobiological networks and mechanisms have only recently started to emerge. Social touch activates a special type of primary afferents, the so-called C tactile fibers, which leads to a sense of pleasantness. Recently, a specific cell type in the dorsal root ganglia was identified in mice initiating the rewarding quality of social touch following their optogenetic activation. Furthermore, ablation of a spinal excitatory interneuron responsive to gentle stroking abolished touch-conditioned place preference. While is not known how C tactile fibers reach the thalamus, the posterior intralaminar thalamic nucleus (PIL) emerged as their target. We showed that it receives input from the spinal cord dorsal horn, and is activated by direct physical contact. In addition, a neuropeptide, parathyroid hormone 2 is activated in its neurons in response to social interactions. PIL neurons project to the medial prefrontal cortex but also have abundant projection to limbic regions, such as the preoptic area of the hypothalamus, the amygdala, and the lateral septum. Experimental activation of social activity-tagged neurons in the PIL increased while their inhibition decreased social grooming. We also showed that preoptic projections were sufficient to exert these behavioral actions. Experimental activation of preoptic amylin neurons also increased contact-seeking behaviour between female mice and also in dam-pup relation. In conclusion, social touch information affects instinctive behavior bypassing the primary somatosensory cortex, e.g. via the preoptic area of the hypothalamus.

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CELLULAR BIOMARKERS OF AUTISM SPECTRUM DISORDER AND SCHIZOPHRENIA

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Schizophrenia (SCH) and autism spectrum disorder (ASD) are chronic and serious mental illnesses which put an enormous burden on the individual, families and society. According to careful estimates there are approximately 100 million people worldwide affected by SCH or ASD. The conditions have multiple genetic risk factors, possibly interplaying with several environmental risk factors. However, the neuropathology of SCH/ASD is still unclear and much remains to be discovered about the neuroanatomical correlates and causes of these conditions.

In my lecture, I plan to outline the logistical, methodological and conceptual challenges while unravelling the complex neurohistological background of these conditions. The involvement of different cell types such as neurons, astroglia and microglia will be discussed. Also, the Primate Brain Collection Initiative will be presented which is an essential step to put human data and disease aetiology in an evolutionary context.

INVESTIGATING THE POSSIBLE ROLE OF A NOVEL NON-CODING RNA IN THE PATHOGENESIS OF GLIOBLASTOMA MULTIFORME

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Glioblastoma multiforme (GBM) is the most common primary tumor of the central nervous system, accounting for 50% of all primary brain gliomas. The median survival of patients with GBM is about 15 months from diagnosis. Standard treatment for GBM is surgical resection, complicated by the high invasiveness of the tumor, followed by radiotherapy and chemotherapy. The most commonly used chemotherapeutic agent is temozolomide (TMZ), a DNA-alkylating agent that induces DNA strand breaks and apoptosis of glial cells. Although TMZ significantly increases survival in GBM patients, resistance to TMZ leads to tumor progression. Several factors may be responsible for the development of TMZ resistance, one being the expression of the enzyme O6-methylguanine-DNA methyltransferase (MGMT). MGMT is a DNA repair enzyme that protects the cellular genome from the mutagenic effects of TMZ and reverses the DNA damage caused by the treatment, leading to reduced efficacy of chemotherapy. The treatment strategy is greatly complicated by genetic and epigenetic heterogeneity within the tumor. Non-coding RNAs (ncRNAs) play a role in the regulation of several epigenetic processes, including chromatin remodeling, gene activation and gene inactivation. We have discovered a novel ncRNA (AS-MGMT) in the 3rd intronic region of the MGMT gene, which is expressed in several GBM cell lines and primary GBM tumor samples. We found that AS-MGMT expression is increased at low O_2 level and mutually exclusive expression of MGMT and AS-MGMT genes was detected. These findings are particularly interesting as the induction of compromised expression of MGMT may be of therapeutic relevance.

RAPID EYE MOVEMENT (REM) BEHAVIOUR DISORDER

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Parkinson disease (PD) is the fastest growing neurological disorder and one of the leading sources of disability globally. Patients with PD frequently suffer with sleep problems which come only second to psychiatric symptoms in the non-motor symptoms category. To date, available treatments for sleep disorders in PD are only partially effective, partly due to the limited mechanistic insight into their oetiology.

A case in point is the idiopathic (*primary*) Rapid Eye Movement Behaviour Disorder (iRBD). iRBD is characterized by the lack of REM-associated atonia, and by the presence of abnormal, dream isomorphic, and at times violent and dangerous motor behaviours. Apart from the injury due to the re-enactment, deficient quality of sleep in iRBD may also contribute to an earlier emergence of non-motor cognitive/psychiatric symptoms, and less favourable prognosis.

During my talk I will discuss some of the recent findings that suggest a role for a cortical predictive processing, orexinergic system and the somatosensory cortex in the genesis of these behaviours in iRBD.

NEUROPLASTIN-CONTROLLED MECHANISMS ARE ESSENTIAL FOR BRAIN DEVELOPMENT AND ADULT PLASTICITY: PRECLINICAL AND CLINICAL EVIDENCE

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Understanding how failed molecular and cellular mechanisms in neurons result in abnormal brain development and reduced adult plasticity may open therapeutic avenues for the treatment of neurodevelopmental disorders (NDDs), neurological alteration, and/or neurodegenerative diseases (NDs). In the last 10 years, we have gathered evidence indicating that the type-I transmembrane domain glycoprotein neuroplastin triggers cell signaling for excitatory synapse formation in young hippocampal neurons through its binding to the cytosolic adaptor protein tumor necrosis factor 6 (TRAF6). Confirming these results, neuroplastin-deficient mice display fewer hippocampal glutamatergic synapses *in vivo* as shown by us and confirmed later by other colleagues. In adult neurons, neuroplastin becomes an obligatory subunit for practically all Plasma Calcium ATPase (PMCA) expressed by neurons. We can show now that inducible ablation of the neuroplastin gene (*nptn*) in mice results in a strong reduction of PMCA levels as well as severe alteration of cytosolic calcium signals. Interestingly, PMCA deficiency is critically linked to impaired cognitive development, NDDs such as autism and epilepsy, and NDs such as Alzheimer's disease in humans. Patients carrying disruptive *de novo* germline variants in *NPTN* have been identified and diagnosed with impaired cognitive development, epilepsy, autistic-like behaviour, and other NDDs. Our new data support the hypothesis that synapse formation and/or PMCA-dependent calcium signal regulation may be disturbed by the mutants of human neuroplastin identified in patients.

NEUROIMMUNE CHARACTERIZATION OF OPTINEURIN INSUFFICIENCY MOUSE MODEL

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Optineurin is a polyubiquitin-binding adaptor protein implicated in inflammatory signalling. Its mutations are associated with amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), neurodegenerative diseases characterised by neuronal loss, neuroinflammation, and peripheral immune imbalance. However, mechanistic role of optineurin mutations in neurodegeneration is unclear. To study the role of optineurin, we analysed optineurin insufficiency mice (Optn470T), designed to mimic ALS/FTD-linked optineurin truncations that fail to bind polyubiquitinated proteins. $Optn^{470T}$ mice did not exhibit ALS and FTD neuropathology or phenotype, but primary microglia and macrophages isolated from these mice exhibited immune imbalance distal to IFN-β secretory pathway and increased TDP-43 protein levels. However, an increase in TDP-43 levels did not trigger cytoplasmic aggregate formation. Interestingly, lipopolysaccharide (LPS) treatment led to an increase in TDP-43 levels in wild-type but not $Optn^{470T}$ microglia and macrophages, suggesting a presence of a TDP-43 plateau and a potential chronic immune imbalance. The latter is a potential therapeutic target for many neurodegenerative diseases necessitating further research into the mechanisms of optineurin-mediated immune regulation.

Oral presentations

NEW CANDIDATE GENE DISCOVERIES IN NEURODEVELOPMENTAL DISORDERS – THE IMPORTANCE OF REEVALUATING GENETIC FINDINGS IN NEURODEVELOPMENTAL DISORDERS BY SYSTEMS BIOLOGY APPROACH

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Disorders of the nervous system development characterized by cognitive impairment and behavioral abnormalities commonly referred to as neurodevelopmental disorders (NDDs) are of significant research and public interest. Although structural variations (including copy number variants – CNVs), SNVs, and indels have become well-described etiological backgrounds for NDDs, there is a question about the changing nature of genetic information and copy number evaluation discrepancy between databases. While genomic testing is now widely available, affordable, and used for diagnosing genetic diseases, determining variant pathogenicity remains challenging in diagnostic decision-making. Therefore, evidence-based knowledge in clinical praxis is needed when working with NDDs.

Here, we present data on reevaluating genetic findings of the custom chromosomal microarray (CMA) in complex NDDs and/or ASD patients. The main objectives of the research were to reevaluate the genetic finding of custom CMA in patients with NDDs and/or ASD and explore a large set of genes for their role in NDD and ASD by systems biology approach.

Using a systems biology approach to integrate information from several databases, we identified 18 potential novel protein-coding candidate genes underlying NDDs that should have priority as a target for future functional analysis.

THE ROLE OF GC-C AGONISTS IN THE BRAIN

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Uroguanylin (UGN) belongs to the family of guanylin peptides. They regulate electrolyte and water transport in intestine via guanylate cyclase C, the only known receptor for guanylin peptides. It is believed that brain is not expressing UGN, we are showing the expression of UGN in different brain regions at mRNA level (PCR, QPCR, RNAScope) and protein level (Western blot, IHC, ELISA) which is regulated by feeding. GC-C is expressed in hypothalamus, midbrain, cerebral cortex, Purkinje cells, amygdala in healthy laboratory animals (age, sex and phase of estrous cycle dependent) and humans, but not in astrocytes. In astrocytes UGN leads to an increase in intracellular Ca^{2+} concentration via GC-C/cGMP independent signalling pathway. Absence of GC-C in GC-C KO mice resulted in the development of smaller ischaemic lesions. WT and UGN KO animals showed a stronger Ca^{2+} response in astrocytes of the peri-ischaemic cerebral cortex compared with the same cortical region of the unaffected contralateral hemisphere. This stronger activation was not observed in GC-C KO animals. Why GC-C might affect Ca^{2+} signalling in peri-ischaemic astrocytes? GC-C is expressed in these cells after MCAO, whereas under normoxic conditions GC-C is expressed mainly in cortical neurons. Stronger activation of the Ca^{2+}-dependent signalling pathway could lead to the stronger activation of the Na^{+}/H^{+} exchanger, tissue acidification and neuronal death.

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Exhibition

TRADITIONAL EASTER EGGS - A UNIQUE METHOD TO DEVELOP MOTORIC SKILLS OF MEDICAL AND DENTISTRY STUDENTS

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Traditional Easter egg dying is a way more complex activity than then it seems at first glance. Such recognition initiated to create a university course, which helps polishing manual skills for medical students through a dramatically alternate way they got used to. The aim of the course is to develop and polish manual skills through alternative ways, which causes not just pleasure but creates artwork. Besides manual skills, this course helps to develop patience, focus, precision, and tolerance of monotony. It is well-known that widely acknowledged doctors were also skilled in different fields of arts (graphics, music, painting, sculpting, etc.). Just as Prof. Dr. János Szentágothai, a celebrated and determinate figure of neuroscience. Within the frames of the course, students can polish their manual skills by absorbing several aspects of traditional Easter egg-dying methods. Activities include engraving and carving with a professional engraver; syringe and medical needle use; wax melting; precision wax applying to the uneven surface; precision painting; acidic etching. On top of it, created artworks can be exhibited as well, which motivates many other students.

Poster presentations

PP1

MOLECULAR BACKGROUND OF SOMATOSENSORY ALTERATIONS IN ADOLESCENT RATS AFTER MILD PERINATAL HYPOXIA

Ana Spajić[1], B. Nikolić[2], S. Trnski [3], M. Drlje[3], M. Bobić-Rasonja[3,4], I. Banovac[3,5], D. Hranilović [2], Z. Petanjek[3,5], N. Šestan[1,6,7,8,9,10], M. Judaš[3], N. Jovanov-Milosevic [3,4]

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Mild to moderate hypoxic events or injury (HI) during gestation or neonatal period may pass unnoticed. Still, it could affect normal brain development and manifest as cognitive or behavioral disorders later in life. In this study, P1 neonates exposed to mild normobaric hypoxia (8% O_2, 2h) and matching controls were studied, aiming to uncover possible long-lasting hypoxia-induced molecular changes in the somatosensory cortex (SSC) and concomitant alterations in somatosensory processing. RNA was isolated from SSC samples of 16 hypoxia-exposed and 15 control P50 rats for RNA sequencing. 703 upregulated and 463 downregulated genes were identified using DESeq. Among the top upregulated genes, we observed those encoding the three receptors associated with somatosensory processing, including Grin2a (a subunit of the NMDA receptor), Gabrb2 (a subunit of the GABAA receptor), and Grm5 (metabotropic glutamate receptor 5). The significance of their upregulation was confirmed by qPCR in the entire sample of 31 SSCs. Subsequent Gene Ontology analysis of the identified differentially expressed genes indicated significant enrichment in biological processes such as synaptic signaling and cell-cell signaling, while processes related to extracellular matrix (ECM) components and cells organization were downregulated. Cytoachitectonic, ECM and synaptic imunohistochemical markers applied in samples at P15 and P50 confirmed the findings of transcriptomic analysis. An analysis of the rats' rearing behavior data (34 control and 36 hypoxia-exposed) unsupported - visually mediated spatial mapping, and supported - somatosensory moderated information about environmental boundaries revealed a highly significant effect of hypoxia only on supported rearing. The results indicate long-lasting changes in somatosensory information processing in SSC due to synaptic and ECM gene expression alterations following a mild perinatal HI.

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PP2

DENERVATION-INDUCED CHANGES OF SYNAPTOPODIN, ARC AND GEPHYRIN IN DENTATE GRANULE CELLS FOLLOWING TRANSECTION OF THE PERFORANT PATHWAY

Fran Božić[1], Dinko Smilović[1], Mario Zelić[1], Thomas Deller[2], Mario Vukšić[1]

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Following brain injury, neurons remodel their spines and dendrites. The molecular mechanisms involved in this remodelling are not fully understood. Studies investigating these mechanisms may help to identify novel targets for therapeutic intervention. Our study focuses on three putative candidate proteins previously associated with synaptic plasticity: synaptopodin, Arc, and gephyrin.
In our study, we transect the perforant pathway of anaesthetised C57Bl/6-J mice, resulting in layer-specific denervation of distal dendrites of dentate granule cells. Sham controls and animals surviving for 3, 7, 14 and 28 days post-lesion are studied. Intracellular injections of Alexa Fluor 568 hydrazide fluorescent dye into identified granule cells are employed to visualise morphological changes and combined with immunofluorescence labelling of synaptopodin, Arc, and gephyrin. The images are obtained using an Olympus FV3000 confocal microscope, and the analysis of spines and fluorescent clusters is performed manually using ImageJ.
Our study hypothesises that synaptopodin, renowned for its role in spine stabilisation, will emerge as a potential keystone in preserving dendritic spines after denervation. It also hypothesises that Arc, a protein implicated in activity-dependent plasticity, will correspond to spine dynamics following denervation. Lastly, gephyrin, a scaffolding protein at inhibitory synapses, is hypothesised to influence the dynamics of the most stable spines in response to the loss of input.
Our findings will provide the first *in vivo* evidence for the role of these proteins in dendritic remodelling after entorhinal denervation. A deeper understanding of their role may help to identify molecular pathways that could be therapeutically exploited in different neurological conditions.

PP3

EXPLORING THE DEVELOPMENT OF HUMAN SUBTHALAMIC NUCLEUS: AN ANALYSIS OF MOLECULAR MARKERS

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The subthalamic nucleus (STN) is a small, biconvex nucleus functionally implicated in the basal ganglia pathways. While extensive research has dissected the developmental origin and molecular markers of STN in animal models, there is an imperative to elucidate the molecular cues governing the development of the human STN, which plays a unique role in human neurobiology. To address this knowledge gap, we analyzed the expression of multiple transcription factors in the human fetal STN from the early fetal period (10-12 PCW, post-conceptional weeks) to newborn. Post-mortem human fetal brain tissue was formalin-fixed, processed for paraffin embedding, and sectioned at 10µm thickness. Standard immunohistochemical techniques were employed to investigate the presence of transcription factors (e.g. PITX2, FOXP2, FOXP1, FOXA1, and BARHL1) and other molecular markers (e.g. calcium-binding proteins). Our findings unveil that the developing human STN shares an intriguing overlap with the transcription factors previously implicated in rodent STN development. Notably, this study represents the first comprehensive exploration of these molecular markers in the developing human STN. Our preliminary findings provide compelling evidence that these transcription factors play a pivotal role in determining the identity of neurons within the developing human STN. This research takes a significant step towards unraveling the cellular and molecular mysteries of the human subthalamic nucleus, contributing to our broader understanding of neurodevelopment in the human brain.

PP4

CAN HUMAN ORAL MUCOSA STEM CELLS IMPROVE SURVIVAL OF NEURONS AFFECTED BY IN VITRO ANOXIA?

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Oral mucosa is, because of its accessibility, a very useful source of stem cells. Since tissue in this region originates from the neural crest cells, which naturally develop in a niche with decreased levels of oxygen, the main goal of this work was to test if human oral mucosa stem cells (hOMSC) might be used to treat neural cells damaged by anoxia. Here we show that hOMSC are more resistant to anoxia than human induced pluripotent stem cells and that they secrete factors which are involved in regeneration: BDNF, GDNF, VEGF and NGF. When hOMSC were added to human neurons damaged by anoxia, they significantly improved their survival. Interestingly, this capability was gradually decreased in hOMSC exposed to neural cells for 14 or 28 days. Moreover, beneficial effect of hOMSC for neural tissue damaged by hypoxia was confirmed in a pilot experiment on mice affected by stroke. In this work we confirmed that hOMSC, in a time-limited manner improve survival of anoxia-damaged neurons. Both in vitro and in vivo results suggest that hOMSC are excellent candidates for clinical trials on patients affected by stroke.

PP5

PRESENCE OF GUANYLATE CYCLASE C IN THE HUMAN BRAIN

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The presence of guanylate cyclase C (GC-C) is well documented in the brain of rodents. It was detected in the midbrain, amygdala, hypothalamus, cerebellum, and cortex. In the human brain of both genders GC-C is determined in the arcuate nucleus of the hypothalamus and the prefrontal cortex but not in other brain regions. Therefore, the goal of this study was to determine the presence of GC-C in those brain regions of human.

In 21 male and 13 female human brain samples, the presence of GC-C protein was determined. Samples were collected *post mortem* within 24 hours. Less than 100 mL od the stomach content was classified as an empty and more as a full stomach. Analysed areas were in the prefrontal cortex Brodmann areas (BA) 9, 10, 11, 32, cerebellar cortex, and hypothalamic arcuate nucleus. Substantia nigra was used as a positive control. Analysis was performed using the ELISA test.

In all BAs, the presence of GC-C was detected. Tests showed more GC-C in the male hypothalamus but after a meal (full stomach) which is in accordance with findings in rodents. More GC-C proteins in females were determined in neurons of BA9, specifically in the left hemisphere, but only when persons died with full stomach.

Less GC-C protein in the female hypothalamus might reflects its weaker influence on satiety. The same could be the case in BA9 where GC-C might underlie gender differences in function of BA9 especially after a meal.

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PP6

MOLECULAR MARKERS DELINEATE REGIONAL DIFFERENCES IN THE HUMAN FRONTAL AND OCCIPITAL CORTEX DURING THE SUBPLATE FORMATION PERIOD

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The human prenatal cortical development is characterized by transient fetal lamination. Subplate (SP) zone, one of the key components of early prenatal neuronal circuitry, is the most prominent fetal cortical compartment and a major site of synaptogenesis and neuronal differentiation. SP is formed between 13 and 15 postconceptional weeks (PCW) and consists of neurons from the deep cortical plate (CP) and early born SP neurons originating from the *preplate* layer (1). SP compartment is not uniform across the brain hemisphere (2) and several regional differences are observed in the parietal somatosensory, occipital visual and limbic cortex (3). SP is thicker and more developed in associative brain areas containing more cortico-cortical connections, and it is thinner in the medial and ventral cortical portions. Using immunohistochemistry on formalin-fixed paraffin-embedded (FFPE) postmortem prenatal human brain tissue, we analyzed expression patterns of diverse cellular and molecular markers in the frontal and occipital cortex using "compartmental approach" (4). Our results showed regional differences in the arrangement and morphology of SP neurons, extracellular matrix (ECM) and axonal content. Namely, the occipital cortex was characterized by a thinner SP and a sharper border between the SP and the IZ (*external capsule*), while the orbitofrontal cortex showed the "double" CP containing projection neurons. Thus, introducing novel molecular markers, these results confirm and extend our initial study (4). In conclusion, regional differences in synapse-rich compartment between the frontal and occipital cortex can be observed early during *in utero* development, even before 15 PCW.

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PP7

CONDURITOL B EPOXIDE ALTERS INSULIN SIGNALING NETWORK THROUGH INSULIN LIKE GROWTH FACTOR RECEPTOR 1

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This study investigated the effects of conduritol B epoxide (CBE), a glucocerebrosidase inhibitor developed as a model for Gaucher disease, on differentiated human neuroblastoma SHSY-5Y cells. Gangliosides are essential glycosphingolipids in cell membranes. Their degradation was disrupted by CBE, leading to their accumulation. Three CBE concentrations (2.5 µM, 10 µM and 40 µM) were tested to investigate the concentration-dependent effects on cell viability and insulin signaling in neuron-like cells. After CBE treatment, cells were exposed to 2 mM of insulin to study effects of ganglioside overload on insulin signaling pathway.

The SHSY-5Y human neuroblastoma cell line differentiated with trans-retinoic acid was used for all experiments. The cells were treated with CBE for 48 hours. The viability of the cell after CBE treatment with or without insulin was tested using MTT assay. Insulin signaling pathway was assessed by western blot using antibodies against the alpha subunit of the insulin receptor (IRα), insulin like growth factor receptor beta (IGF1-Rβ), protein kinase B (AKT) and the beta subunit of glycogen synthase kinase (GSK3β).

Overloading the cells with gangliosides and their precursors triggered a small but significant cell death. This was only observed in the absence of insulin treatment and at the highest CBE concentrations. Insulin challenge showed that CBE did not significantly alter IRα, however IGF1-Rβ levels increased significantly from the baseline. This may potentially lead to an overload of the intracellular signaling network, what is observed at 10 µM as a twofold increase in AKT phosphorylation at serine 473 and drop in GSK3β phosphorylation on serine 21. The accumulation of gangliosides and their precursors in cells can have altering effect on insulin signaling network by activating it via the IGF1 receptor.

PP8

SEX-SPECIFIC RESPONSE TO KETOGENIC DIET IN C57BL/6N MICE

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The antiepileptic ketogenic diet, which had fallen into oblivion, has recently returned to medical practice. Its effects are being studied in the treatment of obesity, diabetes, mental disorders and neurodegenerative diseases. The response to fats is personalized. We investigated whether the response to the ketogenic diet is also gender-specific. C57Bl/6N mice were divided into 2 groups: experimental (KD; 9 males (M) and 7 females (F)) and control groups (SD; 10 males (M) and 10 females (F)). The 12-week-old mice were put on a diet and sacrificed after 12 weeks of feeding. Altromin produced both SD (cat. no. 1324) and KD (cat. no. C1084) diets. KD contained coconut fat, coconut oil and soybean oil. The body weight of the mice was measured weekly. The research was ethically approved by the Ministry of Agriculture (CLASS: UP/I-322-01/22-01/22, REGISTRY NO: 525-09/566-22-4, October 31, 2022). Preliminary results show that the response to the diet is gender-specific. KD-M showed a statistically significant increase in body weight after the second and KD-F after the fourth week of the diet. At the end, the difference in body weight between the KD and SD groups continued to increase. At the same time, the body weight of the SD groups did not increase until the end of the study. We conclude that females are more resistant to KD than males, and we hypothesize that the basis of weight gain in both groups is ketonemia-induced insulin resistance in the satiety centers.

PP9

PHOSPHORYLATED TAU PROTEIN EXPRESSION FOLLOWING INOCULATION OF HUMAN TAU OLIGOMERS AND SYNTHETIC TAU FIBRILS INTO THE RAT MEDIAL ENTORHINAL CORTEX

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The AD tauopathy is first observed in the brainstem and entorhinal cortex before spreading trans-synaptically along specific pathways to other brain regions. In this study, 3–4-month-old wild-type rats were used to determine if different variants of human tau protein induce comparable neurofibrillary changes and propagate in an AD-related pattern. Following inoculation of human tau oligomers and synthetic tau fibrils via stereotaxic injection into the rat medial entorhinal cortex, we measured levels of tau phosphorylated at Ser202 and Thr205 (AT8), Ser396 and Ser404 (PHF1), Ser202 (CP13), and Thr212 and Ser214 (AT100) throughout the central nervous system in samples taken 4, 8, and 11 months after the inoculation. Inoculation of tau oligomers increased the levels of tau protein phosphorylated at AT100 in the hippocampus at the 4-month time point. Inoculation of synthetic tau fibrils increased the levels of tau protein phosphorylated at PHF1 and AT8 at the 11-month time point in the hippocampus, indicating simultaneous phosphorylation of these two epitopes. Understanding the behavior of tau proteins in this rat model of neurodegeneration has the potential to reveal mechanisms underlying the development and progression of AD tauopathy, contributing to future preclinical testing and drug development.

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PP10

EFFECT OF FETAL BOVINE SERUM OR BASIC FIBROBLAST GROWTH FACTOR ON TUBB3 AND SOX2 PROTEIN EXPRESSION IN NEURAL STEM CELLS: THE INFLUENCE OF HOMOCYSTEINE TREATMENT

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In vitro cell culture is a routinely used method which is also applied for in vitro modeling of various neurological diseases. On the other hand, media used for cell culture are often not strictly standardized between laboratories, which hinders the comparison of the obtained results. Here, we compared the effects of homocysteine (Hcy), a molecule involved in neurodegeneration, on immature cells of the nervous system cultivated in basal medium or media supplemented by either fetal bovine serum or basic fibroblast growth factor. We also found that the neuron-specific β-3-tubulin protein expression dose dependently decreased with increasing Hcy exposure. Interestingly, bFGF exerts a protective effect on β-3-tubulin protein expression at a concentration of 1000 µM Hcy compared to FBS-treated neural stem cells on Day 7. Supplementation with bFGF increased SOX2 protein expression two-fold compared to FBS supplementation. One of the possible reasons for dose-dependent reduction in β-3-tubulin with increasing Hcy concentrations is based on deleterious posttranslational modifications of β-3-tubulin protein, which could in turn lead to its conformational instability and faster protein degradation through the proteasome.

PP11

GLUCOSE-DEPRIVED CELLS RETAIN THE ABILITY TO MEDIATE PROTEIN QUALITY CONTROL VIA SELECTIVE DEGRADATION OF MISFOLDED PROTEINS

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Accumulation of misfolded proteins is implicated in age-related neurodegenerative diseases like Alzheimer's and Parkinson's. To prevent harmful effects of misfolded proteins, cells rely on highly conserved protein quality control (PQC) pathways, including ATP-dependent protein degradation by the ubiquitin-proteasome system (UPS) and protein sequestration into specialized quality-control compartments. Earlier studies of PQC mainly focused on actively dividing cells in rich media, however little has been known about PQC in non-dividing cells and in cells encountering glucose deprivation. Using the yeast *S. cerevisiae* as a eukaryotic cell model, we studied PQC in cells subjected to two distinct conditions: acute glucose depletion, a state accompanied by a sudden ATP decrease, and gradual glucose exhaustion, leading to quiescence, a non-dividing state characterized by distinct cellular organization and metabolism. To investigate how cells encountering an acute glucose depletion deal with the misfolded proteins, we grew the cells expressing misfolded proteins tGnd1 and stGnd1 in a rich medium and transferred them to the low-glucose medium. We examined the stability of the model misfolded proteins and observed that cells subject to acute glucose depletion selectively degrade them by the proteasome. Similarly, in yeast cells that were cultured for several days without media replenishment, which leads to gradual glucose exhaustion, we observed that misfolded variants tGnd1 and stGnd1 had a short half-life compared to wild-type Gnd1, indicating selective protein degradation. Furthermore, we showed that E3 ligases Ubr1 and San1 were essential for the degradation of tGnd1 and stGnd1 in quiescent cells, similar to their role in proliferating cells. Overall, our results indicate that quiescent yeast cells have a functional PQC that targets misfolded proteins for selective degradation. Moreover, despite decreased ATP levels during an acute glucose depletion, cells maintain a degradation-mediated PQC, indicating the importance of misfolded protein elimination.

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PP12

NEUROTOXIC EFFECT OF MYRICITRIN IN COPPER-INDUCED OXIDATIVE STRESS

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Oxidative stress (OS) is one of the major pathological mechanisms contributing to synaptic degeneration and functional impairment in neurodegenerative diseases. The aim of our study was to investigate the effects of the flavonoid myricitrin on copper-induced oxidative injury in neuroblastoma SH-SY5Y cells. In a concentration-dependent manner, myricitrin exacerbated toxic effects of copper. It reduced the viability of SH-SY5Y cells by promoting the production of reactive oxygen species, resulting in a marked depletion of ATP and glutathione levels. The pro-oxidant effect of myricitrin was also demonstrated by the reduced activity of aconitase and superoxide dismutase. Cell death induced by myricitrin in the presence of excess copper resulted from both apoptotic and necrotic processes: myricitrin promoted caspase-3/7 activation and DNA condensation and increased the number of cell nuclei stained with propidium iodide. Using a pharmacological approach, we investigated the activation of signalling pathways involved in cell death/survival and OS response. Selective inhibitors of ERK1/2, JNK, and p38 kinases, as well as p53 and PARP-1, did not alter the toxic effects of myricitrin. However, the deleterious effects of myricitrin were attenuated by BAPTA-AM, a selective chelator of intracellular Ca^{2+} stores, and MK-801, a selective NMDA receptor antagonist, indicating the important role of glutamate receptors and intracellular Ca^{2+} ions in triggering cell death. The results obtained suggest that strong antioxidants may act as prooxidants in the presence of excess copper. Therefore, caution is required when flavonoids from the flavonols group are considered as supportive therapy in diseases with disturbed copper homeostasis and redox imbalance.

PP13

THE POSSIBLE ROLE OF BRADYKININ RECEPTOR TYPE 2 IN CEREBRAL GLUCOSE METABOLISM

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Introduction: Bradykinin (BK) is a vasoactive peptide with a proinflammatory role. However, it was shown that by binding to bradykinin receptor type 2 (B2R), it regulates the glucose transporter expression and activity in different organs and tissues. As its impact in cerebral glucose metabolism remains unknown, the aim of this study was to determine whether B2R deficiency affects murine cerebral glucose uptake and the expression of glucose transporters and insulin receptor.

Materials and methods: Five months old male C57BL/6J (WT, n=22) and C57BL/6J/Bdkrb2$^{tm1J^{fh/SmiJ}}$ (B2R-KO, n=22) mice were subjected to blood glucose measurements followed by intraperitoneal tolerance tests. First cohort (n=8 per group) was subjected to optical *in vivo* monitoring of cerebral glucose uptake and *ex vivo* brain imaging using IVIS Spectrum system. From the second cohort (n=4 per group), mRNA expression was assessed with qPCR.

Results: Preliminary results show that B2R deficiency leads to higher basal ($p=0.003$) and fasting ($p=0.008$) blood glucose in B2R-KO mice compared to controls but has no effect on intraperitoneal tolerance of glucose and insulin. *In vivo* optical imaging showed increased cerebral glucose uptake in the first 10 minutes in B2R-KO mice compared to controls ($p<0.001$). However, *ex vivo* imaging showed no difference between groups. Moreover, B2R-KO mice had higher expression of *glut3* ($p=0.02$) and *irs-1* ($p=0.01$) compared to WT mice.

Conclusion: Initial findings indicate that B2R influences early kinetics of cerebral glucose uptake without altering total brain glucose uptake. Additionally, B2R-deficient mice exhibited elevated *glut3* expression, implying its potential role in cerebral glucose metabolism.

PP14

TEMPORAL IMPACT OF MPTP-INDUCED DOPAMINERGIC DYSFUNCTION ON LOCOMOTION AND DOPAMINE LEVELS IN A MOUSE MODEL OF PARKINSON'S DISEASE

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Many mouse models of Parkinson's disease exist as a means of capturing various aspects of the human neurodegenerative disorder. One example is the MPTP model, which involves the administration of 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine (MPTP) to selectively destroy nigrostriatal neurons, therefore recapitulating a major condition of the disease. MPTP-treated mice don't demonstrate an overt phenotype, but do have significantly reduced dopamine levels as a result of nigrostriatal neuronal damage. The aim of this experiment was to investigate how duration of time post-MPTP administration impacts locomotor activity and dopamine bioavailability.

During this investigation we conducted behavioural tests and analysed dopamine levels in the brains of mice at 3 timepoints: 1 week, 2 weeks and 3 weeks post-MPTP administration. 1 day prior to sacrifice, mouse locomotion was tested using an open field paradigm. A stimulant drug (amphetamine) was administered after an initial testing period in order to probe the motor system, and to highlight differences between each of the groups. High-performance liquid chromatography (HPLC) analyses later provided results of relative dopamine levels between the MPTP-treated groups, and a saline-treated control.

Here, we present the results of the open-field test and HPLC analysis. While MPTP treatment alone is insufficient to induce an overt motor phenotype, the stressing of the system using amphetamine allows us to probe differences between each of the temporally-different groups. While it is expected that MPTP-treated mice will have a reduced hyperlocomotion profile relative to control, it is not known to which degree the amount of time post MPTP-treatment will have an impact.

PP15

THE EFFECT OF TAU PROTEIN EXPRESSION ON NEUROLIGIN-1-MEDIATED SYNAPTIC PLASTICITY IN A CELL MODEL OF ALZHEIMER'S DISEASE

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Introduction: Recent evidence suggests a potential role for neuroligin-1 (NLGN1), a key player in synaptic plasticity processes, during the initial stages of Alzheimer's disease (AD) in the hippocampus. Despite overlapping mechanisms, the pathological influence of Tau on NLGN1 has not yet been investigated. The aim of this work is to explore whether there is a direct relationship between the change in Tau and NLGN1 expression.

Materials and methods: Mouse hippocampal neurons (P0-2) were transduced for Tau overexpression (hTau40) and control, respectively. The cells were harvested on day 12 for evaluation of NLGN1, total Tau (tTau), phosphorylated Tau (pTau) Ser262, pTau Ser396 levels by western blot and immunocytochemistry. SH-SY5Y cells were transfected with NLGN1 and hTau40 isoform 2N4R followed by glycine and bicuculine-mediated activation of glutamate receptors for live-cell imaging evaluation. Kruskal-Wallis was used for multiple comparisons followed by Dunn's post-hoc analysis.

Results: A clear attenuation of NLGN1 signal was detected in hTau40 group (-63%, $p<0.001$). A rise in p/t Tau Ser262 was detected in hTau40 (+92%, $p<0.01$), but without significant changes in p/t Tau Ser396, might indicate a role of calcium/calmodulin-dependent kinase 2 as a potential link between Tau and NLGN1. Stimulation of glutamate receptors did not yield any signal in neither of the triple-transfected SH-SY5Y cells indicating a missing link for adequate NLGN1 activation.

Conclusion: This pilot study implies that the overexpression of Tau protein and phosphorylation at Ser262 are related to disruption in NLGN1 levels in hippocampal neurons, providing valuable insight into their potential roles and interaction in early AD pathogenesis.

PP16

STEREOSPESIFIC EFFECT OF P4 INHIBITORS: DISSRUPTION IN GANGLIOSIDES SYNTHESIS SHIFTS GM1 GANGLIOSIDES AND IGF1 RECEPTOR FROM LIPID RAFTS IN HUMAN NEUROBLASTOMA CELLS SH-SY5Y

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Gangliosides - vital cell surface molecules along with other sphingolipids, form lipid rafts when their glycan structures and ceramide anchors drive lateral associations within the membrane. These gangliosides serve as markers for lipid rafts, with others dispersed in the membrane, offering diverse functions.

In an experimental context, SH-SY5Y human neuroblastoma cells underwent differentiation via retinoic acid treatment and were subsequently exposed to three different concentrations: 40μM, 10μM, and 2.5μM of two isoforms of P4 inhibitors targeting ganglioside synthesis. After inhibition cells were exposed to 2mM of insulin to explore ganglioside overload on the insulin signaling pathway. To assess the impact, a series of assays were conducted, including the MTT assay to gauge cytotoxicity, cell viability, and cell proliferation, alongside Annexin V staining to detect apoptotic processes.

The treatment with P4 inhibitors was observed to induce cell death, with an exacerbation of this effect upon the addition of insulin, presumably through mitochondrial damage. Immunocytochemical staining further unveiled stereospecific effects of the P4 inhibitor isoforms, resulting in the redistribution of βAPP and impairing its proper metabolism, leading to long-term cellular damage. Additionally, the disruption of ganglioside synthesis caused the GM1 ganglioside and the IGF1 receptor to shift to non-raft regions of the cell membrane.

PP17

TISSUE CLEARING PROCEDURES FOR PREPARING TRANSPARENT BRAIN SECTIONS AND VISUALIZATION OF FLUORESCENT STRUCTURES WITH VARIOUS TECHNIQUES INCLUDING LIGHT SHEET AND CONFOCAL MICROSCOPY

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Whole organs of laboratory animals can be visualized using light sheet fluorescence microscopy. Tissue clearing procedures are used for achieving transparency of big samples. The main aim of this research was to verify if the clearing procedures can be beneficial even if "classical" fluorescent microscopes were used. LEL Texas Red (Invitrogen) dye was used for blood vessels visualization which was injected in the left heart ventricle prior perfusion. Mice (which naturally produce yellow fluorescent protein in neurons, THY1-YFP) were perfused with 1× PBS and 4 % formalin solution, brains were isolated and cleared. For brain tissue clearing, three methods were used: ECi, PEGASOS and FluoClearBABB. Cleared mouse brain samples were cut on 1 mm thick slices using mold and imaged using inverted fluorescence microscope (The EVOS, ThermoFisher Scientific) and confocal microscope (Olypus FV3000). Additionally, antibody labeling method was used for neuron visualization (NeuN Antibody Vio®R667), for clearing MACS Clearing Kit (Miltenyi Biotec) and imaged using light sheet fluorescence microscope (Ultramicroscope II, LaVision Biotec). PEGASOS and FluoClear BABB methods were preferred for their YFP signal preservation. Method with primary conjugated antibody showed strong signal in neurons and good penetration into deeper parts of mouse brain. Even without using light sheet fluorescence microscopy (LSFM), it was possible to visualize neurons and fluorescently labelled blood vessels in thick samples. In conclusion, the clearing of mouse brain produces thick slices suitable as well for imaging and analysis by fluorescence microscopy.

PP18

THE EFFECTS OF METHYLPHENIDATE ON COGNITION AND HOME-CAGE LOCOMOTOR ACTIVITY IN A RAT MODEL OF SPORADIC ALZHEIMER'S DISEASE

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An Attention Deficit Hyperactivity Disorder (ADHD)-like phenotype may be a risk factor for later development of Alzheimer's disease (AD), and some clinical AD studies show a potentially beneficial effect of methylphenidate (MPH) treatment. We aimed to investigate the effect of oral MPH on circadian locomotor activity and cognitive performance in a streptozotocin-induced rat model of AD (STZ).

Three-month old male Wistar rats (n=40) were injected intracerebroventricularly with citrate buffer (control/CTR) or STZ (3 mg/kg) split in two doses 48 hours apart after which the MPH therapy was initiated daily in a dual-bottle dosage regimen (4 and 10 mg/kg) for 6 weeks to half of CTR and STZ groups. Baseline and 6-week continuous measurements of home cage locomotor activity and cognitive performance were performed using two custom-made home cage devices: the Multicage InfraRed Open Source Locomotor Activity eValuator (MIROSLAV), and an operant conditioning task (VlaDiSlav), respectively.

Throughout the experiment, the locomotor activity of the STZ group was high compared to its baseline and CTR values, particularly during the dark phase. MPH treatment reduced the activity in the STZ+MPH group to the values similar to its baseline measurements. VlaDiSlav learning curves showed a diminished learning rate in STZ group, however, STZ+MPH learning rate was similar to the CTR values.

MIROSLAV and VlaDiSlav continuous measurements suggest that STZ induces a severe learning and activity disorder which both may be ameliorated by MPH treatment, providing further evidence towards a link between AD-ADHD symptomatology, as well as MPH as a potentially effective AD treatment.

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PP19

LIGHT SHEET FLUORESCENCE MICROSCOPY REVEALS THE SPATIAL ARRANGEMENTS OF THE NEURONS AND BLOOD VESSELS IN THE MOUSE BRAIN

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Fluorescence microscopy, especially light sheet fluorescence microscopy (LSFM), revolutionizes the visualization of intricate structures in scientific fields like neuroscience. This study aimed to fluorescently label neurons and blood vessels in the entire mouse brain using LSFM. Thy1-YFP-16 mice expressing yellow fluorescent protein in neurons were utilized, and Lycopersicon Esculentum Lectin Texas Red was administered for blood vessel visualization. Two clearing methods, ECi and iDISCO+, were employed for optimal results. ECi, with a one-day protocol, is recommended due to its efficiency, while iDISCO+ proved superior in visualizing neurons.

The ECi method facilitated good blood vessel visualization, while iDISCO+, utilizing antibody labeling, excelled in visualizing neurons. Ultramicroscope II captured the images. Despite longer durations and the use of more toxic chemicals, iDISCO+ remains the best for neurons, although visualizing both neurons and blood vessels simultaneously is challenging. Such visualization could monitor events and morphological recovery in the mouse brain after ischemic stroke.

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PP20

GLYCANS AND NEURODEGENERATION

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Parkinson's disease and atypical parkinsonism (Progressive supranuclear palsy, Multiple system atrophy, Corticobasal degeneration and Dementia with Lewy body) are progressive neurodegenerative disease caused by pathological accumulation of proteins (alpha-synuclein and tau protein). The main goal of this study was to examine the association between the level of neurodegeneration measured with the radioisotope uptake in the caudate nucleus and putamen using the DaTSPECT method and MRI volume of the putamen with glycane state. Glycan are sugar component of immunoglobuline G that modify it`s activity to pro- or antiinflammatory.

Materials and methods: Twenty-nine patients diagnosed with Parkinson's disease or Atypical parkinsonism participated in the study. Data on patients' DaTSPECT and MRI results were collected from the patient registar. Glycans were analyzed in Genos laboratory. Three types of glycan were evaluate, mature, health and youth. Mature glycan is related to proinflammatory state and glycan of healts and youth to antimmflamatory state. This was a cross-sectional study with hystorical data.

Results: A negative correlation was observed between level of mature glycan and radioisotope uptake in the caudate nucleus and putamen and positive correlation was observed between glycan of youth and health with uptake in the caudate nucleus and putame. No significant association was observed between the MRI volumetry of the putamen and glycan values.

Conclusion: Higher maturity glycan values result in a greater degree of dopaminergic denervation, while reduced dopaminergic denervation was observed with higher values of health glycans and youth glycans.

PP21

RARE CASE OF GORDON HOLMES SYNDROME: A CASE REPORT

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Gordon Holmes syndrome (GHS) is an adult-onset heredodegenerative disorder characterized by cerebellar ataxia, hypogonadotropic hypogonadism, and dementia. It is inherited in an autosomal recessive manner. The main objective of this case report is to present a rare case of Gordon Holmes syndrome.

Case report:

A male patient in his thirties presented with the involuntary movements, speech impairment, behavioral abnormalities, and forgetfulness came to neurology department for a diagnostic work-up. Aside from relatives on his mother's side who had dyslexic speech issues, he had no relevant family history. The patient's parents weren't consanguineous. A neurological examination revealed orolingual dyskinesias, moderately severe hyperkinetic dysarthria with limb and truncal ataxia and choreatic movements. Additionally, dystonic postures on both hands and stereotypical head movements were noticed. Impairment in attention, concentration, memory, visuospatial abilities, abstract reasoning, and executive functions were identified during psychological testing. Magnetic resonance imaging of the brain showed pronounced leukoencephalopathy and generalized brain atrophy. Blood sample was sent for whole exome sequencing that identified a unique homozygous pathogenic mutation, RNF216 NM_207111.4:c.986G>A and diagnose of Gordon Holmes was established. The patient was treated with haloperidol.

The pathogenic variant of the RNF216 gene discovered in our patient is one of the few in the world that results in this clinical presentation of the disease.

PP22

OPTIC NEUROPATHY IN PATIENT WITH DEPRESSION TREATED WITH ANTIDEPRESSANTS: A CASE REPORT

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This abstract is about a 49-year-old patient who has been in psychiatric treatment for 10 years due to depressive affective disorder. In the first years of the disease, depressive episodes were treated with selective serotonin reuptake inhibitors (paroxetine and escitalopram), but in the last year, despite combined therapy with SSRIs and mirtazapine, symptomatology has not been relieved. Depressive mood persists, avolition, significant loss of TT, complete work and social dysfunction. It was decided to introduce a dual antidepressant (venlafaxine), to which the patient responded excellently and which is gradually titrated. Mirtazapine should be kept in therapy for the relief of insomnia. After three months, a stable remission of symptoms is achieved. In the sixth month of therapy with a combination of antidepressants (venlafaxine and mirtazapine), she goes for a routine examination by an ophthalmologist, where the development of optic neuropathy and the possibility that it is caused by psychotropic drugs are suspected. If optic neuropathy is not treated quickly, it might result in irreversible vision loss. It is an uncommon but potentially dangerous side effect of some regularly used antidepressants. The diagnostic abnormalities resembled those of glaucoma patients. However, in order to avoid irreversible vision loss in both situations, early diagnosis and effective treatment are essential. Clinical dilemma: to keep the existing antidepressant therapy, reduce it, or cancel it? The goal of the presentation is to point out the importance of a personalized and multidisciplinary approach to patients treated with psychopharmaceuticals.

PP23

CONSERVATIVE MANAGEMENT OF SIGNIFICANT SUPRATENTORIAL EPIDURAL HEMATOMA IN A CHILD: A CASE REPORT

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In general, epidural hematoma (EDH) is treated by craniotomy and evacuation of the hematoma. The authors present a rare case of conservative treatment of a significant supratentorial epidural hematoma in a 7-year-old boy. The patient was presented clinically with a mild headache, nausea and local swelling of the scalp, but without a neurologic deficit with Glasgow Coma Scale (GCS) of 15. Even as expected, the ophthalmological examination did not show papilledema upon admission to the hospital and after discharge. The brain computed tomography (CT) on admission to the hospital revealed left frontal EDH. Follow-up CT scans and magnetic resonance imaging (MRI) of the brain during the following 11 days after the head injury did not show expansion of the hematoma. This case illustrates how neuroplasticity in the growing brain is a major way that the neurological systems of infants and children differ from those of adults. Also, there is a possibility of conservative treatment of pediatric EDH in patients without neurological deficits, but with careful neurological observation, ophthalmological and neuroradiological follow-up.

PP24

NEW POSSIBILITIES IN TREATING POSTPARTUM DEPRESSION

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The postpartum period is one of the most challenging for maternal mental health, potentially marked by serious mental disorders, including postpartum depression (PPD). This disorder has been insufficiently clinically and experimentally studied, therefore mental health professionals do not know enough about it and it may be unrecognized diagnostically. Recently, neurobiological mechanisms involved in the development of this disorder have been studied more profoundly and new modalities of pharmacological treatment are being developed. Targeting GABAergic signalling in finding new therapeutic agents relies on the known actions of neurosteroids on the specific subtypes of GABA receptors, especially $GABA_A$ Rs including the δ subunit. Allopregnanolone is the neuroactive metabolite of progesterone, a neurosteroid with the ability to allosterically potentiate $GABA_A$ receptors. Treatment with a proprietary formulation of allopregnanolone, brexanolone, given intravenously, has demonstrated significant improvement of postpartum depression in a double-blind, randomised, placebo-controlled trial. It is the first FDA approved drug for this use. The formulation of the same drug called zuranolon made for oral use was approved by the FDA in August of 2023. We will look at the mechanism of action of these drugs, as well as at the potential side effects which ask for caution. To conclude, the advent of these drugs has made a major step forward in caring for maternal mental health in the postpartum period, and it is the duty of public health systems around the world to provide access to this treatment for those who really need it.

PP25

HIGH LEVELS OF ANXIETY, DEPRESSION AND STRESS SYMPTOMS AMONG STUDENTS AFTER THE COVID-19 PANDEMIC

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Introduction: Mental disorders pose a significant and pervasive public health challenge. Many mental disorders tend to peak in incidence during adolescence and early adulthood, with college students being at a heightened risk compared to their non-college peers. This study aims to assess the levels of depression, anxiety, and stress symptoms among students at the University of Osijek after the COVID-19 pandemic.

Materials and methods: This cross-sectional study was conducted in May 2023 using a questionnaire that examined sociodemographic characteristics and mental health status. Mental health was assessed using the validated Croatian version of the Depression, Anxiety, and Stress Scale (DASS-21), which comprises 21 questions related to describing the feelings a person has experienced in the past week. The study was approved by the Ethics Committee of the Faculty of Medicine Osijek.

Results: A total of 691 students participated in the survey, comprising 274 males and 417 females. The overall prevalence of depression, anxiety, and stress symptoms among university students was found to be 44%, 58%, and 39%, respectively. Additionally, it was determined that 13% students exhibited severe to extremely severe levels of depression symptoms, 25% displayed such levels of anxiety symptoms, and 14% had severe to extremely severe stress symptoms.

Conclusion: Following the end of the COVID-19 pandemic, high levels of depression, anxiety, and stress symptoms were identified among students. These findings highlight the urgent need for preventive measures and interventions to enhance the mental health of students.

PP26

EXOPHYTIC CAVERNOMA OF THE PONS – A CASE REPORT

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Cavernomas are vascular lesions in the brain or spinal cord which can potentially lead to neurological symptoms or bleeding.

A Caucasian man in his sixties was brought to the emergency department due to displaying limited movement of the extraocular muscles and facial asymmetry. Neurological evaluation revealed ipsilateral conjugate horizontal gaze palsy, an ipsilateral internuclear ophthalmoplegia and ipsilateral cranial nerve VII palsy. An MRI of the brain revealed a bleeding area in the pons, surrounded by swelling in the nearby tissue. As the patient's symptoms progressed, specifically in the form of convergence insufficiency, he was transferred to the Neurosurgery Department for surgery. To access the lesion located in the dorsal brainstem region, a surgical approach known as the telovelar approach was employed. The lesion had expanded significantly into the fourth ventricle, had an outward growth, and contained bleeding, resembling the characteristics of a cavernous malformation. During the surgery, the vascular lesion was opened, and the caverns within the lesion were coagulated to reduce its size, after which it was carefully separated from the brainstem. An intraoperative examination of the lesion's tissue confirmed the diagnosis of a cavernoma. The patient's recovery progressed without any complications, and there was no change in his neurological deficit.

Cavernomas, often asymptomatic, can cause seizures, headaches, or even more severe issues if they bleed or grow. When diagnosing a cavernoma, it is crucial to differentiate it from cerebral hemorrhage, arteriovenous malformations, hemangiomas, gliomas, cavernous sinus thrombosis, and migraine.

PP27

WHICH DISRUPTS SEXUAL FUNCTION MORE - DISEASE OR MEDICINES?

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It is known that psychiatric disorders are largely associated with increased or decreased sexual drive, which is further compromised by the use of necessary psychopharmacotherapy.
Obsessive - compulsive disorder (OCD) stands out as a very serious psychiatric disorder in which the sufferers' quality of life is compromised by constantly present obsessions and compulsions, and it almost always affects sexual life of the patient.
Following the above, we decided to present the case of our forty-year-old patient with a highly developed obsessive-compulsive disorder, which was most manifested by constant washing of the patient's body, up to thirty times a day in the worst phase. Unfortunately, he forced his wife do the same before and after sexual intercourse. Together they sought the help of the psychiatrist. The patient underwent four different SSRIs over a sufficiently long period of time, without effect, then the treatment was augmented with risperidone and olanzapine, with an equally bad treatment outcome. In the end, clomipramine was prescribed and the patient finally got rid of all the irritating symptoms, his sexual desire returned, but a new problem appeared - erectile dysfunction and delayed ejaculation.
In the end, the question arises - what hinders sexual function more? Is it possible to live with an untreated disease, but still be able to have sex, or is it better that the symptoms of the disease disappeared, but along with them the sexual drive as well? We are faithfully waiting for medicine to take the next step and help our patients.

PP28

ADULT-ONSET ADHD

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ADHD is a common neuropsychiatric disorder of neurodevelopmental etiology, whose global prevalence is between 5 and 7.2% among children and between 2.5 and 6.7% among adults.
The symptoms of ADHD are grouped in three domains: inattention, hyperactivity and impulsivity. Using neuroimaging methods, the differences in the subcortical brain volume in persons diagnosed with ADHD were shown, the most significant ones being reduced volume of the amygdala, accumbens and hippocampus, and bilateral reduction of the volume of the caudate and putamen. Such changes were observed in children, while they were not present in the group of adult-onset ADHD. Finding the most pronounced effects in childhood, while also showing what was described as delayed peaks of subcortical maturation goes to show that ADHD should be viewed as a disorder of brain maturation delay. Despite the extensively described changes, a specific biomarker of ADHD has not been found, and the diagnosis remains clinical, with the condition that some of the symptoms were present before the age of 12. Adult ADHD, while diagnosed, is still not sufficiently researched. The reason for the later appearance of symptoms is assumed to be the protective action of environmental factors or reduced environmental demands, which lead to a reduced manifestation of symptoms. Also, due to the same symptoms being present in ADHD and other mental and developmental disorders, the wrong diagnosis is often made.
In order to better understand this disorder, it is necessary to better investigate it in the adult population and to diagnose it correctly and in time.

PP29

PREVALENCE OF LIPIDOMIC CHANGES AMONG PATIENTS TREATED AT THE PSYCHIATRY CLINIC IN OSIJEK

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Background: Cholesterol is essential for normal brain function and development. The brain accounts for about 2% of total body weight, but it contains about 25% of cholesterol and cholesterol derivatives. As the blood-brain-barrier prevents cholesterol from entering the central nervous system from the rest of body, the brain fully relies on its own synthesis. Dysfunction of the sterol metabolism contributes to many psychiatric and neurodegenerative disorders. Cholesterol intermediates, such as lathosterol and desmosterol are considered better markers of endogenous cholesterol biosynthesis than cholesterol.

Methods: In order to gain an insight into cholesterol metabolism we designed a study to determine the levels of cholesterol intermediates in the blood samples from population of psychiatric patients. Participants were recruited for the study over a 6-month period from hospitalized patients at the Psychiatry Clinic in Osijek. Patients underwent a comprehensive clinical psychiatric examination, accompanied by a questionnaire designed specifically for this research. Blood samples were collected from the patients into serum tubes, and these samples were analyzed by LC-MS/MS.

Results: From the collected results through the implementation of the $\chi 2$ test and Fisher's exact test, elevated oxysterol(7DHC) levels were identified in 21.5% of patients (N=205), predominantly among those treated under the diagnosis of psychotic disorders.
Despite clinical expectations and the assumption that the treatment of psychiatric disorders exposes the organism to increased lipid peroxidation, resulting in anticipated elevation of oxysterol levels, the obtained results indicate that oxysterol levels are specific to the diagnostic category of patients and may be influenced by the therapy administered. Therefore, it is imperative to expand the sample size and conduct a more detailed analysis concerning the psychopharmacological agents used in patient treatment, in order to potentially identify a chronological sequence of earlier onset of psychorganic changes in patients treated with particular groups of psychopharmacological medications.

PP30

cBioPortal *IN SILICO* ANALYSIS REVEALED MARKERS OF EPITHELIAL-TO-MESENCHYMAL TRANSITION IN GLIOMAS

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The aim of this investigation was to analyze and interpret data on mutations, amplifications and deletions of major genes involved in epithelial-to-mesenchymal transition (EMT) and associate their frequency with low-grade (LGG) and high-grade (HGG) gliomas.
We retrospectively collected data on 13 selected genes in gliomas of different pathohistological types and malignancy grades using the cBioPortal database (https://www.cbioportal.org/, accessed May 2023)—a publicly available database for tumor genomics and transcriptomics. The following genes were selected: *CDH1, CDH2, CTNNB1, LEF1, NOTCH1, SNAI1, SNAI2, SOX2, TJP1/ZO-1, TWIST1, VIM, ZEB1* and *ZEB2*. The analysis included mutations of individual genes, changes in the copy number alteration (CNA) and transcript levels (mRNA).
The research processed data from 3497 samples. Only glioblastoma and diffuse glioma had changes in all 13 analyzed genes. Anaplastic oligodendroglioma and anaplastic astrocytoma showed changes in 46.15% of the analyzed genes, oligodendroglioma in 23.08% and oligoastrocytoma in 15.38%. *NOTCH1* gene was statistically more frequently changed compared to the *CDH1, CTNNB1* and *ZEB1* genes ($p < 0,05$). The virtual study showed that mutations in *NOTCH1* and *LEF1* were associated to LGG, while mutations in *CDH1, CTNNB1, TJP1, TWIST1, SOX2, VIM, ZEB1* and *ZEB2* to HGG.
Our study shows consistent changes of genes involved in EMT in gliomas of different grades. The most frequently mutated and amplified genes were *NOTCH1* and *SOX2*. Additional research and validation of the results from the cBioPortal database are needed to confirm the knowledge brought by this study.

PP31

WHAT ARE WE MISSING WITH GLIOBLASTOMA – A METABOLIC PERSPECTIVE

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Glioblastoma (GBM) is the most common and aggressive primary malignancy of the central nervous system (CNS), accounting for almost half of all malignant tumors of the CNS. Despite significant scientific and clinical efforts, outcomes are poor with the median survival of patients with GBM being approximately 14 months. GBM occurrence has been linked to advanced age, high socioeconomic status, exposure to ionizing radiation, whereas female sex hormones, allergy history, and frequent use of particular drugs may have protective effects. The classification of tumors of the CNS, prior to 2016, was based solely on pathohistology of the tumor. However, a paradigm shift took place in 2016 as a result of molecular and genetic analyses of these neoplasms. This was extended upon in the 5th Edition of the WHO classification of CNS tumors, which was published in 2021. First-line treatment consists of maximal surgical resection of the tumor, followed by radiotherapy and chemotherapy. In vitro tests on a number of substances have yielded encouraging results, which are yet to be replicated in individuals with GBM. Understanding genetic peculiarities of GBM cells is crucial for treatment, however it does not provide enough details about their phenotype and metabolic profile. The metabolome of a tissue may be extensively studied using a variety of techniques. Imaging mass spectrometry (IMS) maintains the structural integrity of the sample, while determining the spatial distribution of biomolecules. Metabolomic studies have considerably improved our knowledge, as well as diagnostics and treatment of many tumors and should be utilized for GBM.

PP32

CORRELATION OF SPHINGOID BASES CONTENT IN GLIOMAS WITH DIFFERENT PROLIFERATIVE INDEX

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Background: Gliomas are the most prevalent primary brain tumors. Sphingolipid metabolites and phosphorylated sphingoid bases (S1Ps) are involved in the pathogenesis of gliomas. The aim of this study was to analyse and compare the content of sphingosine (d18:1), sphinganine (d18:0), d18:1-P and d18:0-P in diffuse astrocytoma (grade 2) and glioblastoma multiforme (GBM, grade 4) tissue samples, corresponding peritumoral tissues (PTs), patients' serums (PSs) and healthy control serums (HSs) using liquid chromatography/mass spectrometry (LC/MS) profiling.

Methods: Free sphingoid bases d18:1, d18:0, d18:1-P and d18:0-P were extracted and purified from the tissue homogenates and serums by Sullards et al. [1] modified method. Samples were analysed by Agilent 6550 iFunnel Q-TOF LC/MS by MRM analysis using d14:1 as internal standard.

Results: d18:1 content in all glioma tissues was higher than in corresponding PTs. d18:1 content was significantly higher in HSs than in PSs. d18:1-P was present in all tissue samples in very low concentrations, while quantified in HSs in significantly higher concentrations than in PSs. d18:0-P was quantified only in serum samples with approximately 20 times higher concentrations in PSs than in HSs, while it was not detected in tissue samples. The concentrations of d18:0-P in PSs correlated with the malignancy grade of the glioma type, with the diffuse astrocytoma serum having lower concentration of d18:0-P than GBM.

Conclusions: The difference in d18:1 content in glioma tissue vs. peritumoral tissue was higher for GBM than for diffuse astrocytoma. d18:0-P concentrations in PSs corresponded to the malignancy grade and were significantly higher than in HSs, suggesting potential role as a glioma-associated serum marker.

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PP33

COLLABORATIVE EFFECT OF NOTCH1, NOTCH2 AND BETA-CATENIN IN MENINGIOMA PROGRESSION

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Notch is one of the leading signaling pathways in the development of the central nervous system. Aberrations in regulation of its main molecular actors could pose a threat of developing brain tumors such as meningiomas. Meningioma progression to malignant form usually has a poor prognosis and outcome for patients. Detecting leading molecular actors of meningioma progression could help setting an effective diagnosis and treatment. In this study NOTCH1 and NOTCH2 were analyzed on forty-six formalin-fixed paraffin-embedded sections of human meningioma tissue with different grades. Most prominent result was nuclear translocation of NOTCH1 and NOTCH2 in more than 90% of tumor samples, which was absent in healthy brain tissue from cortex, indicating activation of Notch signaling pathway and its involvement in transcription of targeted genes. These results were correlated with activation of beta-catenin, a central molecule of Wnt signaling pathway, which has a similar role in transcription as NOTCH1 and NOTCH2. Only 26% of samples harbored nuclear expression of active beta-catenin and this result was related to atypical meningioma (p=0,002). In 50% of samples that had nuclear expression of active beta-catenin, NOTCH intracellular domain was weak. To determine the role of NOTCH2, a methylation of its promoter site was tested and was distinctive to atypical meningioma (p=0,000). Our results suggest Notch as early leading process in meningioma development, activated before Wnt signaling which is more pronounced in later stages of meningioma progression.

PP34

EXPRESSION OF AGGRECAN IN THE ADULT HUMAN PREFRONTAL CORTEX

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Perineuronal nets (PNNs) are a specialized form of condensed extracellular matrix (ECM) found surrounding neuron cell bodies and their cellular processes. PNNs are composed of tenascins, link proteins, hyaluronan, and lecticans – a family of proteoglycans that includes aggrecan (AGG). Lecticans have a central domain to which glycosaminoglycan side chains are bound, which can be visualized using *Wisteria floribunda* agglutin (WFA).

We performed qualitative analysis of AGG expression in the adult human prefrontal cortex (PFC) in Brodmann areas 9 and 24 using double and triple labelling immunofluorescence. On double-labeled histological slides, the anti-AGG antibody was combined with anti-calretinin (CR), anti-parvalbumin (PV), and anti-somatostatin (SOM) antibodies. On triple-labeled slides, the anti-AGG antibody was combined with an anti-NeuN antibody and WFA.

Our analysis revealed no apparent differences between the analyzed cortical regions. AGG^+ PNNs were present in all cortical layers, except in layer I. AGG^+ PNNs were mostly found surrounding circular and slightly elongated neurons. Analysis of double-labeled slides revealed that a subpopulation of PV^+ neurons was surrounded by AGG^+ PNNs. We found no evidence of substantial AGG/CR or AGG/SOM co-localization. Analysis of triple-labeled slides revealed the presence of AGG/WFA colocalization, predominantly in layer III. Besides neurons surrounded by AGG^+/WFA^+ PNNs, we found neurons surrounded only by AGG^+ PNNs and neurons surrounded only by WFA^+ PNNs.

In conclusion, AGG^+ PNNs surround a specific subset of cortical neurons in layers II – VI, which includes PV^+ neurons. This suggests that AGG^+ PNNs are involved in highly specific microcircuits of the human cerebral cortex.

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PP35

MORPHOMETRIC ANALYSIS OF GABAERGIC INTERNEURON POPULATIONS IN THE HUMAN PREFRONTAL CORTEX

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GABAergic interneurons play a key role in the function of microcircuits. In the human prefrontal cortex (PFC), almost all GABAergic interneurons can be visualized using four molecular markers: calretinin (CR), parvalbumin (PV), calbindin (CB) and somatostatin (SOM).
We performed morphometric analysis of these interneuron populations in Brodmann areas 9 and 14r of five adult human male specimens. We used double labeling immunofluorescence, combining each interneuron marker with anti-NeuN staining. We selected interneuron cell bodies for manual reconstruction if their entire cell bodies and the most proximal parts of the cellular processes were visible. We analyzed the following morphometric parameters: cell body area, aspect ratio and roundness. We reconstructed a total of 511 CR^+, 359 PV^+, 216 CB^+ and 552 SOM^+ neuron cell bodies. Our analysis found no substantial differences in morphometric parameters between the two analyzed cortical regions. However, morphometric parameters differed between interneuron populations. On average, PV^+ cells had the largest cell bodies (median: 141.50 μm^2), while CR^+ cell had the smallest cell bodies (median: 96.27 μm^2). PV^+ cells also had the largest roundness (0.70) and aspect ratio (0.74), while these parameters were smallest among SOM^+ cells (0.56 and 0.60 respectively), indicating that SOM^+ cells had the most elongated cell bodies.
Our data suggest that each interneuron population can be characterized by a specific morphometric profile. This shows that the major interneuron populations can be differentiated based on both molecular and morphological characteristics, implying that these populations could be involved in different functional microcircuits of the human PFC.

PP36

REORGANIZATION OF THE CORTICAL STRUCTURE IN THE RAT BRAIN AFTER MILD PERINATAL HYPOXIA: HISTOLOGICAL AND *IN VIVO* MRI MULTIMODAL STUDY

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Histological and immunohistochemical findings were cross-referenced intra-subject with multimodal *in vivo* magnetic resonance imaging (MRI) data to disclose possible developmental reorganization in cortical differentiation after the mild perinatal hypoxic event in the rat. A total of 28 Wistar Han (sexes equally represented) rats were subjected to either moderate hypoxia (8% O2, 92% N2/2h, n=14) or normoxia (21% O2, 79%N2/2h, n=14) on postnatal day one (P1), followed by increase blood lactate measurement. Structural and diffusion *in vivo* MRI was performed in 16 rats at age P15, and immediately after the rats were sacrificed, the brains were weighed and processed further for histological (Nissl modification of cresyl-violet staining) and immunohistochemical (Purified Anti-Neurofilament H (SMI-32) evaluation. A significant elevation in fractional anisotropy (FA) values was observed in the anterior cingulate cortex in rats that underwent hypoxia, which correlated well with the observed changes in cytoskeleton intermediate filament organization pattern revealed by SMI32 in the cingulate but also observed in the somatosensory cortex. No brain or body mass differences between hypoxic and control rats were detected at P15. However, MRI revealed regional brain volume changes, particularly an increased volume in the posterior sensory cortices and colliculi. The aforementioned gives additional data and further validation of our model of mild perinatal hypoxia. Further research will be focused on elucidating the molecular pathophysiological mechanisms of perinatal cortical reorganization and its clinical implications for developing new therapeutic strategies and MRI modalities for diagnostic purposes in perinatal medicine.

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PP37

INVESTIGATING EEG PATTERNS AND BRAIN DYNAMICS DURING PHYSICS PROBLEM SOLVING

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Previous studies indicate that students often retain naive, incorrect conceptions about fundamental physics concepts even after receiving instruction. The aim of this study was to compare electrical brain activity of participants who were more or less proficient in applying Newton's laws of motion. Participants were divided into two experimental groups (expert and naive) based on the results of previously conducted testing on understanding of Newtonian mechanics. The problems they solved were designed so that both groups had identical answers for certain problems while providing divergent responses to others. The brain activity of participants was recorded with a 61–channel EEG system with a sampling rate of 200 Hz, out of which the power spectral density (PSD) was derived using the Welch method and clustered afterwards. The naive group had increased beta- and gamma-band PSD activity when they encountered a situation that was not in accordance with naive reasoning. This activity implies additional effort and processing of the statements that are incongruent with their expectations. The expert group did not show a comparable activity. The expert group had stronger PSD activity in the alpha-band which could indicate that they were more relaxed while solving tasks with the application of Newton's laws. The participants did the NASA-TLX test for perceived workload afterwards and the results of the analysis are in agreement with the recorded PSD activity. In conclusion, this study reveals divergent EEG patterns between expert and naive groups, highlighting cognitive effort disparities and potential indicators of expertise in physics problem solving.

PP38

MEASURING OXYTOCIN IN A SPORT CONTEXT - SYSTEMATIC LITERATURE REVIEW

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Research on the sport-related characteristics of oxytocin (OT) is an evolving field. The purpose of this study is to map out, and then narrow down methods allowing reliable and repeated measuring of OT levels as well as the main factors influencing its secretion in a sports context. OT promotes social bonding and trust between teammates, leading to improved cognitive functions, cohesion, and cooperation during training and competition by affecting our psychophysiological state. Suppressing cortisol levels due to OT can help reduce stress and anxiety, it can also enhance performance and recovery due to its anti-inflammatory effect. The advantage of systematically uncovering, categorizing and classifying the potential secretion of OT and its measurement in sports is two-fold. Firstly, in psychology, sociology, pedagogy, and in the context of school bullying, OT may be useful as it influences pro-social behavior and empathy, potentially reducing aggressive tendencies and promoting positive social interactions. Secondly, our findings and analysis of the literature may contribute to therapeutic endeavors in endocrinology, neurology, and by exploring the specific characteristics and effects of OT in the sports environment.

PP39

STUDY OF CENTRAL NERVOUS SYSTEM DEVELOPMENT IN PRESCHOOL-AGED CHILDREN WITH OR WITHOUT SNI OR BTM STATUS USING JUDO SPORT

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This research aimed to assess the possible residual primitive reflexes, motoric, and cognitive status of children aged 4-7 years, as well as the beneficial effects of judo on the central nervous system. Our target group was judo athletes (n=58), and the control group was preschool children who did not practice judo (n=76). The survey was conducted in 2 countries, 3 cities between January and March 2023. We used the INPP (Institute for Neuro-Physiological Psychology) test. The neuromotor skills of the one (p=0.001) and two (p=0.025) years judo groups were significantly better than the control group. There were no differences between Slovak and Hungarian children in the control groups, only the visual perceptual test was significantly different (p=0.049). Judo children showed significantly different results between the two countries (p=0.013). There were compelling differences between the capital city, big city, and medium city for judo groups than for kindergarten groups (p=0.001). We hope that by analyzing sport through our research, we will be able to put together a physical activity program that can be used to develop children in public education institutions.

PP40

THE RELATIONSHIP BETWEEN DIGITAL MEDIA USAGE AND BURNOUT SYNDROME IN MEDICAL STUDENTS

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Objective: To investigate the relationship between the amount of time spent using digital media and the prevalence of burnout syndrome among medical students.
Methods: A total of 339 students from the University of Split School of Medicine and the University of Mostar School of Medicine, representing all 6 years of study, participated in this study. Among them, 73 were male, 263 female, and 3 students did not specify their gender. The questionnaire collected demographic and anthropometric information about the students, including the social networks they used and the amount of time they spent on these platforms. Additionally, the questionnaire assessed students' emotions, behaviors, habits, and attitudes concerning their use of social networks, as well as physical symptoms, emotional indicators, and behavioral changes characteristic of burnout syndrome.

Results: Students who used digital media for more than 3 h/day exhibited higher prevalence of burnout symptoms according to the used questionnaire compared to those using digital media for less than 3 h/day (40.1±21.4 *vs*. 28.6±18.7; P<0.001). Additionally, students who used digital media for more than 3 h/day more frequently reported feelings of fatigue and exhaustion (1.6±1.2 *vs*. 2.2±1.3; P<0.001), a lack of energy and motivation for daily activities (1.7±1.3 *vs*. 2.3±1.3; P<0.001), and a reduced need for social interactions (0.6±1.0 *vs*. 1.3±1.3; P<0.001), compared to students who used digital media for less than 3 h/day.

Conclusions: This study confirmed the significantly positive association between excessive digital media usage and the prevalence of burnout syndrome among medical students.

PP41

SCREENING TESTS FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: This study investigated the sensitivity and specificity of screening tests for obstructive sleep apnea (OSA), including STOP, STOP-BANG, Berlin Questionnaire, Brussels Questionnaire, and the Epworth Sleepiness Scale (ESS).

Methods: A total of 1,286 adult patients were included in the study. These patients were from the Sleep Medicine Center in Split and were referred for diagnosis due to suspected sleep disorders, most commonly OSA. Anthropometric, medical history, and polysomnography/polygraphy findings were used only in encrypted form from the digital database of the Sleep Medicine Center in Split.
Results: Out of the total number of subjects, 1,009 (78%) had OSA, while 277 (22%) did not. Among the OSA patients, 686 (85%) were men, and 323 (15%) were women. Patients with OSA had significantly greater average Apnea-Hypopnea Index (AHI) of 31.54 ± 24.74, compared with 2.21 ± 1.33 ($P<0.001$) in the control group. Additionally, the lowest oxygen saturation in patients with OSA was significantly lower than in controls (78.73 ± 13.90 *vs*. 90.31 ± 6.96) ($P<0.001$). The most common comorbidities were arterial hypertension in 436 (43.2%) of OSA patients and diabetes mellitus in 126 (12.5%). Screening tests with the highest sensitivity were STOP at 83.15% (AUC 0.69, $P<0.001$) and the Berlin questionnaire at 75.89% (AUC 0.69, $P<0.001$), whereas the tests with the highest specificity were STOP-BANG at 88.27% (AUC 0.72, $P<0.001$) and the Brussels questionnaire at 90.25% (AUC 0.59, $P<0.001$).

Conclusion: STOP and Berlin questionnaires exhibited the highest sensitivity for detecting the OSA patients in this study, whereas the highest specificity was observed in STOP-BANG and the Brussels questionnaire.

PP42

THE ASSOCIATION BETWEEN SOCIAL MEDIA USE AND SLEEP QUALITY IN MEDICAL STUDENTS

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Objective: The objective of this study was to investigate the relationship between social media usage and sleep quality among medical students.
Methods: This study included medical students from the University of Split School of Medicine and the University of Mostar School of Medicine. An online questionnaire was administered, comprising questions regarding the frequency and duration of social media usage, the Social Media Use Questionnaire (SMUQ), questions related to the significance of social media, and the Pittsburgh Sleep Quality Index (PSQI). Based on the SMUQ questionnaire, participants were categorized into two groups: those with an SMUQ score higher than ten (severe users) and those with a score lower than ten (moderate users).

Results: Severe users used almost all social networks more than moderate users. Most social media users with an SMUQ score greater than ten spent more than one hour on these platforms. Severe users went to bed later (24h 12min±1h 17min *vs*. 23h 45min±1h 6min, P<0.001), needed more time to fall asleep (21±19min *vs*. 16±14min, P=0.006), woke up later in the morning (7h 31min±1h 6min *vs*. 7h 12min±1h, P=0.006), and were more likely to experience daily symptoms (1.39±0.72 *vs*. 1.05±0.73, P<0.001) than moderate users. Subjective sleep quality was better among moderate users (7.29±2.01 *vs*. 7.88±2.10, respectively, P=0.010).

Conclusion: Medical students identified as severe users spent more time on social media and had worse sleep quality compared to moderate users. This highlights the importance of educating young individuals about the impact of social media on sleep quality.

PP43

DREAMS OF BLIND PEOPLE: A GRAPH THEORY APPROACH STUDY

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Descriptions of individuals' dreams (dream reports) could be represented as a graph with words as nodes and connections between words as edges. This approach was successfully used for identifying speech abnormalities in psychosis and other diseases, but to our best knowledge, this method was not applied to elucidating the specifics of blind subjects' dreams.

To investigate structural and semantic differences in the dream reports of blind people, the following dream reports were retrieved from the DreamBank database: 118 reports of congenitally blind individuals, 75 reports by late blind people, and 140 reposts by sighted controls. Dream reports were converted to structural and semantic graphs, and for each graph, 14 graph attributes and 4 spectral characteristics were calculated.

Overall, in comparison to the sighted controls group, graphs of dream reports by blind people had fewer nodes but higher connectivity in clusters of various sizes and a whole-graph level. In other words, both groups of blind subjects used less varied vocabulary for the description of their dreams, but these individuals referred to the same objects and conceptions more often, which reflects the prevalence of egocentric spatial representations. There were no significant differences between congenitally and late blind people in any case.

In conclusion, the principal specificity of dream reports by blind people is a relatively small number of highly connected ideas.

PP44

ESTIMATION OF SLEEP QUALITY AND SLEEP ARCHITECTURE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: The aim of this study was to investigate subjective assessment of sleep quality in patients with obstructive sleep apnea (OSA) using the Pittsburgh Sleep Quality Index (PSQI) and to compare it to objective parameters measured during whole-night polysomnography.
Methods: A total of 370 subjects (226 men) participated in the study. All subjects completed sleep questionnaires and underwent whole-night polysomnography. Parameters of sleep quality were compared between men and women, and between the good and poor sleepers defined according to PSQI.

Results: More men than women considered themselves good sleepers (65,84% vs 34,16%, P=0.039). Women obtained higher PSQI score (P=0.003), had longer sleep latency (P<0.001), more frequent sleep disturbances (P=0.010), and were taking sleep pharmacotherapy more often (P=0.050) according to the PSQI. Men had higher apnea-hypopnea index (AHI) (31.98±26.01 *vs.* 21.38±21.85, P<0.001), and lower proportion of N3 sleep stage (7.64±6.83% *vs.* 9.97±7.33%, P=0.002). The good sleepers had a shorter sleep latency (19.01±16.22min *vs.* 29.49±24.99min, P<0.001), slept longer (6.47±1.35h *vs.* 5.6±1.69h, P<0.001), and woke up earlier (6.55±1.31h *vs.* 6.82±1.47h, P=0.046) in comparison to bad sleepers.

Conclusion: Analysis of the PSQI sleep components suggests that women perceive their sleep quality as lower than men. On the other hand, men have higher AHI and a lower percentage of N3 stage when compared to women. Good sleepers have estimated that they fall asleep faster, sleep longer, and wake up earlier unlike the poor sleepers. However, polysomnographic parameters such as AHI, sleep duration, latency, and architecture were not significantly different between good and poor sleepers.

PP45

THE ASSOCIATION OF THE METABOLIC SYNDROME WITH THE WHOLE-NIGHT POLYSOMNOGRAPHY/POLYGRAPHY FINDINGS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Objective: The main objective of this study was to investigate the association between metabolic syndrome (MetS) and the results of the whole-night polysomnography/polygraphy (PSG/PG) in patients with obstructive sleep apnea (OSA).
Methods: A total of 2,219 patients were included in this cross-sectional retrospective study. These patients, referred for PSG/PG at the Split Sleep Medicine Centre from 2011 to 2022 due to suspicion of OSA, had their whole-night PSG/PG results, along with demographic, anthropometric, and medical history data, collected from the digital archive.

Results: Out of the total number of patients, 198 (8.92%) met the diagnostic criteria for MetS. Patients with MetS exhibited a higher Apnea-Hypopnea Index (AHI) (37.29±26.13 vs. 25.86±22.98, P<0.001), lower mean and lowest oxygen saturation values (P<0.001), and a longer time spent below 90% oxygen saturation (1 h 20 min±2 h 16 min vs. 33.6 min±1 h 13 min, P<0.001) compared to patients with only OSA. Additionally, patients with MetS had slightly shorter sleep durations (6 h 20 min±1 h 16 min vs. 6 h 22 min±1 h 15 min, P=0.026), significantly lower sleep efficiency (72.60±17.33% vs. 77.08±13.27%, P=0.025), and less rapid eye movement (REM) sleep (11.55±6.58% vs. 14.85±8.45%, P<0.001) compared to OSA patients without MetS.

Conclusion: Patients who have comorbid MetS and OSA displayed more severe OSA with pronounced desaturations during whole-night PSG/PG. Furthermore, patients with both MetS and OSA exhibited significantly impaired sleep architecture and efficiency compared to OSA patients without MetS.

PP46

HOMOIŌMA IN DREAMS OF CONGENITALLY BLIND

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REM sleep is a distinct sleep stage, characterised by rapid eye movement activity, low muscle tone and an increased propensity for vivid dreams. Importantly, REM sleep is crucial for visual cortex development (Hobson et al., 2009) and mental imagery (Foulkes, 1982). Eagleman and Vaughn (2021) posited that REM sleep circuitry amplifies the visual system's activity throughout the night and asserts predominance against other sensory inputs. From this, it could be inferred that one need visual perception to experience visual imagery, which does not seem to be the case in congenitally blind population (CBP). Indeed, it remains unclear to what extent the absence of vision or loss of vision affects the sensory and pictorial sensitivity for oneiric construction. Hence, in our study, we investigated the presence and nature of oneiric visuo-spatial impression by analysing 180 dreams of CBP from the DreamBank database using sensory content dream analysis. A higher presence of auditory, haptic, olfactory, and gustatory sensation in dreams of CBP was demonstrated, as compared to sighted controls. Additionally, oneiric visual imagery in reports of CBP was also noted, in opposition to previous studies. Results obtained here have significant implications, particularly in possible adaptive functional development of the occipitotemporal visual system in the absence of visual stimulation as well as elucidating the nature of oneiric experiences in CBP.

PP47

MEDICATION USE IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Aim: To examine the relationship between the severity of obstructive sleep apnea (OSA) measured by the Apnea-Hypopnea Index (AHI) or Oxygen Desaturation Index (ODI) and the number and types of medications used by patients, as well as to identify the most frequently prescribed medications for individuals with OSA.

Methods: A total of 2,219 patients participated in this cross-sectional retrospective study. Whole-night polysomnography or polygraphy was conducted at the Sleep Medicine Center Split from 2011 to 2022.

Results: Among patients without OSA, the proportion of women (56%) exceeded that of men (44%). The proportion of men increased with OSA severity ($P<0.001$) in the full sample. Patients without OSA had an average age of 46±14.5 years, while those with severe OSA were older, with an average age of 57±11.3 years ($P<0.001$). Arterial hypertension was the most common comorbidity, affecting 965 (43.5%) patients in the study. The most frequently used medications among all patients were those affecting the renin-angiotensin-aldosterone system, which were taken by 547 (24.7%) patients. Higher total number of medications taken was associated with increased OSA severity measured with AHI ($r=0.115$, $P<0.001$) and ODI ($r=0.120$, $P<0.001$). Additionally, there was a negative correlation between the number of medications taken and the mean arterial blood oxygen saturation ($r=-0.085$, $P<0.001$), as well as the lowest arterial blood oxygen saturation ($r=-0.149$, $P<0.001$).

Conclusions: Patients with more severe OSA exhibited a higher prevalence of comorbidities and a greater use of medications. The most common comorbidity was arterial hypertension, and the most commonly prescribed medications were antihypertensives affecting the renin-angiotensin-aldosterone system.

PP48

FINDINGS OF FULL-NIGHT POLYSOMNOGRAPHY/ POLYGRAPHY IN OVERLAP AND ALTERNATIVE OVERLAP SYNDROME

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Introduction: Obstructive sleep apnea (OSA) is the most common sleep breathing disorder. OSA can coexist with COPD and/or asthma, resulting in condition known as the overlap syndrome (OS) and an alternative overlap syndrome (AOS). The objectives of this study were to examine the findings of full-night polysomnography/polygraphy (PSG/PG) in patients with OS and AOS, investigate parameters related to blood oxygen saturation, and assess the severity of OSA using the AHI index. Additionally, we aimed to compare these findings with the patients who had OSA without aforementioned comorbidities.

Methods: Our study included 220 patients, including 22 having OS, 80 having AOS, and six suffering from OSA, COPD, and asthma concurrently. The remaining 112 patients comprised the control group, who had OSA alone. Full-night PSG/PG assessments were conducted on all patients at the Sleep Medicine Center of the University of Split School of Medicine and KBC Split.
Results: Patients with OS exhibited significantly lower mean oxygen saturation (91.88±3.92%, P=0.006) and spent more time with saturation levels below 90% (157.57±170.66 minutes) compared to the control group (93.95±2.46%, 41.97±82.07 minutes, P=0.008). However, there were no statistically significant differences in AHI, ODI, or lowest oxygen saturation levels between the groups.

Conclusion: In summary, patients with OS demonstrated lower oxygen saturation levels and spent more time with saturation below 90% compared to the control group. Their PSG/PG results were less favorable when compared to the group of patients with AOS.

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ADHERENCE TO THERAPY WITH POSITIVE AIRWAY PRESSURE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Objective: This study investigated the adherence to Positive Airway Pressure (PAP) therapy among severe Obstructive Sleep Apnea (OSA) patients and its impact on their quality of life and daytime sleepiness.

Methods: We enrolled 88 severe OSA patients (68 men) between October 2022 and June 2023, who underwent overnight polysomnography or polygraphy (PSG/PG) due to suspected OSA. Data were collected through questionnaires completed either at home or at the Split Center for Sleep Medicine and by accessing the center's digital database, which provided anthropometric, medical history, and polysomnography data.

Results: Women were significantly older than men, with average age of 62.35±10.47 years compared to 53.25±12.39 years in men (P=0.002). At the time of diagnosis, the mean apnea-hypopnea index (AHI) was 50.66±19.08, and the oxygen desaturation index (ODI) was 51.13±2.74. After one month of PAP therapy, patients averaged 88.2±17.7% usage for over four hours a day on 70.1±28.6% of days, with an average daily usage of 5 hours 1 minute±2 hours. On the Calgary Quality of Life Questionnaire studied patients significantly improved their score in the post-PAP period (3.37±1.12 to 1.72±0.92, P<0.001). Epworth Sleepiness Scale scores significantly decreased (6.95±4.94 to 5.34±4.49, P=0.004). OSA severity positively correlated with PAP use (r=0.233, P=0.029). The main reasons for initiating PAP therapy were doctor's recommendations (90.4%) and persistent fatigue (90.4%).

Conclusions: In severe OSA patients, one month of PAP therapy significantly improved their quality of life according to the Calgary Quality of Life Questionnaire and reduced their daytime sleepiness according to the Epworth Sleepiness Scale.

PP50

PROFILE OF SLEEP MACROSTRUCTURE PARAMETERS IN PATIENTS WITH PTSD AND OSA VS PATIENTS WITH OSA WITHOUT PTSD

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Introduction: There is a strong connection between posttraumatic stress disorder (PTSD) and obstructive sleep apnea (OSA). Many polysomnographic studies on PTSD patients have been conducted, but many findings still remain inconclusive.
Methods: A prospective study of polysomnographic and clinical records of patients was conducted in Center for Sleep and Wakefulness Disorders in Psychiatric Clinic Vrapče, Zagreb in 2022 and up to September 2023.

Results: 15 PTSD patients with OSA (1 female, 14 male, mean age ± S.D.: 55.5 ± 7.5 years) and 30 (1 female, 29 male, mean age ± S.D.: 50.6 ± 10.4 years) BMI matched controls with OSA without PTSD patients were studied. Sleep latency was found to be longer in PTSD-OSA cohort (21.60 vs 7.70, p= .040) and portion of N2 sleep stage was lower in PTSD-OSA cohort (49.30 vs 54.80, p = .027). Also, the ratio of non-REM (NREM) AHI in overall AHI is lower in PTSD-OSA patients (0.91 vs 0.98, p=.019), as well as the ratio of total count of NREM apneas and hypopneas in overall count of apneas and hypopneas (0.77 vs 0.86, p=.044).

Conclusions: In our tertiary sleep clinic cohort we found several differences in sleep macrostructure between patients in PTSD-OSA cohort and patients in OSA cohort without PTSD. Patients with PTSD and OSA had longer sleep latency, also the portion of N2 sleep stage was lower in this cohort. Regarding respiratory parameters it was shown that the PTSD-OSA cohort patients had the fewer ratio and total count of NREM apneas and hypopneas.

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OXIME THERAPY ATTENUATES NEUROINFLAMMATION IN MICE EXPOSED TO ORGANOPHOSPHATE COMPOUND

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Organophosphate (OP) compounds that readily cross the blood-brain barrier (BBB) inhibit the physiological function of acetylcholinesterase (AChE) promoting hypercholinergic activity leading to hypoxia, vasodepression, and respiratory arrest, followed by death. Approved therapy for cholinergic toxidrome induced by OP-overstimulation of nicotinic and muscarinic membrane receptors includes permanently charged oxime compounds that don't cross BBB easily making them inadequate for restoring the activity of synaptic AChE. This leads to increased levels and residence time of the neurotransmitter acetylcholine causing seizures and activation of glial cells consequently resulting in neuroinflammation and brain damage. We hypothesized that treatment with uncharged, but ionizable oxime RS194B that crosses the BBB and reactivates OP-inhibited synaptic AChE could act protectively on the brain of mice exposed to an organophosphorus nerve agent sarin (GB). We compared levels of specific proteins expressed in neuronal and glial cells of GB-exposed mice with mice treated by two oximes – the centrally-active oxime RS194B and the one currently in use, pyridinium oxime 2PAM – and untreated control mice. The level of ionized calcium-binding adapter molecule 1 (IBA-1) protein was investigated as a measure of microglial response, and glial fibrillary acidic protein (GFAP) of astrogliosis, whereas neuronal cell viability was detected following neuronal nuclei antigen (NeuN) immunoreactivity. Obtained results indicate the neuroprotective potential of RS194B therapy in mice, especially within 1.5h after OP exposure.
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FROM THE DARKNESS OF ENDOGENOUS PSYCHOSIS TO POLAR BRIGHTNESS

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The patient we present in this paper, a woman of currently forty-five, has been in treatment for endogenous psychosis since she was in her twenties. After being hospitalized for three months, she was treated with long-acting haloperidol (50 mg per month) for twenty years. During this time her everyday functioning was partly iatrogenically conditioned; she felt in a depressed mood, showed no particular interests in her surroundings or hobbies. She worked as a housekeeper and complained that all the mansions she performed were carried out routinely, that she found no happiness in what she did. She was not interested in men and felt emotionally dull and empty.

We then completely revised her pharmacotherapy, replacing haloperidol with aripiprazole during a month's titration. The patient initially showed an improvement on the volitional drive level; she had stronger willpower, more energy, began leaving her home more frequently. She entered an emotional relationship that ended abruptly after a few weeks. She irrationally spent the money she had saved up up until then on clothing, cosmetics and online gambling. She fell into debt and got into unsafe sexual relations. During a night out, after consuming PAT, she had a brief sexual encounter with an unknown man, after which her mother eventually decided to take her to the hospital. What happened to the patient?

Aripiprazole is a new generation antipsychotic, which may have antidepressant, stabilizing and antipsychotic effects depending to the dosage. It is significantly different from other antipsychotics and for this reason opens new possibilities in the treatment of schizophrenia. It is a partial agonist of D2-dopamine, sertononin 5-HT1A-receptors and an antagonist of 5-HT2A-receptors. Patients may feel stronger urges (especially for gambling) with inability to control their impulses, experience an increased sexual drive, be drawn towards compulsive shopping, binge eating and other impulsive or compulsive behaviors.

Some researchers assume that aripiprazole has an agonistic effect on the D3 receptor, which is mainly present in the limbic system, affects the *nucleus accumbens* and therefore stimulates the reward system in an unusually strong manner. This hyperstimulation is particularly enhanced in cases of previous treatment with antipsychotics that function as antagonists of dopaminergic receptors, due to processes of increased regulation of and hypersensitivity to dopaminergic receptors.

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PERSPECTIVE FOR COMPLETE FUNCTIONAL RECOVERY AFTER ANTI NMDAR ENCEPHALITIS

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Anti-NMDAR encephalitis is immunotherapy responsive and a near-majority ultimately acquire a broadly favourable clinical outcome.
The patient we present in this paper, a woman of forty two, has been in treatment for NMDR encephalitis for last two years. Following the course of the acute phase of the disease and the application of high doses of corticosteroid therapy, followed by targeted therapy with monoclonal antibodies over the next two years, a rapid and complete functional recovery was observed, with no residuals. It was necessary to use antidepressants in the early post-hospital period, along with regular psychotherapeutic treatment.
Two distinct models were proposed to explain on the one hand a condition in which a minor inflammatory state as in psychiatric disease culminates in a severe state of inflammation characterized by NMDAR encephalitis and the other a model in which an NMDAR encephalitis might later create favorable conditions for inducing psychiatric disease.
The question arises, how long the pharmacotherapeutic treatment of encephalitis itself should be carried out, given that there is no clear algorithm for the duration of treatment, and all in order to prevent potential decompensation in the form of a psychiatric illness.
Models mentioned above should be kept in mind for further investigations examining the long-term outcome of NMDAR autoantibody immunity in the brain and its functions.

PP54

SELECTIVE INDUCTION OF GLUTAMINOLYSIS-RELATED GENES IN THE PARAHIPPOCAMPAL CORTEX OF SUICIDE VICTIMS

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Altered functional connectivity in human brain networks has been reported in mood disorders. A moderating hub between resting state networks (RSNs) and the medial temporal lobe (MTL) is the parahippocampal cortex (PHC), where abnormal activity has been reported in depressed patients and suicide attempters. Alterations in neuronal mitochondrial function may contribute to depression and suicidal behavior, however, little is known about the underlying molecular level changes in relevant structures. Specifically, expressional changes related to suicide have not been reported in the PHC. Here, we compared the protein expression levels of genes encoding tricarboxylic acid (TCA) cycle enzymes in the PHC of suicide victims by reverse phase protein array (RPPA) and mRNA levels by RT-PCR. Postmortem human brain samples were collected from 12 control and 10 suicide individuals. The entorhinal cortex (EC), topographically anterior to the PHC in the parahippocampal gyrus, served as a control. RPPA analysis revealed that the protein levels of DLD, OGDH, SDHB, SUCLA2 and SUCLG2 subunits were significantly elevated in the PHC but not in the EC. Accordingly, the mRNA levels of respective subunits were also increased. The subunits with altered levels participate in enzyme complexes participating in the oxidative decarboxylation branch of glutamine catabolism. Our data hint on a potential role of glutaminolysis in the PHC in the pathophysiology of suicidal behavior.

PP55

DEFICIENCY OF GD3 SYNTHASE HAS PROFOUND EFFECTS ON NEUROPLASTIN EXPRESSION AND MICRO-LOCATION IN MOUSE BRAIN

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Neuropastin (Np) is a glycoprotein necessary for long-term potentiation, regulation of neuronal calcium homeostasis and associative memory formation. Np exists in isoforms Np55 and Np65 encoded by the *Nptn* gene. The localization of Np within specific membrane subdomains e.g. lipid rafts (LR) depends on the surrounding lipid milieu. In this study we investigated the effect of ganglioside composition on protein and gene expression as well as submembrane localization of Np in brains of GD3 synthase deficient (*St8sia1 null*) mice with impaired synthesis of gangliosides. Neuroplastin gene expression was investigated by RT-qPCR, protein expression of Np isoforms by Western blotting. Immunohistochemical staining was performed on frozen brain slices using an antibody specific for both isoforms. LR and non-raft (nLR) fractions were isolated by ultracentrifugation in sucrose gradients, and submembrane localization of isoforms analyzed by Western blotting. Results revealed lower amounts of Np55 and Np65 in cortices and cerebella of *null* mice compared to their WTs, while *Nptn* gene expression remained unchanged. Immunohistochemical analysis revealed lower intensity of Np staining in the cortex and cerebellar molecular layer of *null* mice compared to WT mice. The amount of both isoforms positioned within cortical LR of *null* mice were lower than those in LR derived from WTs. Results demonstrate that gangliosides affect Np expression, membrane positioning and therefore probably functions as well. This work broadens the understanding of the intricate network encompassing glycosphingolipids and synaptic proteins as important assemblage in the formation and stabilization of functional synapses and the molecular basis of cognition.