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DECEMBER 8, 2020 (Tuesday)	
10:45-11:00	**Opening Ceremony**
11:00-12:00	**Plenary Lecture:** **Pico Caroni** (University of Basel, Switzerland): A brain network to implement flexible learning
12:00-12:30	**FlashTalks**
13:00-15:00	**Oral sessions:**
	NEURAL CONTROL OF BEHAVIOR chaired by: **Artur Pałasz** (Medical University of Silesia, Katowice, Poland) **Martine Migaud** (University of Tours, France): Hypothalamic neurogenesis and seasonal control of reproduction **Maria Bolla** (Instituto Italiano di Tecnologia, Genoa, Italy): Alterated circadian rhythm in the Snord116-deleted mouse, an experimental model of Prader-Willi syndrome **Marton Mayer** (Institute of Experimental Medicine, Budapest, Hungary): Behavioral effect of GABA release from forebrain cholinergic neurons **Kenichi Makino** (Hokkaido University, Japan): Anterior cingulate cortex fluctuates willingness for learning depending on the success and failure **Christina Miskolczi** (Institute of Experimental Medicine, Budapest, Hungary): Early-life social isolation is linked to abnormal social behaviour in adulthood and disrupted network organization in the prefrontal cortex

13:00-15:00	**THREAT AND FEAR –** **A MULTOMODAL AND MULTIDISCIPLINARY APPROACH** chaired by: **Vanessa van Ast** (University of Amsterdam, the Netherlands) **Vanessa van Ast** (University of Amsterdam, the Netherlands): How we remember - emotional episodic memories change over time **Anna Tyborowska** (Donders Centre for Cognitive Neuroimaging, Nijmegen, the Netherlands): Neurophysiological markers of defensive freeze-fight reactions in adolescence **Jeroen van Dessel** (KU Leuven, Belgium): How the emotional brain responds to impending negative events: common and distinct elements across childhood disorders **Michał Szczepanik** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): Vicarious fear learning with naturalistic stimuli - preliminary results of an fMRI study **Anna Kaźmierowska** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): The power of human fear. Observations from human-human and human-rat studies on social transmission of threat.
15:30-16:30	**Poster Session I**
17:00-18:30	**Oral sessions:** **ASTROCYTES AND NEUROIMMUNOLOGY** chaired by: **Cleide dos Santos Souza** (Sheffield Institute for Translational Neuroscience, UK) **Cleide dos Santos Souza** (Sheffield Institute for Translational Neuroscience, UK): Astrocytes in Neurodegeneration: the influence of a bad neighbourhood **Monika Myszczyńska** (University of Sheffield, UK): Uncovering novel drug therapies and targets for amyotrophic lateral sclerosis (ALS) using AI **Claudia Cristiano** (Federico II University of Naples, Italy): Anti-inflammatory and behavioural effects of a novel formyl peptide receptor 2 agonist in two mouse models of autism spectrum disorder **Aleksandra Mielnicka** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): Tracking vesicular gliotransmission to decoding Ca2+ signals

17:00-18:30	**DOGS (CANIS FAMILIARIS) AS A NEW TRANSLATIONAL MODEL** **FOR HUMAN MENTAL CONDITIONS** chaired by: **Anna Kis** (Research Centre for Natural Sciences HAS, Budapest, Hungary) **Anna Kis** (Research Centre for Natural Sciences HAS, Budapest, Hungary): The dog as a model for hemispatial neglect. Behavioural and psychophysiological parallels **Henrietta Bolló** (Research Centre for Natural Sciences HAS, Budapest, Hungary): Affective disorder-like symptoms in the dog? A sleep deprivation experiment **Eszter Petró** (Research Centre for Natural Sciences HAS, Budapest, Hungary): A new translational approach to study the neurocognitive bases of autism **Barbara Csibra** (Eötvös Loránd University, Budapest, Hungary): Development of a human-analogue 3-symptom domain ADHD questionnaire for dogs
19:00-20:00	**Plenary Lecture:** **Dayu Lin** (New York University, USA) Neural Mechanisms of Aggression
20:00-21:00	**TOPIC DISCUSSIONS** **How drugs of abuse affect innate motivation circuits?** chaired by: **Anna Błasiak** (Jagiellonian University, Kraków, Poland) **Dayu Lin** (New York University, USA) **Luigi Bellocchio** (Neurocentre Magendie, Bordeaux, France) **How hippocampal inhibitory microcircuits contribute to memory?** chaired by: **Steffen Kandler** (University of Basel, Switzerland) **Pico Caroni** (University of Basel, Switzerland) **Pablo Mendez** (Cajal Institute, Madrid, Spain)

	What is the best approach to model neurological diseases? chaired by: **Tomasz Prószyński** (Łukasiewicz Research Network, PORT Polish Center for Technology Development, Wrocław, Poland) **Camila Esguerra** (University of Oslo, Norway) **Maryam Afzali** (Cardiff University, UK) **Cleide dos Santos Souza** (Sheffield Institute for Translational Neuroscience, UK) **Is there anything unique about adult neurogenesis?** chaired by: **Michał Ślęzak** (Łukasiewicz Research Network, PORT Polish Center for Technology Development, Wrocław, Poland) **Alejandro Schinder** (Leloir Institute, Buenos Aires, Argentina) **Martine Migaud** (University of Tours, France) **Juan Manuel Encinas** (Achucarro Basque Center for Neuroscience, Leioa, Spain)

DECEMBER 9 (WEDNESDAY)	
11:00-12:00	**Plenary Lecture:** **Karin Roelofs** (Radboud University, Nijmegen, the Netherlands): Human defensive reactions and their role in decision making
12:30-14:30	**Oral sessions:**
	COMPUTATIONAL METHODS IN NEUROSCIENCE chaired by: **Tomasz Pięciak** (AGH University of Science and Technology, Kraków, Poland) **Maryam Afzali** (Cardiff University, UK): Quantifying Tissue Microstructure using Diffusion Magnetic Resonance Imaging **Łukasz Kuśmierz** (RIKEN Center for Brain Science, Wako, Japan): Heavy tails in the brain **Fabian Schubert** (Goethe University, Frankfurt am Main, Germany): Local Autonomous Online Regulation of Echo State Networks **Olgierd Borowiecki** (Nicolaus Copernicus University, Toruń, Poland): Spectrums, not dichotomies. Acting as an ecological-enactive entity

12:30-14:30	**ENDOCANNABINOID MODULATION OF BRAIN FUNCTIONS** chaired by: **Urszula Skupio** (Neurocentre Magendie, Bordeaux, France) **Luigi Bellocchio** (Neurocentre Magendie, Bordeaux, France): Cannabinoid signaling in the brain: cell type / subcellular localization underlies differential biochemical and behavioral outcomes **Roman Serrat Rene** (NutriNeuro, Bordeaux, France): Astroglial mitochondrial calcium dynamics determine synaptic integration **Daniel Heinz** (Max Planck Institute of Psychiatry, Munich, Germany): Yin-Yang effects of the endocannabinoid system on panic-like behavior **Tibor Štark** (Masaryk University, Brno, Czech Republic): Adolescence – the stone(d) age of psychosis
12-30:14:30	**EMOTIONAL EXPRESSION AND PERCEPTION** **A FUNCTIONAL AND EVOLUTIONARY ACCOUNT** chaired by: **Mariska Kret** (Leiden University, the Netherlands) **Iliana Samara** (Leiden University, the Netherlands): Detecting attraction: deceptively simple, endlessly complicated **Eliska Prochazkova** (Leiden University, the Netherlands): The choreography of human attraction: physiological synchrony in a blind date setting **Diana Fabiola** (Leiden University, the Netherlands): Emotional contagion in different interaction contexts: face-to-face vs video call **Julia Folz** (Leiden University, the Netherlands): Going beyond facial expressions: the additional value of investigating subtle emotional cues and emotional body expressions **Mariska Kret** (Leiden University, the Netherlands): Emotion Processing in Homo and Pan
15:30-16:30	**Poster Session I**
16:30-16:55	**Job Opportunities**

	Oral sessions:
17:00-18:30	**SYNAPTIC PLASTICITY** chaired by: **Sandra Jurado** (Institute of Neuroscience CSIC-UMH, San Juan de Alicante, Spain) **Pablo Mendez** (Cajal Institute, Madrid, Spain): Interneuron diversity in hippocampal memory circuits **Marcin Wyroślak** (Wrocław Medical University, Poland): GABAergic tonic inhibition shows cell type-dependent plasticity in the hippocampus **Agata Szlaga** (Jagiellonian University, Kraków, Poland): Medial septum directly inhibits the nucleus incertus theta phase-locked neurons - optogenetic and electrophysiological in vivo and ex vivo studies **Marta Pratelli** (University of California San Diego, USA): A link between neurotransmitter identity and drug-induced behavioral alterations
17:00-18:30	**EFFECTIVE CONNECTIVITY TECHNIQUES** **FOR MODELLING NEURAL FUNCTIONS** chaired by: **Balint File** (Pázmány Péter Catholic University, Budapest, Hungary) **Zoltán Somogyvári** (Wigner Research Centre for Physics HAS, Budapest, Hungary): Complete Inference of Causal Relationships in Neural Dynamical Systems **Zsuzsanna Fodor** (Semmelweis University, Budapest, Hungary): EEG functional connectivity and network structure during memory maintenance mark vulnerable brain networks in Mild Cognitive Impairment **Vaibhav Diwadkar** (Wayne State University, Detroit, USA): Recovering immediate and delayed brain network dynamics: Applications of convergent cross mapping **Balint File** (Pázmány Péter Catholic University, Budapest, Hungary): Reorganization of Functional Networks During Low-Frequency Electrical Stimulation of the Cortical Surface
19:00-20:00	**Plenary Lecture:** **Karl Friston** (University College London, UK) Me and my Markov blanket

DECEMBER 10 (THURSDAY)	
	Oral sessions:
11:00-12:30	**ZEBRAFISH IN CNS AND PNS DISEASES RESEARCH** chaired by: **Kinga A. Gaweł** (Centre for Molecular Medicine Norway, Oslo, Norway) & **Camilla Esguerra** (University of Oslo, Norway) **Camilla Esguerra** (University of Oslo, Norway): New insights into the early mechanisms of epileptogenesis in a zebrafish model of Dravet syndrome **Nancy Saana Banono** (University of Oslo, Norway): Characterization of Zebrafish Cacna1c Mutant- a Model for Schizophrenia **Justyna Jędrychowska** (International Institute of Molecular and Cell Biology, Warsaw, Poland): The role of voltage-gated potassium channels in the development of ear in zebrafish **Anna Sarosiak** (Institute of Physiology and Pathology of Hearing, Kajetany, Poland): Development of a zebrafish model for nonsyndromic sensorineural hearing loss
11:00-12:30	**MODULATION OF EMOTIONAL RESPONSES** chaired by: **Mirosław Wyczesany** (Jagiellonian University, Kraków, Poland) **Charlene Lam** (University of Hong Kong, Hong Kong): The Relationship of Memory Reconsolidation and Return of Fear: Clinical and Methodological Implications of a Novel MultiCS Conditioning Paradigm **Sara Spadone** (University G. d'Annunzio, Chieti, Italy): Beta band communication flow within DAN controls attentional processes **Agnieszka K. Adamczyk** (Jagiellonian University, Kraków, Poland): Implicit induction of emotional control – the role of attentional gating **Tomasz Ligeza** (Jagiellonian University, Kraków, Poland): Acute aerobic exercise enhances processing of positive compared to negative pictures
20:00-21:00	**Meet the Speakers**

	Oral sessions:
13:00-15:00	**NEUROBIOLOGY OF ADDICTION** chaired by: **Jan Rodriguez Parkitna** (Institute of Pharmacology PAS, Kraków, Poland) & **Małgorzata Frankowska (**Institute of Pharmacology PAS, Kraków, Poland) **Anita Hansson** (Central Institute of Mental Health, Mannheim, Germany): Dopamine and opioid system adaptation in alcohol addiction **Paweł Grochecki** (Medical University in Lublin, Poland): Binge mephedrone administration during adolescence potentiates ethanol rewarding effect in adult rats **Maria Nalberczak-Skóra** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): Why is it so hard to quit? The role of the dentate gyrus in seeking behavior of alcohol dependent mice **Magdalena Walczak** (Jagiellonian University, Kraków, Poland): Cholinergic modulation of dopaminergic neurons' activity- in vivo electrophysiological and pharmacological studies on NR1DATCreERT2 mice
13:00-15:00	**PAIN IN LEARNING CONTEXT** chaired by: **Wacław M. Adamczyk** (Jagiellonian University, Kraków, Poland) **Przemysław Bąbel** (Jagiellonian University, Kraków, Poland): A modified model of learning mechanisms of placebo effects in pain **Wacław M. Adamczyk** (Jagiellonian University, Kraków, Poland): Do you really need sensitization to elicit allodynic response? **Bjoern Horing** (University Medical Center Hamburg-Eppendorf, Hamburg, Germany): Three methodological considerations for pain and placebo research **Juliane Traxler** (KU Leuven, Belgium): Pain by mistake - investigating a link between error-related negativity and avoidance behavior
15:30-16:30	**Poster Session II**
16:40-16:55	**WORKSHOP** **Dariusz Zapała** (Cortivision, Lublin, Poland): A portable fNIRS system for measuring hemodynamic response during movement

	Oral sessions:
17:00-18:30	**NEUROGENESIS** chaired by: **Joanna Danielewicz** (Achucarro Basque Center for Neuroscience, Leioa, Spain) **Juan Manuel Encinas** (Achucarro Basque Center for Neuroscience, Leioa, Spain): Induction of Proinflammatory Neural Reactive Stem Cells by Seizures **Ane Rodriguez-Bodero** (Achucarro Basque Center for Neuroscience, Leioa, Spain): Time-lapse monitoring of neural changes in hippocampus during in vitro eplileptogenesis **Anton Chizhov** (Ioffe Physical-Technical Institute, Saint Petersburg, Russia): Coupled experimental and modeling representation of the mechanisms of epileptic discharges in rat brain slices **Theodora Mourtzi** (University of Patras, Greece): Evaluation of the effects of the proneurogenic microneurotrophin BNN-20 on a Parkinsonian patient-derived cellular model and on the success rate of adult NSC transplantations in the Substantia Nigra of a preclinical mouse model of Parkinson's Disease
17:00-18:30	**VISUAL PERCEPTION** chaired by: **Łukasz Okruszek** (Institute of Psychology PAS, Warsaw, Poland) **Łukasz Okruszek** (Institute of Psychology PAS, Warsaw, Poland): Processing of the complex social displays in the posterior superior temporal sulcus subregions **Rafał Skiba** (University of Geneva, Switzerland): Developing a Dynamic Causal Modeling of the network governing dynamic emotional expressions **Maya Jastrzębowska** (École Polytechnique Fédérale de Lausanne, Switzerland): Recurrent processing in the visual cortex underlies (un)crowding **Łucja Doradzińska** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): ERP correlates of consciousness and attention during perception of self-related stimuli

17:00-18:30	**MOTOR CONTROL** chaired by: **Rob van der Lubbe** (University of Twente, Netherlands) **Rob van der Lubbe** (University of Twente, Netherlands): No support for the functional equivalence hypothesis: frontal areas are more involved during motor imagery than during motor execution/ preparation of a response sequence **Magdalena Siemiatycka** (University School of Physical Education, Wrocław, Poland): Cortical activity related to muscle relaxation of the dominant and non-dominant hand **Mateusz Woźniak** (Central European University, Budapest, Hungary): Mental replay of self-associated body movements involves activity in mirror neurons network
19:00-20:00	**Plenary Lecture:** **Alejandro Schinder** (Leloir Institute, Buenos Aires, Argentina): Remodeling of hippocampal circuits by experience and neurogenesis
20:00-21:00	**Social Meetings**

DECEMBER 11, 2020 (Friday)	
11:00-12:00	**Plenary Lecture:** **Adam Hampshire** (Imperial College London, UK) Cognitive and mental health impact of COVID-19, insights from the Great British Intelligence Test
12:30-14:30	**Oral sessions:**
	NEURON-MICROGLIA INTERACTIONS IN HEALTH AND DISEASE chaired by: **Urte Neniskyte** (Vilnius University, Lithuania) **Rosa Paolicelli** (University of Lausanne, Switzerland): Synaptic consequences of selective microglial TDP-43 depletion **Urte Neniskyte** (Vilnius University, Lithuania): Phosphatidylserine scrambling is required for developmental axon pruning **Jorge Valero** (Achucarro Basque Center for Neuroscience, Leioa, Spain): Phagocytic microglia actively regulates adult hippocampal neurogenesis **Mar Puigdellivol** (University of Cambridge, UK): The microglial P2Y6 receptor mediates microglial phagocytosis of neurons in multiple models of neurodegeneration
12:30-14:30	**CROSSMODAL BRAIN PLASTICITY** chaired by: **Katarzyna Cieśla** (Baruch Ivcher Brain, Cognition and Technology Institute, Israel) **Katarzyna Cieśla** (Baruch Ivcher Brain, Cognition and Technology Institute, Israel): Improvement of speech-in-noise perception by audio to tactile sensory substitution **Łukasz Bola** (Harvard University, Boston, USA): Functional selectivity to facial expression sounds in the fusiform gyrus of congenitally blind individuals **Joanna Plewko** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): Letter and speech sound association in early blind children and adults **Gabriela Dzięgiel-Fivet** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): Neural network for tactile reading – similarities and differences to print reading

12:30-14:30	**PSYCHIATRY AND ALZHEIMER'S DISEASE** chaired by: **Witold Libionka** (WSS Gdańsk, Poland) **Andre Aleman** (University of Groningen, the Netherlands): Using noninvasive neurostimulation to target frontostriatal brain circuits: Implications for treatment of negative symptoms in schizophrenia **Anna M. Sobczak** (Jagiellonian University, Kraków, Poland): Time-frequency dynamics of resting state in euthymic bipolar disorder patients **Anna Tkachev** (Skolkovo Institute of Science and Technology, Moscow, Russia): Blood plasma lipid alterations in psychiatric disorders **Maciej Dulewicz** (Medical University of Bialystok, Poland): The cerebrospinal fluid postsynaptic protein concentration in Alzheimer's Disease **Aleksandra Fesiuk** (Nencki Institute of Experimental Biology PAS, Warsaw, Poland): Circulating miRNA biomarkers for Alzheimer's disease (AD) diagnostics
15:30-16:30	**Poster Session II**
17:00-19:00	**FUTURE OF NEUROSCIENCE** **Viktor Jirsa** (Aix-Marseille University, France): Translational neuroscience: from network theory to personalized medicine **Panayiota Poirazi** (Foundation for Research and Technology-Hellas, Greece): Active dendrites and their role in neuronal and circuit computations **Dominik Paquet** (Ludwig Maximilian University of Munich, Germany): Developing a new generation of human brain disease models using CRISPR editing and iPS cells
19:00-19:30	**Awards / Closing Ceremony**

DECEMBER 8, 2020 (Tuesday)

PLENARY LECTURE

11:00 – 12:00

chaired by: **Steffen Kandler** (Biozentrum, University of Basel, Switzerland)

A brain network to implement flexible learning

Pico Caroni

Friedrich Miescher Institute, University of Basel, Switzerland

Adaptive behavior critically depends on re-adjusting to alternative goals when new evidence contradicts previous conclusions, and cost-benefit considerations favor alternative learning. How such flexible learning might be implemented in the brain is not well understood, but a possible framework could involve systems dedicated to evaluating current experience against expectations, and downstream learning systems recruited for assignment of new feature/item-value associations. I will discuss recent studies from our lab identifying and functionally dissecting a specific hippocampal-cortical-striatal subnetwork involved in the implementation of adaptive context-related flexible learning.

FLASHTALKS

12:00 – 12:30

chaired by: **Marta Klimczak & Michał Zaręba** (Neuronus Forum Committee, Jagiellonian University, Krakow)

Aliaksei Chareshneu: NACHRDB: Solving the puzzle of structure-function relationships in nicotinic acetylcholine receptors (nAChRs)

Judyta Juranek: Coordinated bi-directional trafficking of synaptic vesicle and active zone proteins in peripheral nerve fibers

Gniewosz Drwięga: Control of midbrain dopaminergic neuron activity by brainstem nucleus incertus – electrophysiological and optogenetic studies on urethane anesthetized rat

Kamil Pradel: Superior colliculus innervates contralaterally located rostromedial tegmental nucleus – a neuroanatomical study

Łukasz Chrobok: Circadian influence of orexins upon retinorecipient neurons in the rat lateral geniculate complex

Jacek Wróbel: Nasal respiration is necessary for the emergence of aberrant oscillatory activity and behavioural hyperactivity in the ketamine model of psychosis

Klaudia Nowicka: Physiological and pathological appetitive learning – can we understand addiction by peeking inside the brain?

Marilia Sousa: What happens after chronic opioid cessation? Studies in a pain facilitatory area of the brain

Filip Janiak: Divergent excitation two photon microscopy for 3D random access mesoscale imaging at single cell resolution

Liubov Vasileva: More than 2.5 years of stable chronic recordings of single-units in the rabbit amygdala

Edeth Edwin: Corpus Callosum T1-weighted signal features and fluid intelligence

Katarzyna Gugnowska: Endogenously driven interbrain synchrony in musical interaction

Louis-David Lord: Dynamical exploration of the repertoire of brain networks at rest is modulated by psilocybin

Ewa Beldzik: The pre-supplementary motor area reflects conflict processing irrespectively of reaction times
Przemysław Adamczyk: Hypofunction of the left hemisphere as substrate of impaired conventional metaphor processing in schizophrenia – an fMRI study

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Biological Session I

NEURAL CONTROL OF BEHAVIOUR

13:00 – 15:00
chaired by: **Artur Pałasz** (Medical University of Silesia, Katowice, Poland)

Hypothalamic neurogenesis and seasonal control of reproduction

Martine Migaud

University of Tours, France

Adult neurogenesis is recognized as the process of producing new neurons from adult neural stem cells. The hypothalamus, a structure critically involved in the control of neuroendocrine functions, ranging from reproduction, to energy intake/expenditure balance, has recently been shown to harbor adult neural stem cells within a neurogenic niche. In the ependymal lining of the third ventricle, tanycytes act as neural stem cells supporting this continuous neurogenesis process. In sheep, a large long-lived mammalian model, we have recently shown that the hypothalamic neurogenic niche harbours adult neural stem cells (NSCs), the tanycytes, capable of generating new neurons and glial cells. In this seasonal species, the function of reproduction is limited to one period of the year and the timing of this restricted sexual activity period is driven by the photoperiod and the pineal hormone, melatonin. We have shown a seasonal peak in hypothalamic cell proliferation rates occurring around 55 days after the onset of the sexual activity period, concomitant to an increase in the expression of doublecortin, a marker expressed in young migrating neurons, indicating a simultaneous enhancement of the rate of neurogenesis. We provided evidence that this peak of neurogenesis is pineal dependent, suggesting a regulatory role for melatonin in this process. Furthermore, the disruption of hypothalamic neurogenesis following the administration of the antimitotic cytosine-b-D-arabinofuranoside (Ara-C) leads to an alteration of the timing of reproduction. Together, our results correlate the cyclic increase of hypothalamic neurogenesis to seasonal reproduction and suggest that the photoperiod-regulated hypothalamic neurogenesis plays a role in the seasonal reproductive physiology.

Alterated circadian rhythm in the Snord116- deleted mouse, an experimental model of Prader-Willi syndrome

Maria Bolla, Matteo Falappa, Laura Cancedda, Valter Tucci
Instituto Italiano di Tecnologia, Genoa, Italy

Prader-Willi syndrome (PWS) is a genomic imprinted disorder that is characterized by brain developmental, behavioral and metabolic abnormalities. Snord116 is a small nuclear RNA that controls the expression of many genes, including different clock genes in the suprachiasmatic nucleus. Here, we analyzed the effects of the loss of paternal expression of Snord116 in the circadian rhythms of mice during light-dark (LD) and dark-dark (DD) where they express the capability of entrainment and free-running respect to external events, respectively. We found that loss of paternal expression of Snord116 in mice alters the circadian period during free-running when the animals run according to their internal clock. In particular, mutant mice present with a reduced shortening of their circadian period in DD in comparison to their wild-type littermates. On the other hand, the circadian period during LD shows an unaltered circadian rhythm in mutants compared to wild-type mice. Our study indicates that Snord116 is involved in the regulation of circadian rhythms in mice and points out a new endophenotype for a pre-clinical investigation into the pathomechanisms of PWS. Moreover, this research promotes the knowledge of how imprinted genes can contribute to the alteration of circadian rhythms.

Behavioral effect of GABA release from forebrain cholinergic neurons

Marton Mayer, Katalin E. Sós, Virág T. Takács, Zsuzsanna Bardóczi, Katalin Sviatkó, Balázs Hangya, Manó Aliczki, Éva Mikics, Tamás F. Freund, Gábor Nyiri

Institute of Experimental Medicine, Budapest, Hungary

The basal forebrain cholinergic system comprises several nuclei that provide innervation to cortical areas. It contributes to the regulation of arousal, attention and memory, including fear and extinction learning, and it is implicated in anxiety and post-traumatic stress disorder. We have recently shown that cholinergic terminals synaptically release not only acetylcholine, but GABA as well, the release of which can be modulated independently. Although previous studies demonstrated that the alteration of GABAergic cotransmission is possible and has functional consequences in other non-cholinergic brain regions, the role of GABA release from forebrain cholinergic cells is unknown. We created a conditional knockout mouse strain (ChAT-vGAT-cKO) showing decreased GABA release from cholinergic neurons. Our results from behavioral phenotyping of this strain revealed that decreased GABA release from cholinergic neurons led to increased hippocampal theta activity during sleep and increased cognitive performance in an operant learning task, possibly due to a relatively more efficient cholinergic effect. However, ChAT-vGAT-cKO mice showed significant deficits in fear extinction learning after cued fear conditioning. These results suggest that inefficient GABA release from cholinergic cells may explain certain fear-related pathological conditions.

Anterior cingulate cortex fluctuates willingness for learning depending on the success and failure

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We achieve learning by repeating trial-and-error. In the process, successful experiences could maintain willingness for the learning, whereas failure experiences could decrease it. In this study, we assumed that anterior cingulate cortex (ACC) fluctuated the willingness for learning. To clarify this hypothesis, we designed a two-hole nose-poke test as a learning task. The trial outcomes in this test are correct (success), incorrect (failure), omission (no-poking) trials. We regarded the omission trials as an index of willingness, which reflects the demotivational state to perform the task. We inactivated the ACC by local injection of muscimol. ACC inactivation induced omissions after incorrect trials, but not correct trials. Thus, ACC activity is necessary to support the willingness. Moreover, the ACC inactivation also increased the probability that consecutive omission trials occurred. Therefore, ACC activity is also required to rescue from the sustained demotivational state. On the other hand, ACC activation using a DREADD chemogenetic system reduced omissions after incorrect trials, but not correct trials. Furthermore, the ACC activation also decreased the probability that consecutive omission trials occurred. These results indicated that ACC activation increased the willingness for learning. Taken together, our results suggest that ACC activity contributes to the control of learning willingness.

Early-life social isolation is linked to abnormal social behaviour in adulthood and disrupted network organization in the prefrontal cortex

Christina Miskolczi, Laszlo Biro. Biborka Bruzsik, Huba Szebik, David Lorincz, Zoltan Kristof Varga, Laszlo Szente, Orsolya Horvath, Jozsef Halasz, Mate Toth, Eva Mikics

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Brain regions modulating social behaviour undergo dynamic changes in early life, rendering them vulnerable to social adversities experienced during this period. Here we aimed to characterize changes induced by post-weaning social isolation (modelling childhood neglect) in mice and investigate underlying disturbances in the prefrontal cortex (PFC), a key modulator of social behaviour, with a focus on parvalbumin (PV) interneurons, a neuronal population tied to developmental maturation. Mice were weaned at P21 and were housed socially (4 mice/cage)

or were isolated (alone) until adulthood. In adulthood, social behaviour and aggression was investigated via the resident-intruder(vRI) test. Mice were perfused under resting conditions or 90 minutes following RI. Using immunohistochemistry and confocal imaging, we investigated c-Fos co-activation patterns of PFC subregions, and subregion-specific activation of parvalbumin interneurons under resting conditions or following RI. Isolated mice display social disturbances in adulthood, shown as increased defensive and abnormal aggressive behavior. RI caused hyperactivation in the medial PFC of isolated animals and disturbed co-activation patterns between PFC subregions. In isolated mice PV+ neurons also showed differences in response to an acute social challenge (RI) compared to socially-reared animals. In conclusion, isolation leads to abnormal network activity in the PFC, which could underlie behavioural disturbances seen in adulthood.

Cognitive Session I

THREAT AND FEAR – A MULTIMODAL AND MULTIDISCIPLINATORY APPROACH

13:00 – 15:00

chaired by: **Vanessa van Ast** (University of Amsterdam, the Netherlands)

How we remember: emotional episodic memories change over time

Vanessa van Ast

University of Amsterdam, the Netherlands

Our emotional memories seem to be a reliable record of our experiences. But nothing is further from the truth: recollection of past experiences changes over time and so do the accompanying emotions (emotional episodic memory). However, classic theories of memory cannot easily explain such dynamics. Furthermore, past research on emotional memory has traditionally focused either on alterations in content or the emotional expression of memory. Based on recent data from experimental studies in our lab using paradigms that combine these measures, I will present new insights in the way emotional experiences can simultaneously alter the content and psychophysiological expression of existing memories. Ultimately, delineation of the fate of such dynamic episodic emotional memories may help to understand the etiology and treatment of emotional memory disorders.

Neurophysiological markers of defensive freeze-fight reactions in adolescence

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Defensive stress reactions, such as freezing and active fight-or-flight, are relevant for coping with threat. Recently, animal models of the neural circuitry implicated in these defensive reactions have been translated to humans. However, it remains unclear whether those insights also translate to human adolescent maturation. In this study, 17-year old adolescents (n=68) were tested with an fMRI-adapted shooting task previously used to induce threat-anticipatory freezing and switch to active fight responses in adults. Similar to adults, when adolescents prepare for shooting under threat their heart-rate decelerates, and activity in subcortical and thalamic structures increases. During the subsequent switch to active shooting, the perigenual anterior cingulate cortex (pgACC) of adolescents becomes active. Differently from adults, adolescents preparing for shooting under threat activate their amygdala. This effect was related to the amount of callous unemotional traits (a juvenile precursor of psychopathy), as well as negative amygdala-PAG connectivity. Crucially, PAG activity was not threat-specific during this preparatory stage of freezing - as seen previously in adults. These findings may point to the emergence of an adult-like neuro-

physiological profile of freeze during late adolescence, whilst highlighting the continued maturation of key regions in the automatic defense response circuit.

How the emotional brain responds to impending negative events: common and distinct elements across childhood disorders

Jeroen Van Dessel[1], Silke Beckers, Matthijs Moerkerke[1], Edmund Sonuga-Barke[2,3], Sarah Morsink, Saskia Van der Oord [4,5], Jurgen Lemiere[1], Hilde Sijmons, Marina Danckaerts[1]

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Negative reinforcement processes allow individuals to avoid negative outcomes and are used to promote adequate behaviour. Identification of the neural mechanisms responsible for the effectiveness of negative reinforcement is important so that treatments for different psychiatric disorders can be applied under the correct conditions. In the present study, male adolescents with anxiety disorder, attention-deficit/hyperactivity disorder and matched controls performed the Escape Monetary Loss Incentive task in the MRI scanner under three conditions. Warning cues signaled the relationship between performance and monetary loss to differentiate the brain's responses to contingency (CONDITIONAL LOSS AVOIDANCE trials) and valence (CERTAIN LOSS; CERTAIN LOSS AVOIDANCE trials). The analysis focused on loss anticipation and feedback periods. Participants rated the emotional and the value significance of cues. Atypical processing of contingent loss cues was seen for adolescents with anxiety, while differences in valence processing were seen for ADHD adolescents.

Vicarious fear learning with naturalistic stimuli - preliminary results of an fMRI study

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People often learn about threat and safety socially, where behaviours and emotional expressions of others serve as powerful cues. The process can be studied using a protocol of Observational Fear Conditioning, in which the subject watches another person undergoing a differential conditioning task, before being confronted with the task themself. To amplify the social aspect of the procedure, we invited pairs of friends and streamed live video to the participant undergoing fMRI scanning, eschewing standardized recordings of an actor. Electric shocks, paired with visual conditioned stimuli (CS) and administered only to the person being observed, were used as unconditioned stimuli (US). We collected data from 90 participants. In the preliminary analysis we confirmed that the observational (social) US elicited robust responses in the "core fear network" of Amygdala, Anterior Insula and Anterior Cingulate, as well as in visual areas, including face-specific Fusiform Gyrus (all bilateral). In response to direct presentation of CS, we observed activation of the right Anterior Insula, alongside a temporal modulation effect in bilateral Amygdala, ACC and subcortical areas, indicative of response extinction. The results confirm the effectiveness of fear acquisition with less controlled stimuli and allow further investigation of neural background underlying ecologically-relevant vicarious fear learning.

The power of human fear. Observations from human-human and human-rat studies on social transmission of threat

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Studies in both rats and humans have shown that learning about threats from conspecifics is possible but the nature of social communication differs between these species. While humans prefer to learn observationally, rats need to interact with one another in order to learn about the threat vicariously. We conducted two studies in order to 1) examine the brain correlates of the observational fear learning in humans and 2) investigate whether human fear can be transmitted to rats through social interaction. In study 1, participants were asked to watch a close friend being fear-conditioned and in study 2, fear-conditioned humans were asked to interact with previously handled rats. Preliminary fMRI results showed that brain networks related to fear and empathy for pain were activated in the participants during observation. Remarkably, strong involvement of bilateral amygdala was observed. Regarding the human-rat experiment, the c-Fos mapping performed in this region of interest indicated increased activity in two amygdalar nuclei - medial and lateral - following the interaction with a fear-conditioned human. These findings show that bridging the gap between human and rat studies is possible and suggest a similar brain mechanism underlying social transmission of fear in both human-human and human-rat dyads.

POSTER SESSION I

BIOLOGICAL POSTERS

BASIC NEUROSCIENCE

1. Circadian rhythm of the antimicrobial peptide attacin in the brain of Drosophila melanogaster

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One of the sporadic forms of Antimicrobial peptides (AMP) protect against pathogens by permeabilizing their cell membrane, which leads to cellular leakage and cell death. Nowadays intensive research on bactericidal AMP seems to be particularly important due to a growing problem of antibiotic resistance. Attacins are one of *D. melanogaster* classes of AMP, which respond to Gram-negative bacteria infection. In order to detect expression of Attacin A gene in the brain of *D. melanogaster* PCR method was used. Additionally brain sections of the strain expressing fusion protein AttacinA::GFP under UAS control were observed with a fluorescence microscope. Furthermore, a quantitative Real-Time Polymerase Chain Reaction (qRT-PCR) method was used to evaluate daily changes in Attacin A gene expression in heads of *D. melanogaster*. The present study provided an evidence for the Attacin A gene expression in the brain of *D. melanogaster*. Moreover, there were daily differences between time points studied with maximum at ZT20 (four hours before lights-on) and minimum at ZT16 (four hours after lights-off) in a light/dark cycle. Further research will evaluate effects of an injury on Attacin A level in the brain.

2. Divergent excitation two photon microscopy for 3D random access mesoscale imaging at singlecell resolution

Filip Janiak[1], Phillip Bartel[1], Michael R Bale[1], Takeshi Yoshimatsu[1], Emilia Komulainen[1], Kevin Staras[1], Lucia Prieto-Godino[2], Thomas Euler[3,4], Miguel Maravall[1], Tom Baden[1,4]

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Studying brain-wide computation requires the ability to simultaneously monitor activity of arbitrary groups of neurons largely independent of their individual 3D positions. Using a standard 2-photon imaging, this remains a challenging task. Here, we use a simple optical trick to dramatically ameliorate this problem, thus allowing for rapid random-access 3D mesoscale imaging. With an investment below £1,000, we simplified a Sutter-MOM 2-photon setup into a non-collimated design, thereby extending the standard 0.5 mm planar field of view to a 3D 3.5 x 3.5 x 0.6 mm using a standard x20 objective. These simple modifications allow running arbitrary 3D scan-paths across a volume with a maximal travel time of 2 ms between any two points. Our design opens a wide range of eminently useful scan options, including mesoscale random-access scans as well as vertical and 3D curved scans that acknowledge the 3D structure of biological samples. We demonstrate the capability of this setup using a wide range of examples from mice, zebrafish and Drosophila. Our setup allows simultaneous recordings in the eye and brain of larval zebrafish, or intelligent plane bending to acknowledge the natural 3D curvature of the zebrafish brain in a "SPIM-like" recording configuration.

3. NACHRDB: Solving the puzzle of structure-function relationships in nicotinic acetylcholine receptors (nAChRs)

Aliaksei Chareshneu[1,2], Purbaj Pant[1,2], Ravi Jose Tristao Ramos[1,2], Tugrul Gokbel[3], Crina-Maria Ionescu[1,2], Jaroslav Koca[1,2]

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The nicotinic acetylcholine receptor (nAChR) is evolutionary ancient allosteric membrane protein mediating synaptic transmission. This prototypic pentameric ligand-gated ion-channel is involved in neurophysiological processes (from learning to motor control), diseases (Alzheimer's, Parkinson's diseases, schizophrenia, epilepsy), and addictions (alcohol, tobacco). Since its isolation in 1970, extensive studies produced huge amounts of structural-functional data. However, the cumulative knowledge on nAChRs, spanning 50 years of research, is not systematically accessible. The multitude of receptor types, residue numbering schemes, and methods used, together with diverse terminology and scattered nature of existing findings make it harder to summarize the current knowledge and apply it efficiently to promote further discoveries. There is no single resource providing an access to and visualization of such extensive information. Bridging this gap, we developed NACHRDB (https://crocodile.ncbr.muni.cz/Apps/NAChRDB/) – web-accessible manually curated database providing fast access to relevant structural-functional data on nAChRs and facilitating its interpretation through integration of residue-level functional annotations with interactive visualization. Besides, NACHRDB contains predictions of potentially allosterically relevant residues, based on atomic charges' and channel lining profiles. We believe that NACHRDB can guide the further studies on nAChRs and serve as a key starting point in unification of the state-of-art knowledge in broad field of ion channels.

4. Immunodetection of calcium-binding proteins in dorsal root ganglia of the guinea pig (Cavia porcellus, Rodentia) at midgestation

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Many findings suggest that calcium binding proteins (CaBPs) such parvalbumin (PV), calbindin D-28k (CB), and calretinin (CR) may be involved in some developmental events. A striking similarity in the milestones of onset and differentiation of specific fetal movement patterns was found in guinea pig and human (Kan et al., 2009). These CaBPs are also useful neuroanatomical markers differently labelling subpopulations of GABAergic neurons. Somatosensory neurons comprise main component of dorsal root ganglia (DRG) transmitting important information such as temperature, touch, pain, muscle extension etc.The aim of this study was to examine the presence of immunoreactive structures containing PV, CB or CR in DRGs at midgestation of the guinea pig (E30, E31). Two methods were applied; the paraffin scraps were stained with the cresyl violet according to the Nissl method, for immunodetection DAB technique with using primary antibodies against these CaBPs. The present study show that the most abundant protein engaged in DRG functioning was PV (most numerous PV-positive cells) and the least was CR. In conclusion PVseems to have considerable impact on developmental events which take place in this period of the guinea pig.

5. Neurobiological activity of Rhinella dorbignyi (Duméril&Bibron, 1841) toad toxic secretion on Nauphoeta cinerea cockroaches

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Rhinella dorbigny is a toad specie exclusive from the Pampa Biome, in Southern America. The neurobiological activity of Rhinella dorbignyi toad toxic secretion (RDTTS) has never been evaluated so far. RDTTS biological activity was investigated against Nauphoeta cinerea cockroaches locomotory and neuromuscular behaviors. The cockroach exploratory behavior was recorded using a video-monitoring system (id Tracker) and the analysis accomplished by an ad-hoc script developed at Matlab®. The in vivo cockroach nerve-muscle preparation was mounted as described elsewhere. Overall, when RDTTS (2.5, 5, 7.5 e 10 µg/g of animal weight) was administered there was a maximum increase in the total track of 627±77cm (for the least dose) and a concomitant decrease in the immobile episodes of 370±33, compared to the control saline (p<;0.0182, n=40, respectively). The analysis of the cockroach neuromuscular function showed that RDTTS at the same doses, induced a preliminary increase in the amplitude of muscle twitches (118.4± 6% and 112.6±2%, p<;0.005), with 5 and 7.5 µg/g of animal, followed by a neuromuscular blockade, in 120min recordings (47±7%, 65±4%, 16±3%, 15±4%, respectively for each dose) (p<;0.005, n=9). Altogether, the results indicate that RDTTS disturbs the cockroach exploratory behavior mainly by affecting its neuromuscular function.

6. Matrix metalloproteinase 9 sin neuronal plasticity – methodological approach

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Matrix metalloproteinase 9 (MMP-9) plays a major role in synaptic plasticity, although the exact mechanisms of its action remain unclear. There are several factors which make studying MMP-9 challenging, including low MMP-9 concentration in the non-stimulated brain; restricted time window of its activity at the synapse; and overall high structural similarity and substrate specificity to other matrix metalloproteinases. Here, we present our approaches to study MMP-9 in the context of synaptic plasticity. Our studies have been performed on hippocampal organotypic cultures obtained from mice and rats. First, we investigated timing of MMP-9 release during whole neuronal network remodelling evoked by cholinergic agonist (carbachol) treatment. The second aim has been to image MMP-9 release from a single dendritic spine. For that we used the MNI-glutamate uncaging technique combined with two-photon imaging. It allowed precisely releasing of glutamate in the spine neighbourhood to trigger dendritic spine plasticity. With a use of variety techniques including in situ zymography, two-photon imaging and protein-based fluorescent biosensors, we are investigating MMP-9 release after evoking plastic changes in neuronal network. We discuss advantages and disadvantages of each technique for MMP-9 detection and our findings on timeline of MMP-9 release from dendritic spines.

7. Robust and cost-effective and tracking of antennal pointing response to looming stimuli inhouse cricket, Acheta domesticus

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Studies in the field of comparative ethology could pose a significant challenge considering the experimental design. Perception of visual stimuli in case of mammals could be easily tracked by observing the ocular movements, however, in the case of studies aiming at exploring such processes in insects, the immobility of typical insect' eye render this approach unsuitable. A common answer to this problem is to study antennal movements, which usually occur in response to the occurrence of novel stimuli in insect surroundings. A particularly strong response may be observed in response to so-called looming stimuli (the appearance of swiftly growing objects in the visual field). *Acheta domesticus* exposed to such a stimulus would usually abruptly point one of its antennas towards it. By manipulation of the characteristics of the stimulus, one can conduct the studies analogous to the classical paradigms employed in studies of attention in species with mobile eyes. The poster describes the method of facing the challenges posed by the relative swiftness of antennal movement and limitation of traditionally used tracking software with the help of the DeepLabCutmarkerless pose estimation framework based on deep neural networks.

8. The mTOR-driven phosphorylation of TBC1D5 is spare for proper neuronal connections in mature neurons in vitro.

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Retromer complex is the protein complex responsible for recycling proteins from endosomes to trans-Golgi network and cell surface. TBC1D5 is a regulator of the retromer. In our laboratory,TBC1D5 phosphorylation sites by mTOR were identified and confirmed. Our previous results showed that the overexpression of unphosphorytable mutants of TBC1D5 causes impairment of retromer function and simplification of the dendritic tree in developing neurons. However, thus it has remained unknown if TBC1D5 affects mature neurons. I tested a hypothesis that mTOR via TBC1D5 regulates the function of the retromer in mature neuron synaptic transmission. Rat hippocampal neurons in vitro were transfected with plasmid encoding GFP(control), TBC1D5-GFP-WT or its variants with mTOR-phosphorylated residues substituted by alanines, and excitatory currents were recorded using the patch clamp method. In addition, colocalization between pre- and post-synaptic markers was analyzed. As a result we showed that neurons overexpressing TBC1D5-GFP WT and unphosphorytable mutants of TBC1D5 are indistinguishable from control cells. Thus, retromer regulation by mTOR, which is essential for dendritogenesis in developing neurons, is not critically important for basic communication of mature neurons. This work has been supported by Polish National Science Centre OPUS grant 2017/27/B/NZ3/01358.5.

DEVELOPMENT

9. Investigation into the role of Hippo pathway component FRMD6 in axon growth

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The growth of axon, and the maintenance of its morphology greatly underlines the fundamental functions of neurons. This project aims at investigating how protein FRMD6, an architecture regulatory Hippo signaling component, might affect the axonal growth of neuronal cells. We have first used molecular gene-editing techniques to obtain differential levels of FRMD6 in neuronal cultures, for example HT-22, SHSY-5Y and mouse cortical neurons. It was initially noted that the modification of Willin levels greatly changes the number and length of axons. FRMD6 can also move to the tip of a fast-growing axon upon exposure to neurotrophic factors (e.g. BDNF, EGF), a phenotype that considered as a polarity regulator. As the cell cytoskeleton dynamics greatly shapes how neuronal cells adapt to a new morphology, we moved on to looking at the dynamics of F-actin filaments by applying 3D-SIM super-resolution imaging techniques. It was first shown that Mcherry-Willin potentially interacts with actin-GFP. Moreover, the down-regulation of FRMD6/Willin changes the organization of actin filaments in both fixed and live-cell samples. Lastly, a few cell mobility-related assays were performed, and results suggest that up-regulated Willin expression slows down cell proliferation, migration, however, increase the adhesion of cells to the extracellular matrix.

10. Lipocalin 2 – a promising link between immune system and brain development

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Epidemiological studies indicate that maternal infection during pregnancy is a risk factor for neurodevelopmental disorders. However, mechanisms underlying this phenomenon remain unclear. The aim of our studies is to characterize the role of Lipocalin 2 (Lcn2), an innate immune response protein highly expressed in inflamed brain, in the regulation of neuronal circuitry development. To mimic maternal infection the pregnant mice received three i.p. lipopolysaccharide or PBS injections on E16-18, representing infection in the second-trimester pregnancy in humans. Fetal cortex and hippocampus were isolated 24 hours after the last injection to evaluate Lcn2 mRNA expression. To address how lack of Lcn2 during prenatal infection may influence electrophysiological properties of hippocampal pyramidal neurons in adult brain, we performed excitability recordings on brain slices from Lcn2 WT and KO mice. Our results indicate that Lcn2 mRNA is significantly upregulated during maternal infection-induced fetal brain inflammation. We also observed that the absence of Lcn2 in developing brain results in higher excitability of hippocampal neurons in adult brain, but only in mice exposed to prenatal infection. These results suggest that Lipocalin 2 could be a promising link between immune response and brain development. This work was supported with NCN grant 2017/27/B/NZ4/01639.

11. Comparing neuronal differentiation of human induced pluripotent stem (iPS) cells from different tissue of single donor

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The technology of generating stem cells from somatic cells opened new perspectives such as cellular replacement, regenerative therapy and disease modelling. An interesting approach is modelling of cellular interactions within the human brain using pluripotent stem cells. However, iPS cells' fate is guided by expression of specific genes and epigenetic modulation.The aim of this study was to elucidate whether the origin of tissue used for reprograming and obtaining of iPS cells determine their fate during differentiation. Peripheral blood mononuclear cells and keratinocytes from the same donor were reprogrammed using the Sendai-virus reprogramming system. The transgene-free iPS clones were verified by RT-PCR, alkaline phosphatase staining and teratomas formation. The differentiation of human iPS cells into 2D dopaminergic neurons and 3D multicellular midbrain organoid-like structure was performed.We observed that number of neuroectodermal structures were higher in teratomas generated from keratinocytes-derived iPS lines. Analysis of neuronal progenitors' and neurons' markers revealed differences. iPS cells, generated from different origin cells, showed differences in neuronal differentiation propensity. 3D organoid model showed a potential to become a universal in vitro system to study human brain biology. The project was supported by the grant from the National Science Centre in Poland 2015/17/B/NZ5/00294 and N41/DBS/000120.

METABOLISM

12. The effect of the novel atypical antipsychotic drug lurasidone on cytochrome P450 (CYP) enzyme activities in human liver

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The present study aimed at examining the inhibitory effect of the new atypical neuroleptic lurasidone on the main human cytochrome P450 (CYP) enzymes in pooled human liver microsomes and cDNA-expressed CYP enzymes (Supersomes). CYP enzyme activities were determined using CYP-specific reactions: caffeine 3-N-demethylation (CYP1A2), diclofenac 4'-hydroxylation (CYP2C9), perazine N-demethylation (CYP2C19), bufuralol 4'-hydroxylation (CYP2D6), testosterone 6β-hydroxylation (CYP3A4), and HPLC method. Inhibition constants (Ki) of CYP-specific reactions were obtained using a non-linear regression analysis (Program Sigma Plot 8.0; Enzyme Kinetics). Lurasidone moderately inhibited CYP1A2 (Ki = 12.6 and 15.5 μM in microsomes and Supersomes), CYP2C9 (Ki = 18 and 3.5 μM in microsomes and Supersomes) and CYP2C19 via a mixed mechanism (Ki = 18 and 18.4 μM in microsomes and Supersomes), and CYP3A4 via a competitive mechanism (Ki = 29.4 and 9.1 μM in microsomes and Supersomes). Lurasidone competitively, though weakly diminished the CYP2D6 activity (Ki= 37.5 and 85 μM in microsomes and Supersomes). The observed inhibition of different CYP enzymes by lurasidone may be of pharmacological and clinical importance. The obtained Ki values indicate that pharmacokinetic interactions with lurasidone may occur during combined therapy. Acknowledgements: Przemysław Danek acknowledges the support of InterDokMed project no. POWR.03.02.00-00-I013/16.

13. Effect of 2-hydroxyglutarate on metabolism of human neuroblastoma cells

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The increased level of 2-hydroxyglutarate (2-HG) is a hallmark of glioblastomas and neurological damage. 2-HG affects several cellular processes including epigenetic regulation of gene expression. To identify the effect of 2-HG on metabolism of human neural cells, cultured neuroblastoma (SHSY-5Y)were used to a) assign the specific uptake of both 2-HG enantiomers; b) to identify the changes in cellular metabolism by 1H-NMR method; c) investigate the expression of the indispensable enzymes for essential amino acid catabolism. Our results demonstrate that human neuroblastoma cells a) are capable to dispose the both enantiomers of 2-HG from their extracellular milieu with comparable specific rate; b) their oxidative metabolism is inhibited by 2-HG; and c) incorporate the essential amino acids in the energy metabolism. Therefore it could be concluded that human neuroblastoma cells are capable to use some of the essential amino acids as the alternative substrates for their energy metabolism, and their metabolism is compromised by both enantiomers of 2-HG. This is in line with our hypothesis that 2-HG initiated metabolic changes contribute to transformation of cancer metabolism and etiology of neurological damage. This work was supported by the Ministry of Health of the Slovak Republic. 2018/13-UKMTO-9, VEGA grant 1/0255/20 and APVV-18-0088.

14. Bovine brain endothelial cells metabolize glutamate locally via glutamate dehydrogenase action

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Glutamate levels within brain parenchyma must be tightly regulated because of its excitotoxic potential. Accordingly, both astrocytes and brain capillary endothelial cells have been reported to metabolize the excitatory neurotransmitter glutamate into alpha-ketoglutarate via glutamate dehydrogenase (GDH). Using western blotting and immunofluorescence, here we show that GDH is expressed in cultured mouse, bovine, and human endothelial cells (EC). This was further confirmed in mice lacking GDH expression in parenchymal cells. Cultured bovine and mouse brain EC were shown to take up stable isotope labelled glutamate and to anaplerotically metabolize it via alpha-ketoglutarate in the TCA cycle. This was inhibited by bithionol, which suggests that this metabolic process is at least partially dependent of GDH action. Bovine EC that were subjected to a mitochondrial stress test in the presence of medium supplemented with only glutamate in the absence of glucose were capable of supporting mitochondrial function, albeit at lower levels than cells with access to glucose. Bovine EC were subjected to a glycolysis stress test, where they showed no difference in extracellular acidification, when only glutamate was provided; this indicates no profound metabolism to lactate takes place in endothelial cells, and that they may only transport astrocyte-generated lactate into the blood.

15. Expression of glucose transporters in the hippocampus of female rats subjected to the western diet and forced physical activity

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Recently more attention has been paid to the contribution of an unhealthy diet to the development of the central nervous system (CNS). The positive effect of physical activity on CNS has been demonstrated in numerous clinical and experimental studies and growing evidence supports the role of physical activity as a brain and nervous system disease-preventing factor. Female adult rats were fed with the prepared chow reproducing the human western diet and subjected to wheel running physical activity for 6 weeks. A control group of lean rats were fed with a standard diet. The aim of our study was to verify the hypothesis that regular physical activity can mitigate the changes in the hippocampus protein expression of GLUT-1, GLUT-3, and GLUT-8 transporters induced by exposure to the western

diet. We observed the significant increase of the protein expression of GLUT-8 transporter in the hippocampus of rats subjected to the western diet (WD) and forced physical activity (PA), as compared the control and rats fed with WD. Our results provide contribution to the understanding of changes in brain structure and function induced by western diet and physical activity. This research is supported by the National Science Center 2015/19/D/NZ7/02408.

16. Quantitative assessment of Enterococcus faecalis in gut microbiota in two strains of laboratory rats fed with ketogenic diets based on fat of animal or plant origin

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The gut-brain axis is associated with biochemical signalling between the gut microbiota and the central nervous system. Ketogenic diet (KD) directs the metabolism towards fat consumption as an alternative source of caloric demand thus a state similar to starvation is created. KD is used to manage drug-resistant epilepsy in children.
The aim of this study was to test the hypothesis that the influence of ketogenic diet on Enterococcus faecalis may differ depending on the rat strain and the composition of the diet. Adult twenty male Wistar and Long Evans rats were fed with KD composed of animal fat (KDA) or plant fat (KDB). Real-time qPCR was performed to assess the number of Enterococcus faecalis in the faeces of animals after 28 days of feeding. We observed a statistically significant increase in the number of Enterococcus faecalis in the faeces of Long Evans rats after 28 days of KDA and KDB feeding. In addition, KDA feeding impacted the Enterococcus faecali differently in Long Evans and Wistar strains. In conclusion, our results show that the effect of KD on the amount of Enterococcus faecali depends on the composition of the diet and rat strain.

17. The effect of short- and long-term treatment with NMDA receptor antagonist on the activity of cytochromeP450 in rat liver

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Cytochrome P450 (CYP) enzymes are engaged in the metabolism of endogenous and exogenous substances. Hepatic CYP activity is controlled by the neuroendocrine system. The hypothalamus has glutamatergic innervation and expresses various glutamate receptors. However, their role in hormonal regulation of CYP is not known. The aim of this study was to determine the effect of short- and long-term treatment with CP-101,606 (selective GluN2B subunit NMDA receptor antagonist) on the activity of cytochrome P450 in the liver. Male rats were administered intraperitoneally CP-101,606 (20 mg/kg) for five days or three weeks. The activities of cytochrome P450 isoenzymes in liver microsomes were measured as a rate of testosterone hydroxylation in specific positions (HLPC). The obtained results showed that five-day administration of CP-101,606 caused a decrease in the activity of CYP2A, 2B, 2C11 and CYP3A, while chronic treatment exerted no significant effects on the activities of these CYP enzymes. Short, but not long-term treatment with CP-101,606 down-regulates cytochrome P450 enzymes. The obtained results indicate a novel neuroendocrine mechanism of cytochrome P450 regulation involving glutamate system. Further molecular studies are in progress to explain this regulation. (OPUS 12 grant no 2016/23/B/NZ7/02283, National Science Centre, Kraków, Poland; Institute of Pharmacology PAS).

EPILEPSY

18. The influence of ketogenic diet on the number of parvalbumin neurons in hippocampal formation of rats after electrical kindling

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Epilepsy is a neurological disorder accompanied by changes in nervous tissue, as the decline of GABAergic interneurons. The aim of this experiment was to verify the influence of ketogenic diet – an antiepileptic therapy with neuroprotective properties – on the number of GABAergic, parvalbumin-positive (PV+) interneurons, in the hippocampus of electrically kindled rats. Four dietary schemes of feeding with standard or ketogenic food were applied. The stimulation administered by the electrodes localized on the animal's ears was used for evoking seizures. The dissected tissue was stained immunochemically for parvalbumin, and cells were counted in the hippocampus. Although the statistical analysis did not show any significant differences, some trends in the data were observed. A slightly higher average number of PV+ cells, as well as the least decline of cells' number in comparison to control group, was observed in the hippocampus of rats receiving the ketogenic feed only during the electrostimulation. The lack of statistically significant dependences can suggest that ketogenic diet has no prominent influence on PV+ cells, however the observed trends may indicate its neuroprotective properties in case of application only during electrostimulation. Nevertheless, to confirm the neuroprotective influence of ketogenic diet, further investigation needs to be carried out.

19. Analgesia induced with cerebellar stimulations and blockade of peroxisomal proliferator-activated γ-receptors in kindled rats

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Antiepileptic effects induced with cerebellar transcranial direct current stimulation (TDCS), and the role of peroxisomal proliferator-activated γ-receptors (PPARγ) in its development has been shown (Godlevsky, Pervak, 2017; 2019). The work aimed to investigate pain reactions under conditions of cerebellar TDCS and blocking PPARγ with bisphenol A diglycidyl ether (2,2'-[(1-methylethylidene) bis(4,1-phenyleneoxymethylene)] bis-oxirane (BADGE, 100.0 mg/kg, i.p.). All investigations performed on rats with the kindling syndrome induced by i.p. injections of pentylenetetrazol (PTZ; 30.0 mg/kg daily, for three weeks), and pain tests undertaken in 30.0 min after TDCS and in 60.0 min after BADGE administration. The latency of painful reaction in the hot plate test significantly increased (by 27.2% on average P <; 0.05 vs. control) after transcranial stimulation (600 μA, 10.0 min, anode on the skull surface) oriented to the cerebellar cortex. TDCS performed after BADGE administration increased the latency by 11.7% (P >; 0.05 vs. control). In tail pinch test averaged score of painful reaction decreased after TDCS by 35.2% (P <; 0.05), while being performed after BADGE administration it exceeded control value by 13.2% (P >; 0.05). Gained data are in favor of the analgesic effects caused by cerebellar TDCS, which at least mediated via PPARγ.

20. Neoangiogenesis as a mechanism of chemical kindling seizures development

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The antiseizure effectiveness of axitinib – specific blocker of tyrosine B kinase established on the kindling seizures model (Chubach et al., 2015) assumes participation of neoangiogenesis in chronic brain epileptization. The aim of the work was confined to investigation the presence of newly created vessels in brain cortex of kindled rats. Kindling was induced via daily subthreshold pentylenetetrazol (PTZ, 30.0 mg/kg, i.p.) injections during three weeks. Brains for histological investigations were got from rats responded with generalized clonic-tonic fits to each of the three last PTZ administrations. Control animals were injected i.p. with 0.9% NaCl solution. Region of interest investigated between 2.0 to -1.5 mm anterior and posterior, relative to bregma. Six microscopic fields-of-view (each covering an area of about 0.50 mm2) in the region of interest at 40× to 200× magnification wereanalyzed. Gained results revealed the presence of characteristic buds of vessel growth in neocortical regions of fully kindled animals, while such changes were absent in the brains of control animals ($P < 0.01$). Hence, neoangiogenesis, promoted by the accumulation of vascular endothelial growth factor, increased permeability of the brain-blood barrier, which might be necessary for chronic epileptization of the brain, induced via PTZ-induced kindling.

21. Genetic variants of CYP2C9, CYP2C19, CYP3A4 among children of Ukraine suffering from drug-resistant epilepsy

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The aim of the research was to study the frequency of genetic polymorphisms - CYP2C9, CYP2C19, CYP3A4 in children with drug-resistant epilepsy (DRE) and to determine their potential role, as well as the role of other factors in the development of pharmacological resistance. Genotyping of CYP2C9 * 2, CYP2C9 * 3, CYP2C19 * 2, CYP3A4 * 1B by the method of allele-specific PCR was performed in 83 children and adolescents, suffering from DRE. Results: Alleles of genes that provide the slowing down of AED metabolism - CYP2C19 * 2 in 39.76%; CYP2C9 * 2 and CYP2C9 * 3 for 20.48%; CYP3A4 * 1B at 12.05%; a combination of these polymorphisms was found in 10.84% of children suffering DRE. In our experimental model of DRE, chronic administration of the inhibitor (Sultiame) and activator (Carbamazepine) of the enzyme system of cytochrome P450 was used against the background of the epileptic status caused by multiple corneal kindling. Prior chronic administration of Sultiame increased and Carbamazepine decreased the anticonvulsant effect of Lamotrigine. The results of genetic and experimental studies allow us to predict the response to the use of various AEDs, increase the effectiveness and safety of treatment.

22. Differential utilisation of ketone bodies in hippocampus and cerebral cortex of mice fed with ketogenic diet

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The high fat, low carbohydrate ketogenic diet (KD) has been shown to be effective in managing drug-resistant epilepsy and other brain diseases. The rationale for the use of KD is based on its neuroprotective properties, but mechanisms responsible for these effects are only partially explained. The aim of this study was to evaluate how the composition of KD affects the cerebral utilization of ketone bodies (KB), the additional energetic fuel for neurons during KD. 9-weeks-old male mice were divided into three groups and fed with standard rodent chow (SD - control) or one of two differently composed ketogenic chows (KA, KP) for 4 subsequent weeks. KDs were isocaloric and had a similar ketogenic ratio (4.2:1) but were composed of fat of either animal (KA) or plant origin (KP). Western blotting was employed to evaluate the level of ketone body transporter (MCT1) and the marker of ketones utilisation (OXCT1) in hippocampus and frontal cortex. The level of MCT-1,was upregulated by both KDs in hippocampus, but

not in the frontal cortex. Expression of OXCT1 was increased in hippocampus by KA, without changes in the cortex. The data suggest that hippocampus poses a higher ability to transport and metabolize KB than cortex.

23. Methyl-CpG binding domain 3 promoter activity in a rat model of seizure evoked by intraperitoneal injection of pentylenetetrazol (PTZ)

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Animal models for seizures and epilepsy have played a fundamental role in advancing our understanding of basic mechanisms underlying epileptogenesis and epilepsy. During epileptogenesis and epilepsy, several changes occur, including alterations in gene and protein expression. Methyl-CpG binding domain 3 (MBD3) protein is a reader of DNA methylation marks which changed its expression in epileptogenesis. The aim of this study was to determine changes in MBD3 protein expression after acute seizure in the rat brain. Single intraperitoneal injection of pentylenetetrazol (PTZ, 40mg/kg) was used to evoke tonic-clonic seizure in rats (n=16). Control rats (n=16) were injected by saline. Animals were sacrificed in selected time points: 1h, 4h, 8h and 24h after injection. Changes in MBD3 protein level were examined in the hippocampus, entorhinal and somatosensory cortex using Western Blot with anti-MBD3 antibody, whereas changes on RNA level were examined using RT-PCR. Western Blot analysis showed an increased level of MBD3 protein in the somatosensory cortex 4h after PTZ injection. The PTZ did not affect MBD3 protein expression in the hippocampus and entorhinal cortex. No differences were observed in RNA level. Thisresults showed that seizures influence MBD3 protein expression and therefore MBD3 may play important role in epileptogenesis or epilepsy.

NEURODEGENERATION

24. Neurolemmocytes reaction after peripheral nerve transplantation

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The significance of damaged peripheral nerves functions restoring problem is important, because peripheral nerve injuries are more common in young working age. The aim of our research is electron microscopic examination of nerve fibers regeneration after neuroplasty and correction with Lipin. Experimental animals are divided into: control group - 1, neuroplasty after injury (2 cm defect) without pharmacotherapy - 2; the same with pharmacotherapy - 3. Lipin was administered (16-18 mg/kg) subcutaneously in two weeks after neuroplasty daily for 10 days. Electron microscopy examined the distal segments of the damaged tibial nerve in 12 weeks after neuroplasty. Lemocytes with manifestations of myelin destruction, partly lysed cytoplasm are detected after neuroplasty. The amount of new formed fibers is insignificant. The study of lemocytes after neuroplasty with Lipin correction indicates that the number of newly formed myelin fibers is increased. Small myelin fibers on transverse sections prevail, they are surrounded by active lemmocytes, as evidenced by the presence of a well-defined granular endoplasmic reticulum and ribosomes, the nuclei contain predominantly euchromatin. Thus, the study shown that the usage of Lipin in the conditions of peripheral nerve plastic activates biosynthetic processes in lemmocytes and contributes to the myelination of newly formed fibers.

25. The Involvement of Aryl Hydrocarbon (AHR) and Constitutive Androstane (CAR) receptors in DDE Neurotoxicity

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Dichlorodiphenyldichloroethylene (DDE) is the toxic compound belonging to organochlorines and it is the most stable metabolite of DDT. DDT was previously commonly used worldwide as pesticide in agriculture but nowadays it is still exploit in controlling disease-vectors responsible for malaria and zika virus diseases. Population studies suggest that the exposure to DDE may be related to the occurrence of mental and psychomotor retardation, impairment of cognitive skills, autism and attention deficit and hyperactivity disorder (ADHD)-like behaviors as well as Alzheimer's and Parkinson's diseases. The results of the present study showed that p,p'-DDE- and o,p'-DDE (both 10 μM) induced LDH release and caspase-3 activity in primary neuronal cells, and selective AHR and CAR antagonists decreased these effects. In addition to apoptotic and neurotoxic effects, DDE isomers affected mRNA and protein expression levels of AHR, ARNT and CAR. The immunofluorescence labeling and confocal microscopy revealed that AHR and CAR receptors were localized at neocortical cells and the exposure to p,p'-DDE significantly increased AHR and CAR staining. Therefore, we identified new mechanisms of neurotoxic action of DDE which, in addition to inducing apoptosis involved AHR and CAR signaling. Acknowledgement: This study was supported by the National Science Center grant no. 2015/19/B/NZ7/02449.

26. Novel transgenic mice model to study presymptomatic phase of Parkinson's Disease: attempt of CRISPR/Cas9 exploitation for genetically evoked progressive degeneration of noradrenergic neurons

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Parkinson's Disease (PD) is characterized by inevitable loss of dopaminergic cells, however clinical data show that noradrenergic degeneration might start before in PD. The aim of this study was to determine whether genetically evoked, selective loss of locus coeruleus (LC) neurons may negatively influence the dopaminergic system. We created two mouse models with progressive degeneration of noradrenergic system, based on deletion of Rrn3 gene encoding transcription factor TIF-IA. First, we applied the conditional inactivation of Rrn3 by the Cre-loxP system expressing Cre recombinase under DBH promoter. Mutant TIF-IADBHCre mice revealed ptosis, reduced locomotor activity and shorten life span associated with enhanced expression of various neurodegenerative markers within dopaminergic system: upregulation of micro- and astroglia, pro-inflammatory proteins, enhanced level of oxidative stress, and changes in many transcripts related to PD. To omit the problems associated with targeting the peripheral noradrenergic cells, in a second model a Cre-dependent lentiviral vector carrying the Rrn3 deletion created by the CRISPR/Cas9 system was directly delivered to LC of DBHCre mice (study in progress). If we provide additional evidences that prolonged, selective noradrenergic degeneration impairs dopaminergic system functioning, mice with ongoing neurodegeneration of LC neurons may became a valuable tool for study presymptomatic phase of PD. NCN: 2017/25/B/NZ7/02406

27. Synthetic neuromelanin as a trigger of inflammation in the brain – new mouse model of Parkinson's disease

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Parkinson's disease (PD) is a neurodegenerative disease that is an increasing threat to an aging society. The idiopathic form of PD accounts for over 90% of all cases, and the current etiology is still unknown. One of the reasons hindering research on this form of PD is the lack of an appropriate animal models. Among mouse models

of the disease, those based on the administration of neurotoxins such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) or 6-hydroxydopamine (6-OHDA) to the substantia nigra (SNpc) or striatum are predominantly used. In these models, there are metabolic disturbances causing oxidative stress in the SNpc or striatum, which ultimately leads to the death of dopaminergic neurons. However, the models used so far have serious limitations, most of all they do not fully reflect the processes occurring in the course of the disease and do not consider the involvement of inflammation in the etiology and pathogenesis of PD. In this study we show that the administration of synthetic neuromelanin, which activates microglia, induces the inflammation and may be involved in degeneration of dopaminergic neurons. Neuromelanin under physiological conditions acts as a neuroprotector, however, released from dying dopaminergic neurons is an important factor activating microglia and causing neuroinflammation. Since one of the causes of Parkinson's appear to be the death of dopaminergic neurons overloaded with neuromelanin and consequent pathological activation of microglia, the use of synthetic neuromelanin reflect the natural pathological processes occurring during the development of the disease. Project was supported by National Scientific Center in Poland 2015/17/B/NZ5/00294 and 2019/03/X/NZ4/00115

28. Coordinated bi-directional trafficking of synaptic vesicle and active zone proteins in peripheral nerve fibers

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Synaptic transmission is mediated by neurotransmitters that are stored in synaptic vesicles (SV) and released at the synaptic active zone (AZ). While in recent years, major progress has been made in unravelling the molecular machinery responsible for synaptic vesicle docking, fusion and exocytosis, the mechanisms governing active zone protein and synaptic vesicle trafficking at the active zone still remain a mystery. We performed stop-flow nerve ligation to examine axonal trafficking of endogenous AZ and SV proteins. Rat sciatic nerves were collected 1h, 3h and 8h post ligation and processed for immunohistochemistry and electron microscopy. All animal procedures were approved by the Lund University Local Ethical Committee, following NIH guidelines. We observed a time dependent accumulation of both AZ and SV proteins at both proximal/distal or proximal only (Rab3) ligation sites and noticed a high level of colocalization between SV and AZ proteins, present on same synaptic vesicles. Our data uncovers a robust bi-directional, co-trafficking of SV and AZ proteins in peripheral nerves and implies that any pathological disruption of axonal trafficking will not only impair trafficking of newly synthesized proteins to the synapse but will also affect retrograde trafficking, leading to neuronal dysfunction and likely neurodegeneration.

29. Itaconic acid causes a mitochondrial dysfunction in the cells of brain tissue

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Itaconic acid (IA) is an anti-inflammatory metabolite produced by LPS- stimulated macrophages. The function of IA is extensively studied in immune cells but its effects on the nervous tissue are not investigated, though there is evidence that IA can be synthesized by murine microglia. IA functions are mostly studied in bone marrow-derived macrophages. IA has been shown to inhibit succinate dehydrogenase and to activate the NRF2 pathway. The aim of this study was to investigate whether IA has any effects on the mitochondria of brain tissue. We studied mitochondrial oxygen consumption rates (OCRs) using high resolution respirometry in mitochondria isolated from the forebrains of adult rats and in permeabilized cerebellar granule cells (CGCs) isolated from 7 days old rat pups. The OCRs were recorded with I-st and II-nd complex substrates in the presence of 1-5mM IA. We found that 1-5mM IA decreased mitochondrial respiratory chain Complex-I-driven OCR by 44-62 % and Complex-II-driven OCR by 35-62% in isolated brain mitochondria. 1-5 mM IA decreased maximal ADP stimulated respiration in CGCs by

40-70% respectively. We also show that IA sensitizes brain mitochondria to calcium-induced opening of the mPTP. These results indicate that IA causes mitochondrial dysfunction in cells of the brain tissue.

30. Beneficial role of sulforafane in perinatal hypoxic ischemic insult

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Hypoxic-ischemic insult (HI) is one of the most severe complications during parturition, the most affected organ is brain with neurodevelopmental impairments. There are limited therapeutic possibilities till present. We tested the effect of activation of Nrf2 transcription factor by Sulforafane (SFN) in protecting brain against HI damage. Animal model of HI injury of seven days old Sprague -Dawley rats were employed and divided into four groups: Sham, Sham with SFN, HI and HI with SFN. SFN was applied 24h prior (5mg/kg,ip) to exposed left common carotid artery (anaesthetized), then ligated and incubated in a hypoxic chamber (pO2 8%) for 90 min in HI groups. Glucose uptake was evaluated by PET imaging with 18F-FDG, after 24hr, 7 days and 5 weeks after HI insult with total activity. Analysis of activity was performed using PMOD software and Schiffer rat brain MR atlas. We have observed significant changes in HI injury namely hippocampus and surrounding cortex in PET imaging and partially thinner cortex and larger cerebral ventricles in histology. The pretreatment with SFN led to significant protection in hippocampus after 24hr of insult as represented by both normalizations of interhemispheric ratio and increase in 18F-FDG activity.

31. Neuroprotective effects of daidzein derivative on hydrogen peroxide-induced apoptosis in SH-SY5Y cells

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Progressive neuronal loss has been associated with many neurodegenerative diseases. Cell death can be induced by chronic brain inflammation accompanied by excessive production of reactive oxygen species. Therefore, this study is investigating the neuroprotective properties of daidzein derivative use of which might serve as a potential treatment to slow down neurodegeneration. SH-SY5Y cells were differentiated for seven days using 10μM of retinoic acid. Subsequently, cells were pre-incubated for 30 minutes with daidzein derivative and then the neuronal loss was induced by 50μM of hydrogen peroxide for 24 hours. Cell viability was assessed by XTT assay. Neuronal apoptosis was detected using FITC Annexin V Apoptosis Detection Kit with propidium iodide. Caspase 3/7 activity was measured using Caspase-Glo® 3/7 Assay System. Bcl-2 expression was assessed using Bcl-2 Human ELISA Kit. Seven days differentiation of SH-SY5Y cells using retinoic acid induced morphologic change from epithelial-like shape to mature neuron morphology. The daidzein derivative significantly diminished neuronal death induced by hydrogen peroxide. The reduced caspase 3/7 activity and induced expression of Bcl-2. Daidzein derivative protects differentiated SH-SY5Y neuronal cells against hydrogen peroxide-induced cell death. Mechanism of neuroprotective activities includes reduction of caspase 3/7 activity and increased expression of Bcl-2.

32. Administration of Mesenchymal Stem Cell (MSCs) into cerebrospinal fluid as a new tool to study brain encephalopathy

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Encephalopathy is brain disturbance caused by e.g. virus infections, mechanical disturbances, drug poisoning or reduction of oxygen in the blood combined with reduced blood flow. All of mentioned factors might lead to damage of brain tissue, increased local inflammatory response and seizures. Previously known clinical therapies allows only for reducing the degree of damage (hypothermia) or alleviating complications (drug treatment). Despite a lot of research and attempts using new therapeutic approaches, there is still no effective treatment that enable the regeneration of damaged brain tissue. In this study we administered mesenchymal stem cells (MSCs) into cerebrospinal fluid of NOD-SCID mice. We have optimized dose of injected cells to monitor distribution of MSCs and safety of the procedure. This data can be used in various brain damage models, like hypoxia-ischemia encephalopathy (HIE), chronic-traumatic encephalopathy (CTE) or metabolic encephalopathy (ME). We believe that our research will lead to a better understanding of central nervous system and will to development of more effective therapies. Project was supported by National Scientific Center in Poland 2018/31/B/NZ3/01879.

33. Seeding mechanisms of fibrillar tau repeat peptide aggregates

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Neurofibrillary tangles are pathological hallmarks of Alzheimer's disease (AD), but the prion-like propagation of tau aggregates may underlie AD progression. Deciphering the minimal region in the tau microtubule-binding domain that acts as the locus for tau fibrillization is, therefore, essential to comprehend the prion-like property of tau. Phosphorylation at Ser202/Thr205/Ser208 readily fibrillizes tau; however, whether tau phosphorylation induces prion-like properties and mechanisms by which prion-like tau induces native tau aggregation remains elusive. Herein, we examined the effect of peptide aggregates of repeats 1-4 (R1-R4) of tau microtubule-binding domain on intracellular tau phosphorylation and aggregation in biosensor (BS) cells expressing aggregation-prone, P301S tau. We found that R2 and R3, but not R1 and R4, aggregated into β-sheet-rich fibrillar aggregates under *in vitro* conditions. Unlike R1 and R4, aggregates of R2 and R3 seeded the aggregation of intracellular P301S-Tau in BS cells. Additionally, aggregates of both R2 and R3 peptides induced P301S-Tau phosphorylation at Ser262 and oligomerization in BS cells. Our data link R2 and R3 regions to the prion-like nature of tau and may suggest the role of R2 and R3 on increased phosphorylation of neurofibrillary tangles in progressive AD and other tauopathies.

34. Similarities and differences in the responses of wild type and triple synuclein knockout mice to sub-chronic MPTP treatment

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Aggregation of alpha-synuclein, with formation of toxic intermediates, and the loss of normal alpha-synuclein function are believed to contribute to the dysfunction of dopaminergic neurons of the substantia nigra (SNpc) in Parkinson's disease and plays a pivotal role in MPTP-induced pathology. The synuclein family consists of three closely related proteins, alpha-synuclein, beta-synuclein and gamma-synuclein, that can compensate, at least partially, for the loss of a family member function. We used a TKO mouse line lacking all three synucleins to study the role of the synucleins in the MPTP-induced pathology. Animals received daily i.p. injection of 30 mg/kg MPTP or a vehicle for five consecutive days. Three weeks after the last injection comparative analysis revealed that MPTP treatment causes similar extend of SNpc dopaminergic neuron loss, similar changes in dopamine metabolism in

the striatum, similar behaviour in basic motor tests, and only changes of some gait parameters assessed using NoldusCatWalk system were different for WT and TKO mice. In conclusion, we demonstrated that members of the synuclein family are dispensable for the manifestation of major effects of sub-chronic MPTP treatment. Behavioural studies were funded by RFBR grant 19-315-90049, HPLC analysis - by RFBR 18-04-00515, morphometric analysis - by RSF 19-14-00064.

35. Histone deacetylase – new potential therapeutic target in the treatment of AD-related pathology – study in the APP NL-F knock-in mice

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Alzheimer's disease (AD) is a chronic neurodegenerative disease, which is associated with learning and memory impairment in the elderly. In a number of recent studies, histone deacetylase (HDAC) has been found to be a novel promising therapeutic target for neurological disorders, particularly for AD. Aim: The present study aims to biochemically characterize new knock-in mouse model of AD, in particular in case of the expression of brain Hdac1, Hdac2 and Dnmt1 genes. To address this issue, at 3 months of age, female mice (AppNL-F knock-in and control C57BL/6J mice) were killed by rapid decapitation. Hippocampal and frontal cortices were dissected and stored at -80°C until biochemical analysis. Using qRT-PCR we measured mRNA expression of Hdac1, Hdac2 and Dnmt1 in both brain areas. The mRNA expression of Hdac1, Hdac2 and Dnmt1 was significantly higher in hippocampus in 3 months of age APPNL-F females, in comparison with control C57BL mice, while where was no changes in mRNA expression of all analyzed genes in frontal cortex. Together our findings support feasibility of using APP NL-F mice as AD model and demonstrated the disturbances in expressions of analyzed genes. Supported by the grant no. JPND/13/2019 National Centre for Research and Development

36. Collateral ganglionic degeneration: novel neuropathological phenomenon in the somatosensory system

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Retrograde axonal transport of intraneural injected adriamycin has been utilized to selectively denervate specified target tissues. These experiments were aimed at the study of neuropathological changes of C-fiber primary sensory neurons following adriamycin treatment. Adriamycin (40 µg, 2 µl) was injected into the exposed sciatic nerve of adult male Wistar rats under general anesthesia. Seven hours to 40 days later the L4-L5 dorsal root ganglia (DRGs) and the spinal cord were removed and processed for histochemical and immunohistochemical analyses.The appearance of adriamycin in neurons and satellite cells was observed already 7 hours after intraneural injection, followed by a gradual decrease in the number of TMP+, CGRP+ and IB4+ neurons from the 9th day after the treatment. The ATF3-based quantitative morphometry revealed that DRG neuronal degeneration ensued 15–21 days after the treatment and affected DRG neurons relating to untreated nerves. Similarly, depletion of neuronal markers was observed in the spinal dorsal horn in somatotopic areas unrelated to the treated nerve. These findings may be explained by collateral damage to adjacent DRG neurons relating to intact peripheral nerves. We propose the term collateral ganglionic degeneration to denote this phenomenon. This study was supported by grants from GINOP (NKFIH GINOP-2.3.2-15-2016-00034).

37. The effects of acute and chronic treatment with an agonist of the zinc-sensing GPR39 receptor or memantine on episodic-like and spatial memory in healthy and GPR39 knock-out mice.

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Zinc ions (Zn2+) regulate neuronal activity in several brain structures. The neuromodulatory effects of Zn2+ include regulation of synaptic plasticity and memory functions. Mounting evidence also shows that Zn2+ is a crucial factor in the development of toxic forms of amyloid beta protein and subsequent Alzheimer's dementia (AD). Therefore, efforts to pinpoint the mechanisms underlying Zn2+-dependent cognitive functions might aid AD research. One of the most understudied targets in this regard is the Zn2+-sensing metabotropic receptor (GPR39). In this study we compare the impact of a GPR39 agonist (T-CG 1008) on episodic-like (ELM) and spatial memory (SM) with memantine (MEM) – a drug used to slow down AD progression. Acute application of 10 mg/kg of T-CG 1008 to old WT mice reversed an age-related deficit in two of three ELM components. The same treatment had no effects on ELM deficits caused by consolidation interference in adult WT mice. We also did not observe any effects of acute or chronic MEM (5 mg/kg) on ELM or chronic T-CG 1008 on ELM or SM. However, chronic MEM did cause a SM deficit in GPR39 KO mice. This study provides first evidence for a GPR39 role in declarative memory.

38. Molecular rehabilitation and neuro-protective role of piperamide derivative (D4) on the neurodegeneration upstream pathways of Late-onset proteinopathies

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NF-kB translocation is the key point in upstream neuroinflammatory pathways leading to the inflammatory response of the innate immune system. The NF - kB complex consists of structural homolog subunits, including c-Rel, RelB, p52, p65, and p50. Among the p65 subunit has an important function of NF-kB translocation and DNA binding. NF-kB translocation may occur due to acetylation and phosphorylation LYS 310 and SER311 amino acids in chain A of the p65 subunit in response to IKK-α/β activity. NF-kB translocation inhibitors can void the NF-kB complex to shift into the nucleus through inhibiting IKK-α/β directly by binding to its active site or bind to LYS 310 and SER311 to protect them from acetylation and phosphorylation and protect NF-kB complex in the inactive form inside cytosol. In this study, we have developed an NF-kB translocation inhibitor, D4 and have performed various in silico, in vitro and in situ studies on the anti-neuroinflammatory function of D4. It showed the ability to inhibit IKK-α/β in both genome and proteome levels and protect LYS310 of the p65 subunit of NF-kB from the acetylation process, therefore, it can be considered as a promising anti-neuroinflammatory agent with function on the upstream process of inflammatory pathways.

39. The effect of UV filters: 4-methylbenzylidene camphor (4-MBC), octyl methoxycinnamate (OMC) and benzophenone-3 (BP-3) on neuronal and astroglial cells in primary cultures and the influence of BP-3 on apoptotic marker in vivo

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4-MBC, OMC and BP-3 are UV filters commonly used in cosmetics, but little is known how they affect the central nervous system. While neurons are cells most vulnerable to damage, many studies implicate that astroglial damage can trigger neuronal dysfunction and neurodegeneration. This study aimed to evaluate the effect of mentioned compounds on neuronal and astroglial cells viability. Cells were isolated from rodents, cultured in appropriate media and exposed to each UV filter (0,1-100 μM) for 48 or 72 hours. The level of the extracellular lactate dehydrogenase (LDH), cell viability in MTT reduction test and caspase-3 activity were estimated. BP-3 (100 mg/kg) was also administered dermally to rats during pregnancy and to offspring. Caspase-3 was quantified using Western blot and immunofluorescence staining.Results demonstrated significant increase of extracellular LDH level in both cell types after exposure to 4-MBC and OMC (100 μM). Also decrease of viability in MTT test in neurons and elevated caspase-3 activity in astrocytes were observed. BP-3 had less cytotoxic effect in vitro and increased caspase-3 expression in vivo in males, but not in females. In summary, the tested UV filters can damage neurons and astrocytes, but they exert such effects at relatively high concentrations. This research was supported by the National Science Centre grant (DEC-2014/15/B/NZ7/00892).

40. Post-stroke Metformin Treatment Using Permanent Middle Cerebral Artery Occlusion in Rats

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Experimental studies when transient middle cerebral artery occlusion (MCAO) is used, consistently suggest post-stroke treatment of metformin as beneficial not only in reducing acute infarction, but also in promoting long-term functional recovery. Experiments were approved by the Animal Experiments of Hiroshima University. Adult male Wistar rats were used (N=19, 194–290g, 7 weeks). Rats were divided into the following groups, received intraperitoneal metformin injections (50 mg/kg/day) (metformin group) or equal volumes of saline injections (control group) after permanent MCAO and sacrificed after 48 or 120 hours. Neurological deficits were based on Rotarod test. Image J were used to measure the infarct area in each section. Stroke areas were 28.6% in control group (N=5) and 26.3% in metformin group (N=4) after 48 hours (p>;0.05), respectively. Stroke area was significantly lower in metformin group (N=5) than in control one (N=5) (15.9%vs.20.8%) after 120 hours (p=0.03). Rats with metformin treatment remained longer on the rotarod longer than rats of control group after 120 hours (27.8±11.8 sec.vs.8.8±2.7 sec) (p<;0.05). Post-stroke metformin treatment reduced area of stroke and improved neurological status of rats compared to control group after 120 h, although it was not found in both groups after 48 h.

NEUROPHYSIOLOGY

41. Relaxin-3/RXFP3 signalling in the PVN inhibits magnocellular neurosecretory neurons via M-like current activation and contributes to binge eating behaviour

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Relaxin-3 (RLN3) is an orexigenic neuropeptide expressed in the brainstem nucleus incertus. RLN3 stimulates food

intake by activation of RXFP3 receptor in the hypothalamic paraventricular nucleus (PVN). Moreover, RLN3/RXFP3 signalling has been implicated in the binge-eating disorder (BED) – the most common eating disorder worldwide, affecting women twice as frequently as men.This study focuses on RLN3/RXFP3 signalling in the rat PVN and its potential role in binge-eating behaviour.This was achieved using ex vivo patch-clamp recordings, single-cell reverse-transcription PCR, tract-tracing and immunostaining studies, as well as behavioural testing on rat model of binge-eating behaviour.The pharmacological blockage of RXFP3 in the PVN of female rats prevents the occurrence of binge-eating behaviour. Moreover, RXFP3-mediated inhibition of PVN magnocellular neurons depends on an M-like potassium conductance in male and female rats. No sex differences were observed in the RXFP3-mediated inhibition of PVN neurons. Notably, higher intra- and peri-PVN RLN3 fibre densities observed in female compared to male brains may constitute an anatomical substrate for sex differences in BED susceptibility. These data provide evidence for important physiological role of PVN RLN3/RXFP3 signalling in governing food intake and its involvement in binge-eating behaviour. Funding: NSC, Poland UMO-2017/24/T/NZ4/00225 and UMO-2016/21/B/NZ4/00204; MSHE, Poland 0020/DIA/2014/43.

42. Control of midbrain dopaminergic neuron activity by brainstem nucleus incertus – electrophysiological and optogenetic studies on urethane anesthetized rats

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Dopaminergic (DA) neurons localized in the ventral tegmental area (VTA) and substantia nigra pars compacta of the mammalian brain are involved in the control of motivation and motor functions. Based on our preliminary results we hypothesized that nucleus incertus (NI) – brainstem structure implicated in stress response, may control DA neuron activity. Therefore, the aim of current study was to verify this hypothesis using single-unit extracellular recording of DA neurons' activity combined with targeted optogenetic stimulation of NI-VTA neural pathway. Prior to the main experiment animals (Sprague Dawley rats) received stereotaxic injections of viral vectors: CAV2-Cre (into the VTA) and AAV-DIO-Chrimson-tdTomato (into the NI), resulting in expression of Chrimson (a red light-sensitive cation channel) and orange fluorescent protein selectively in NI neurons that innervate VTA. Two weeks later, using red laser light (635 nm) delivered to the brain with fiber optics, NI was optogenetically stimulated and extracellular responses of the midbrain DA neurons were recorded. Obtained results revealed that the selective stimulation of NI neurons innervating VTA significantly inhibit fraction of DA neurons. These results, and observed, NI originating tdTomato-positive fibers in VTA, strongly suggest the existence of neuronal pathway that directly inhibits VTA DA neuron activity.

43. Extracellular domain intersubunit interaction of aromatic residues αF14 and βF31 substantially modulates GABAAR gating

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GABAA receptors (GABAARs) are pentameric ligand-gated ion channels that play a crucial role in adult brain inhibition. Local intersubunit interactions between charged amino acids stabilizing the ligand binding are well described but the importance of other intersubunit interactions via non-charged residues is poorly understood. Cysteine substitution was used in two aromatic residues αF14 and βF31 located at the top of α1β2γ2L GABAAR extracellular domain. Whole-cell current responses to saturating [GABA] and single channel activity were recorded from single αF14C or βF31C mutant and a αF14CβF31C double mutant expressed in HEK 293 cells. Kinetic analysis of macroscopic recordings revealed marked alterations: prolongation of rise time, strong reduction of extent and speed of macroscopic desensitization and acceleration of deactivation for αF14C and β31C mutants but far smaller effects for the double mutant relative to WT. Disruption of a disulfide bridge with DTT in αF14CβF 31C mutant resulted in a phenotype closer to singly-mutated receptors. Single-channel analysis and modeling with macroscopic model simulations indicated major effects of mutations on all gating steps: preactivation, opening/closing and desensitization with a minor impact on αF14C binding. These novel results show a critical role of αF14/βF31

intersubunit interaction in GABAAR activity. Supported by NCN grant MAESTRO2015/18/A/NZ1/00395.

44. The influence of SNPs in MKLs genes on neurons function

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Megakaryoblasticleukemia 1/2 proteins (MKL1, MKL2) are Serum Response Factor (SRF) transcriptional co-activators, involved in remodeling of dendritic spines morphology that harbor excitatory synapses in the brain. Since neuronal development is controlled on transcriptional level, single nucleotide polymorphisms (SNPs) in transcription factors or signaling pathways often result in neurodevelopmental disorders. In our study, we investigated SNPs impact on MKLs genes neuronal function. We introduced point mutation in MKL1-, MKL2-Flag-tagged constructs (5 and 6 mutations, respectively) by site-directed mutagenesis. We tested transcriptional properties of modified plasmids by luciferase reporter system. Transcriptional activity and localization of control/ mutated MKLs constructs was analyzed in primary cortical cultures in basal condition and after brain-derived neurotrophic factor (BDNF) stimulation. MKLs overexpression in neurons elevates SRF-driven transcription, enhances its stimulation by BDNF and changes the cellular localization of MKLs-Flag constructs, from cytoplasmatic to more dispersed in MKL2, reverse to MKL1. We showed that the cysteine conversion to arginine at position 647- MKL2, proline to leucyne at position 244- MKL1 affects the subcellular localization of the protein and reduces its transcriptional properties compared to WT MKLs. Altogether our results demonstrate that SNPs in MKLs gene may affect protein function. This work was supported with NCN grant: 2019/33/B/NZ4/01450.

45. Menthol changes intracellular signaling pathways by activation of adrenergic-like receptors and protein kinase A in Periplaneta americana

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Menthol is an essential oils component; its action on TRPM8 receptors is well known, although it also appears to have other effects on insects. We verified the hypothesis, that menthol changes the intracellular signaling pathways, acting on octopamine (adrenergic-like) receptors in Periplaneta americana. In extracellular recordings from the dorsal nerve cord, menthol decreased the response to mechanical stimulation as well as spontaneous activity of the nerve. In in-situ microelectrode recordings from DUM neurons, menthol caused deep hyperpolarization, followed by a decline in the generation of spontaneous action potentials. The same effect was observed after octopamine; the effect of menthol and octopamine was not observed after previous administration of phentolamine. Moreover, menthol increased free calcium ion level in isolated DUM neurons, which was reversed by protein kinase A inhibitor. Menthol had no direct effect on acetylcholinesterase (AChE), but it increased the efficiency of bendiocarb in inhibiting AChE. Potentiation of menthol was abolished by antagonists of octopamine receptor – phentolamine and inhibitor of protein kinase A. Our results clearly indicate, that menthol can change functioning of the nervous system through activation of octopamine receptors and then, protein kinase A pathway. This work was supported by the National Science Center, Poland [NCN 2014/15/N/NZ9/03868].

46. Brain state dependent changes in dopaminergic neurons' responses to the aversive stimuli

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The ventral tegmental area (VTA) constitutes the stem of reward and motivation system in the mammalian brain. For a long time, it has been assumed that dopaminergic neurons respond to reward and aversive stimuli homogeneously across the entire population – with increase or decrease of their activity respectively. However, recent studies revealed a subpopulation of VTA dopaminergic neurons that is excited by the aversive stimuli. Given that both the level and the pattern of VTA dopaminergic neurons' activity depends on ongoing brain states under urethane anaesthesia, we put forward a hypothesis that responses of VTA dopaminergic neurons to the aversive stimuli are also dynamically modulated. We conducted in vivo, extracellular recordings of dopaminergic neurons' responses to the electrical footshock applied to the urethane anaesthetised rats. Dopaminergic neurons were juxtacellularly-labelled or optogenetically tagged. Consistently with previous studies, we have recorded two subpopulations of VTA dopaminergic neurons – excited or inhibited by the aversive stimuli. Interestingly, we have observed VTA dopaminergic neurons that are inhibited during REM-like brain state but change the response to excitation during NREM-like brain state. This study extends the previous hypothesis about two distinct subpopulations of VTA dopaminergic neurons displaying opposite responses to the aversive stimuli. Founding: grant PRELUDIUM2019/33/N/NZ4/03011.

47. The influence of pipecuronium and rocuronium bromides on LCC-channels in the nuclear membrane of cerebellar Purkinje neurons and cardiomyocytes

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The Spontaneously active Large Conductance Cationic channels (LCC-channels) are highly expressed in the nuclear membranes of cerebellar Purkinje neurons and cardiomyocytes. Ion currents through the LCC-channels in the inner nuclear membrane of cardiomyocytes and cerebellar Purkinje neurons were registered using the patch clamp method in configuration «nucleus attached» or «excised patch». Previously we have tested the effect of a number of n-choline receptor modulators (activators and inhibitors) on the LCC-channels. Among them tubocurarine, atracurium, dithylinum and neurotoxin II were the most effective. Under the influence of rocuronium and pipecuronium bromides, current through LCC-channels decreased in a dose-dependent manner. In particular, 2 mM of pipecuronium bromide reduced the current through the LCC-channels by 68 % and 55 % in the nuclei of Purkinje cerebellum neurons and cardiomyocytes, respectively. Same concentration of rocuronium bromide caused a decrease of this parameter by about 50 % in both objects. The pharmacological sensitivity of the LCC-channels in the Purkinje neurons and cardiomyocytes nuclear membranes is almost identical, indicating that there is a single population of these channels in the studied tissues. Thus, the sequence of inhibition efficiency is as follows: d-tubocurarine > neurotoxin II >dithylinum ≈ atacurium ≈ pipecuronium bromide > rocuronium bromide.

48. The role of fructose 1,6-bisphosphatase in a crosstalk between neurons and astrocytes

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Several lines of evidence suggest that a molecular crosstalk between different types of cells in the central nervous system, plays a crucial role in supporting neuronal metabolism and plasticity, which is important during formation of the longterm potentiation, an energy-demanding process required in memory consolidation. However, little is known about roles of glucose metabolism enzymes in the cross-talk between neurons and astrocytes. This study seeks to examine a role of an essential regulatory glycogenogenic enzyme, fructose 1,6-bisphosphatase 2 (FBP2), in neuronal-astrocytic crosstalk. FBP2 is a moonlighting protein and, as such, it can prevent apoptosis by binding to mitochondria, it can be also involved in supporting cells' proliferation while transported into the nucleus. Results presented here show prominent differences in quantity and activity of FBP2 between astrocytes cultured alone and co-cultured with neurons or in neuron-conditioned medium. Interestingly, these changes are probably not related to catalytic role of the enzyme. This may point to participation of FBP2 in some non-enzymatic processes in astrocytes. Obtained data suggests that the factor responsible for observed changes in FBP2 expression is transferred to astrocytes in extracellular vesicles. Both the factor and the reason of observed changes remain

unknown.

49. GABAA Receptor Binding Site Involvement in Modulation by Protons

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GABAA receptors (GABAARs) facilities inhibitory signalling in the nervous system. Receptor kinetics can be modulated by protons but molecular mechanism of this action are not fully elucidated. To find pH-sensor residues structural homology models of the α1β2γ2 receptor were built and pKa's of respective amino acids were estimated. β2E155, located at the GABA binding site, showed pKa values similar to physiological values and dependence on the receptor state, indicating possible role in modulation by pH. Kinetic properties of responses to GABA modulated by pH, mediated by WT and mutated (β2E155(C,Q,L)) GABAARs were examined using patch-clamp technique. Mutants showed distinct susceptibility to modulation by pH. Cysteine mutant exhibited WT-like pH-dependence, but lysine mutant current amplitude was not affected by pH, although the kinetics maintained some dependence on pH. Obtained results showed that mutation of β2E155 to hydrophobic residue induced an impairment of modulation by protons while in the case of the polar substitutions the protons still affected the receptor. These data indicate that the binding site area plays a role in modulation by pH, although it is not responsible for the complete effect. M.A.M. and M.M.Cz. contributed equally to the presented work. Supported by National Science Center grant 2018/29/N/NZ1/02834 (M.A.M.) and DEC-2015/18/A/NZ1/00395 (J.W.M & M.M.Cz.)

NEUROPSYCHIATRY

50. Maternal high-fat diet during pregnancy and lactation alters transcriptomes profile in the frontal cortex of adolescent offspring rats

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Evidence from studies of recent years underline that maternal unbalanced diet and obesity lead to morphological, molecular and functional changes in the offspring brain, predisposing to the occurrence of mental diseases. The goal of this study was to assess the impact of modified maternal diets on changes in offspring transcriptomes profile in the frontal cortex. Wistar rat dams were maintained ad libitum on high-fat, high-carbohydrate or mixed (rich in carbohydrate and fat) diet during gestation and lactation. Transcriptome sequencing was done in the frontal cortex of male and female offspring rats sacrificed at postnatal day 28.Functional analysis revealed that the most impacted biological processes are related to ribosomal proteins and microtubule motor activity. Genes differentially expressed in offspring exposed to high-fat diet were associated with the molecular pathways implicated in dopaminergic signaling and the etiology of Parkinson's and Alzheimer's diseases. In conclusion, maternal high-fat diet considerably alters the profile of gene expression compared to other diets. These results underscore the complexity of fetal environmental reprogramming by early maternal nutrients. This study was funded by the NUTRICIA Foundation (grant no. RG-1/2018) and grant UMO-2016/21/B/NZ4/00203 from the National Science Centre, Poland.

51. The effect of 1-methyl-1,2,3,4-tetrahydroizoquinoline (1MeTIQ) on recognition memory in rat model of schizophrenia

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In schizophrenia, positive symptoms are reduced by antipsychotics but negative and cognitive ones seem to be resistant to the pharmacotherapy. Novel object recognition test (NORT) is a tool to verify the memory impairment in animal models of schizophrenia.1MeTIQ is an endogenous substance, that exhibits neuroprotective, anxiolytic and anti-oxidative properties. Male Sprague-Dawley rats were divided into 6 groups that received injections: saline; ketamine, 1MeTIQ, 1MeTIQ + ketamine, olanzapine, olanzapine + ketamine. Using NORT, we calculated exploration times for each object and discrimination index (DI). After NORT, we decapitated animals and dissected hippocampus for further HPLC analysis of metabolism rate of monoamines. Results were compared using t-student test and one-way ANOVA, followed, when appropriate, by post-hoc Duncan's test. In T2 phase of NORT, all groups, except the ketamine-injected animals, explored the novel object significantly longer. Ketamine significantly lowered DI ($p<0.05$). In HPLC analysis, significant changes of noradrenaline metabolism rate were observed in all groups. Ketamine disrupts memory processes measured in NORT and 1MeTIQ partially improved recognition memory. Obtained data suggest that NA may be involved in hippocampal memory processes. Financial disclosures: Study was financed from the National Science Centre Grant No. 2017/25/B/NZ7/01096.

52. The influence of tryptophan metabolites – kynurenine and kynurenic acid administered at early stage of development on the behavior of adult rats

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Exposure to endo- and exogenous substances at an early stage of development, may cause changes within the brain that may persist in adulthood. Kynurenine (KYN) and kynurenic acid (KYNA) are metabolites of tryptophan. The aim of this study was to assess the effect of KYN and KYNA supplementation during early postnatal developmental period on the behavior of adult rats. Male Wistar rats were used. In first experiment, rats received KYN solution (50 mg/kg) intragastrically on postnatal days (PND) 2-21. In second experiment, experimental group received KYNA in drinking water solution (25 mg/l) starting on PND 1 until adulthood. Control groups received tap water. Behavioral tests were conducted starting on PND 49. The following tests were used: the elevated-plus maze (EPM) test, forced swimming test and locomotor activity test. Our study revealed that neither KYNA supplementation in drinking water nor intragastric KYN administration during breastfeeding period did affect the behavior of adult rats. There was no difference between control and experimental groups in the EPM, despair test and locomotor activity test. This study shows that KYN and KYNA supplementation at early stage of development does not result in behavioral changes in adult male rats.

53. Brain serotonin deficiency contribute to dominance behaviour in male and female rats

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Tryptophan hydroxylase 2 (TPH2) is a rate-limiting enzyme of brain serotonin synthesis and genetic removal of this enzyme results in central serotonin depletion. Brain serotonin manipulations are associated with central nervous system processes, including social behaviour and aggression. The goal of the current study was to examine

aggressive behaviour of male and female rats with life-long serotonin depletion. To analyze aggressive behaviour Tph2-deficient (TPH2-KO) and wildtype (WT) control rats were subjected to resident-intruder paradigm. In this experiment, an unfamiliar rat (intruder) of similar body weight, age and sex was introduced into the home cage of the individually housed resident animal. Animals were allowed to interact for 10 minutes and the number of offensive episodes was analyzed. We report that both male and female TPH2-KO rats showed more episodes of dominance behaviour as compared with WT controls. Additionally, TPH2-KO animals demonstrated significantly lower latency to the first dominance behaviour. The present study confirms the role of central serotonin in the regulation of dominance behaviour. This study was supported by the grant ERA-NET Neuron II JTC 2015 Respond and by the Statutory Activity of the Maj Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland.

54. Functionally selective activation of 5-HT 1A receptors as a potential method of treating side effects of tetrabenazine, an orphan drug in Huntington disease

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Tetrabenazine (TBZ) is useful in the treatment of hyperkinetic movement disorders and is mainly used for chorea. The mechanism by which TBZ exerts antichoreic effects is by decreasing the amount of dopamine by the avid bind to vesicular monoamine transporters and by directly blocking dopamine receptors. However, the use of TBZ has been associated with numerous adverse effects directly related to its mechanism of action, these include depression, suicidality, parkinsonism and other extrapyramidal symptoms (EPS). Since parkinsonism can be modelled in rodents by measuring catalepsy, and because serotonin 5-HT 1A receptor (5-HT 1A R) agonists have been reported to attenuate the effects on EPS-like measures, the aim of this study was to characterize the effects of 5-HT 1A R biased agonist (NLX-112) in comparison to 5-HT 1A R partial agonist (buspirone) in TBZ-induced-catalepsy in rats 4,5 . The results show potent anticataleptic effect of NLX-112 with minimal effective dose of 0,16 mg/kg in the cross-legged-position and in the bar tests. Buspirone was inactive in TBZ-induced-catalepsy tests in the whole range of doses used. In summary, an effective dose of NLX-112 that selectively activate 5-HT 1A R can minimize side effects induced by TBZ such as parkinsonism, which raises the possibility for better tolerated therapy of chorea. Supported by: N42/DBS/000103.

55. Behavioural assessment of acute and long-term antidepressant and anxiolytic efficacy in mice

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An impressive number of mice models to assess anxiety and depression are available today. However, the "gold standard" treatments do not always consider the comorbidity of major depression and anxiety disorders. Additionally, several studies suggest that drugs used commonly to treat depression, have anxiogenic effects following acute administration. Here, we investigate the efficacy of two commonly used antidepressants: fluoxetine,desipramine and one promising treatment: ketamine. We subjected C57BL/6J mice to number of anxiety- and depression-related behavioural tests: forced swim test (FST), social interaction (SI), and elevated zero maze (EZM) to test both acute (2hr) and long-term (24hr and 7 days) administration of fluoxetine (10 mg/kg, s.c.), desipramine (10 mg/kg, s.c.) and ketamine (3 mg/kg, s.c.). Our FST results showed acute antidepressant-like efficacy of a single administration of fluoxetine and desipramine ($p<;0.0001$), whereas ketamine exerts persistent antidepressant efficacy after 24hr ($p<;0.05$) and 7 days ($p<;0.01$) post-administration. Both fluoxetine ($p<;0.005$) and desipramine ($p<;0.001$) induce a significant social aversion phenotype in the SI test, reflecting rapid anxiogenic effect 2hr post-administration. Surprisingly, ketamine ($p<;0.05$) exerts acute anxiolytic efficacy in the EZM whereas desipramine ($p<;0.005$) has an opposite anxiogenic effect. Taken together, these results confirm the distinct characteristic of the acute response to various antidepressants.

56. The phenomenon of maternal potentiation in infant rats' isolation calls

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Few-day-old pups being separated from their mother and/or the nest produce ultrasonic vocalizations (USVs) to elicit maternal retrieval behaviour. This suggests that pup USVs may function as calling signals and/or a marker of the pup's distress. Maternal potentiation (MP) of rodent pup USVs is a promising model of early life social bonds that can be a useful tool in research. Short interactions with mother just before isolation have been found to increase USV in the offspring. Our aim was to validate the MP model in rat pups. Thus, by examining calls emitted by ten-days old pups before and after interactions with mother, we assessed the impact of a brief reunion with the dam on the early communicative behaviour. The results show that short contact with mother induced an increase in the number of USVs in re-isolated pups and a prolongation of the mean call duration. In addition, potentiated USVs were characterised by the greater percentage of the frequency modulated calls and the lower percentage of short calls. These data suggest that infant rats display maternal potentiation which may have implications for understanding the development of filial bonds. This study was supported by the Polish National Science Centre grant NCN 2016/23/B/NZ7/01131.

57. Maternal dietary fat intake in association with autism spectrum disorders - preclinical study

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Autism Spectrum Disorder (ASD) is a severe neurodevelopmental brain disorder that remains poorly understood. ASD is characterized by impairments in communication, social interaction and stereotypic patterns of behavior. Maternal nutrition is essential to fetal brain development and an impoverished diet has been associated with strong increases in the risk of neurological diseases and other adverse neurodevelopmental outcomes. Our goal in this study was to determine whether maternal high-fat diet (HFD) was associated with risk of ASD in the offspring. Wistar rat dams were maintained ad libitum on control chow or an HFD during pregnancy and lactation. Profiles of mRNA expression in the prefrontal cortex of male offspring rats sacrificed at postnatal day 28 were determined using TaqMan Low Density Array Cards. The results indicate that the offspring exposed to maternal HFD showed significant changes in gene expression associated with the risk of ASD, such as Shank 1, Cacna1d, Cacna2d3 and Nlgn3. Given the known importance of fatty acids in brain development and the correlation between maternal consumption and accessibility for the developing fetus, our results suggest that maternal HFD is associated with a risk of ASD. Supported by research grant 2018/29/N/NZ7/02703 from the National Science Centre.

58. Kappa opioid receptor agonists block the expression of social-conditioned place preference

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Social contact is often rewarding. Here we investigate how the endogenous opioid system controls the conditioned preference of a context associated with social interaction. Juvenile male C57BL/6N mice were tested in a social

conditioned place preference task (sCPP). First animals were placed for 30 minutes in a cage divided into two compartments, containing two novel bedding types. Next day conditioning started, with animals being placed for alternating 24h periods either together with their littermates or in isolation, with different types of bedding associated. The conditioning phase comprised of 3 social and 3 isolation periods. On the final test day animals were treated with an opioid antagonist or agonist and then tested again for context preference. As expected, mice preferred the socially conditioned context. Treatment with selective or non-selective mu or delta opioid antagonists (cyprodime, naltrindole, naltrexone) had no effect on preference. However, treatment with opioids that have partial or full kappa agonist activity (nalmefene, U50488) abolished the expression of sCPP. Pre-treatment with a selective kappa antagonist (norbinaltorphimine) prevented nalmefene effects on sCPP expression. We find that partial activation of kappa opioid receptors is sufficient to block the expression of place preference conditioned by social interaction.

59. A new genetically modified mouse with inactivation of the proenkephalin gene

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Enkephalins derived from the Penk gene are the most abundant opioid peptides in the forebrain and the primary activators of mu and delta opioid receptors. Here we describe generation of novel genetically modified mice with inactivation of the Penk gene and their initial characterization. We have generated by homologous recombination a mouse strain with floxed variant of Penk, with loxP sequences placed in the second exon of the gene flanking the coding sequence. Correct recombination of the floxed sequence was confirmed, however, we also observed that the presence of the loxP sites interfered with Penk expression causing severe reduction in mRNA and protein levels in the striatum and other brain areas. In order to convert the strain to complete gene inactivation ('ko') we crossed the animals with a germ-line expressed Cre (SynCre). 'Flox' mice were viable, had normal weight gain, and showed no obvious impairments. No fertility deficits in males were observed. We have also assessed the levels of Met- and Leu-enkephalin, to test if inactivation of the Penk gene could be to an extent compensated by Leu-enkephalin derived from prodynorphin. Once initial characterization is completed the model will be used to test the role of enkephalins in reward-driven behaviors.

60. Investigation of molecular adaptive changes in cerebellum after chronic administration of antidepressant drugs

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Depression is a mental disorder for which current treatment has many limitations. Despite thorough research in this field, the biological mechanisms underlying this psychiatric disorder are still poorly understood. Some studies suggest the role of cerebellum in pathophysiology of depression. Neuroimaging techniques confirmed decreased volume and grey matter concentration. The aim of this this experiment was to evaluate the molecular adaptive changes in cerebellum after chronic administration of antidepressant drugs. Drugs with different mechanisms of action were selected: imipramine, reboxetine and S-citalopram. Saline was used for the control group. Drugs were administered to rats (n=8/group) intraperitoneally for 21 days. Cerebellums were isolated and protein expression was determined using Western blot analysis. Study involves different molecules that allow evaluation of synaptic signalling. Tested proteins were: BDNF, mTOR, GluN2B subunit of NMDA receptor, GluA1 subunit of AMPA receptor, PSD95. Their involvement in depression pathophysiology and antidepressant mechanism of action has been widely investigated. Preliminary results show statistically significant upregulation of AMPA subunit concentration after S-citalopram administration. Further analysis is in progress, other changes in protein expression are observed. Full results will be presented at the conference.

61. Influence of the maternal high-sugar diet during pregnancy and lactation on the locomotor activity of the offspring as an early symptom of the risk of mental disorders

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Recent literature data have shown that prenatal exposure to high-sugar and/or high-fat diet may predispose offspring to develop mental disorders later in life. Changes in locomotor activity in laboratory rodents usually accompany mental disorders such as anxiety and depression. In the presented study we examined if maternal high-sugar diet during pregnancy and lactation affects general locomotor activity in juvenile and adult offspring in both males and females. The Wistar dams were fed with high-sugar diet (HSD) or normal chow (control group) three weeks before matching, during pregnancy and lactation. Next, we investigated the velocity and the locomotor activity in the open-field test in 28 and 70-day-old offspring. Both velocity and locomotor activity were strongly diminished in the HSD group in 28-day-old male offspring and slightly increased in 70-day-old male rats. No changes were detected in the female group. Together, these findings reveal influence of maternal diet on the offspring locomotor activity and velocity and those changes in behavior might be an early sign of risk for mental disorders in children of mothers on sweet diet during pregnancy and lactation. The results suggest that male offspring are more vulnerable to the impact of maternal diet on the locomotor activity than females.

62. The impact of the prenatal high-fat diet on the locomotor activity and velocity of the offspring in the open-field test as a sign of the risk of the behavioral disorders.

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Based on the recent findings on the influence of high-fat maternal diet (HFD) on the health of the offspring we decided to asses general locomotor activity in the offspring exposed prenatally and in early life period to HFD. Diminished locomotor activity in laboratory rodents is usually associated with mental disorders like depression and anxiety. Wistar dams were fed with the HFD or normal chow (control group) three weeks before matching, during pregnancy and lactation. Next we investigated the velocity and the locomotor activity in the open-field test in juvenile (28-day old) and adult (70-day old) offspring in both males and females. Both velocity and locomotor activity were strongly diminished in the HFD group in juvenile male offspring and normalized in adult male rats. No changes in the female group were found. In conclusion, the obtained results indicate that maternal diet influence the locomotor activity and velocity in the male offspring group and those changes in behavior might be an early sign of risk for mental disorders in children of mothers on HFD during pregnancy and lactation. In addition, the results suggest that female offspring are more resistant to the impact of maternal diet on the locomotor activity than males.

63. Behavioral Alterations in Rats Prenatally Exposed to Valproic Acid

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A large body of evidence shows that the anticonvulsant medication, valproic acid (VPA), used during pregnancy increases prevalence of autism spectrum disorder in the newborn. To examine translational value, we investigated whether prenatal exposure to VPA may also induce autistic-like behaviours in laboratory rats. Aim: We performed the Social Play Test on rats that underwent prenatal exposure to VPA to study potential social deficits in adolescence. Pregnant Sprague-Dawley rat dams received a single i.p. injection of VPA (300 mg/kg) or

vehicle at gestational day 13. The 30-35 days-old offspring were then tested in pairs using Social Play Test. Prenatal exposure to VPA significantly decreased the number of pinning and pouncing episodes. Additionally, VPA treatment reduced overall play time and increased latency to the first episode of playful behavior. The present study demonstrates that prenatal exposure to VPA leads to impairments in social behavior in juvenile male rats. Our study confirms that prenatal exposure VPA model results in autistic-like behavioral phenotypes. Current research in our laboratory investigates whether rat prenatal VPA exposure could be useful in ASD pharmacotherapy. Supported by NSC grant: 2016/23/B/NZ7/01131.

64. The Effects of Perinatal Fluoxetine Treatment on Social and Non-Social Investigation

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Selective serotonin reuptake inhibitors (SSRIs) are increasingly prescribed as medication for various affective disorders during pregnancy. SSRIs crosses the placenta and affect serotonergic transmission in the fetus. Whether this leads to lasting neurobehavioral consequences for the child remain unclear Recent rodent research has also linked perinatal SSRI exposure to alterations in both social and non-social aspects of behavior. However, this research has mainly focused on behavior within simplified environments. The current study investigates the effects of perinatal SSRI exposure on social and non-social investigation behaviors of adult rat offspring upon introduction to a seminatural environment. During the perinatal period (gestational day 1 until postnatal day 21), rat dams received daily treatment with either an SSRI (fluoxetine, 10 mg/kg) or vehicle. Adult male and female offspring were observed within the first hour after introduction to a seminatural environment. The results showed that perinatal fluoxetine exposure altered aspects of non-social, but not social, behaviors. More specific, both fluoxetine exposed males and females spent more total time on walking/running than controls, while fluoxetine exposed females also had a higher number of episodes with walking/running compared to control animals. Furthermore, fluoxetine exposed females spent less time exploring objects and specific elements in the physical environment.

COGNITIVE POSTERS

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65. GABAergic neurotransmission in human brain characterized by single- and paired-pulse TMS with EEG co-registration and pharmacological GABAA activation

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Amongst numerous neurotransmitters γ-aminobutiric acid (GABA) is of particular importance, as it represents the main inhibitory agent of the central nervous system. The present study aims to characterize the state of GABAergic neurotransmission in human brain using non-invasive, available methods, in a way that will subsequently allow for comprehensive comparison of various patient groups with the healthy population. We combined transcranial magnetic stimulation (TMS) over the primary motor cortex (M1) with electroencephalography (EEG) and recorded TMS evoked potentials (TEPs) before and after pharmacological activation of $GABA_A$ receptors with alprazolam. In addition, we applied paired-pulse TMS in order to asses local $GABA_A$-mediated inhibition. 20 healthy young volunteers participated in two sessions (alprazolam, active placebo - cetirizine). Three types of TMS stimuli were applied: suprathreshold single-pulse (120 % resting Motor Threshold - rMT), subthreshold single-pulse (80% rMT), and paired-pulse (80% + 120% rMT, 2.5 ms inter-stimulus interval). Our results show that alprazolam modulates amplitudes of early TEP waves following a single suprathreshold TMS stimulus and this modulation resembles changes induced locally by the paired-pulse TMS. The effect of paired-pulse TMS in TEPs is reduced following the administration of alprazolam. Observed TEP changes possibly reflect the state of GABAergic neurotransmission in human brain.

66. Endogenously driven interbrain synchrony in musical interaction

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When people coordinate their behaviour, their brain activity synchronizes. However, the extent to which interbrain synchrony is based on the alignment of endogenous processes between players or the shared auditory input remains unclear. The current study disentangles this by investigating EEG interbrain synchrony (Phase Locking of Amplitude Envelopes, PLAE) in 14 piano duos. First, we compared PLAE in periods of high behavioural synchrony that differed in whether pianists were motorically familiar with the partner's part. PLAE in the delta and gamma band was modulated by familiarity, being higher in the unfamiliar condition, despite identical shared sensory input. Second, we compared PLAE in periods without sensory input, when pianists were planning either the same or a different tempo. PLAE in the gamma band at right posterior electrodes was higher when pianists planned to play at the same tempo. These findings illustrate that interbrain synchrony during coordinated behaviour is not merely driven by shared sensory input but also the alignment of endogenous processes. Specifically, when sensory feedback was present, interbrain synchrony was modulated by players' orientation towards their own internal action representations or the others' action. When sensory feedback was absent, interbrain synchrony was modulated by the temporal similarity of planning.

67. The types of cognitive flexibility in different cognitive tasks

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Cognitive flexibility is an ability or a trait that plays important adaptive functions, underlying human adjustment to the changing environment. In the literature, cognitive flexibility is defined in several ways, but most often as a capacity to accommodate to changing conditions. Moreover, some researchers single out two types of cognitive flexibility: adaptive and spontaneous. Unfortunately, studies rarely make a distinction between the two types. As a consequence, it is not clear which type of cognitive flexibility is measured by any given task. Similarly, the definition of the concept per se becomes less obvious too. The aim of the present study was to run a comparison of different cognitive flexibility tasks and determine the types of cognitive flexibility they probe into. The volunteers (N=125) performed a battery of computer and paper tasks measuring perseverance, learned irrelevance and set – switching performance, as well as, verbal fluency and divergent thinking, including thinking flexibility. The results have shown no significant relationships between the tasks and the two types of cognitive flexibility and a negative correlation between flexibility measured by perseverance and learned irrelevance task (Dreisbach and Goschke, 2004) and switching measured by task set – switching (Rogers et al., 1998).

68. Valence and Origin role in Interpretation of Ambiguous Stimuli in Terms of Warmth vs. Competence: Behavioral Phenomenon and its Neural Correlates

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The warmth and competence are fundamental dimensions of social cognition. The affective state of an individual may affect the way people interprets the neutral stimuli in the environment. As previous findings showed, it is possible to alter the perception of neutral social stimuli in terms of warmth vs. competence, by eliciting an incidental affect wit use of emotion-laden words. In the current experiment, we expected valence and origin of an affective state, factors ascribing emotionally laden words, to be able to switch the interpretation of the neutral object. In a series of two experiments (behavioral and EEG), we have demonstrated that negative valence and reflective origins promote the interpretation of unknown objects in terms of competence rather than warmth. Furthermore, electrophysiological response-locked analyses revealed differences specific to negative valence while decision making and decision executing. The results of current experiments show that usage of warmth and competence in social cognition is susceptible to the affective state manipulation. What is more, the results are coherent with an evolutionary perspective on social cognition: valence effects, as well as predictions of dual mind model of emotion: origin effects.

69. Grasparatus for transcranial magnetic stimulation research

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One of the important aspects of cognitive neuroscience research is its ecological validity. The organization of an experiment itself, as recent studies show, may after all affect various mental processes, and thus influence the results of the test itself. Among others, the use of real objects as experimental stimuli is crucial. Moreover, similarly to functional magnetic resonance imaging (fMRI) studies, in transcranial magnetic stimulation (TMS) research there are movement constraints on top of any space limitations, as well as metal stimulus restrictions (especially when presented close to the body). To overcome these challenges, we built a nifty presentation tool called "Grasparatus". Following its successful application in our fMRI studies on haptically guided functional grasping of tools (Nowik et al., 2019, MethodsX, 6, 1353-1359), several adjustments were nevertheless required. Here we show a proposed way how to adapt Grasparatus for TMS research. The technical description of this new apparatus and the procedure for its use are presented. All these adaptations of Grasparatus allow to use real objects, firmly or semi-attached, so that different interactions with stimuli are possible while the participant's brain is stimulated. Such modifications of Grasparatus move TMS studies to more advanced and ecologically valid level.

70. Chronotype is associated with marginal to medium effect size structural brain differences

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Based on the prefered time of sleep and wakefulness, humans can be characterised as early, intermediate or late chronotypes. The anatomical basis of chronotype variability remains, however, still poorly explored. Brain imaging data from 116 healthy young adults (73 women) were analysed using cortical thickness and grey matter voxel-based morphometry approaches. Early chronotypes were found to have thinner cerebral cortex in the right superior frontal gyrus and superior parietal gyrus compared to intermediate chronotypes ($p<0.05$). As the primary voxel-based morphometry comparison revealed no group differences ($p<0.05$), an additional exploratory analysis was performed with a less conservative threshold. Early chronotypes had higher grey matter volume in the left cerebellar lobule VI compared to intermediate chronotypes, as well as in the left thalamus and the right cerebellar lobule IX, hippocampus and cerebellar lobule VI compared to late chronotypes ($p<0.001$ uncorrected). Late chronotypes were found to have higher grey matter values than early chronotypes in the left superior occipital gyrus, and in the right middle cingulate gyrus compared to intermediate chronotypes ($p<0.001$ uncorrected). Despite the less

conservative threshold, voxel-based morphometry results do not necessarily reflect false positive findings as the majority of clusters was replicated in an additional correlational analysis and the effect sizes of differences fall between those reported in earlier studies. Altogether, in line with the existing literature, we show that chronotype is linked to marginal to medium effect size structural brain distinctions. Furthermore, we connect circadian phenotypes with anatomical differences in several new brain areas.

71. I don't see you, but my brain does: a study on the variation of pupil size in conditions of sensory unawareness

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Several neuroscientific studies have shown how some emotional stimuli can be processed without awareness. In addition to specific brain activation (e.g., amygdala, pulvinar, superior colliculus), increasing evidence has shown changes in some physiological parameters, such as in heart rhythm, skin conductance and pupil dilation. This research's goal was to measure the physiological response, through the recording of pupil diameter, of emotional stimuli (e.g., emotional faces/bodies) presented in non-conscious conditions in healthy participants. The Continuous Flash Suppression (CFS) paradigm was used to produce the stimulus suppression. An infra-red eye-tracker was used to measure pupil diameter throughout the task. All participant performed both conditions: a test condition (target stimuli are presented only to the non-dominant eye, unconscious condition) and a control condition (target stimuli are presented to both eyes, conscious condition). We found a greater pupil dilation for emotional stimuli suppressed through CFS compared to stimuli presented in the conscious condition, indicating an implicit physiological response towards emotional stimuli. Furthermore, a greater dilation for faces compared to bodies in the condition of unawareness was found, although no significant difference emerged between the emotions presented. These data suggest that the emotional content may represent a relevant evolutionary variable that induces significant psychophysiological alterations.

72. Event-Related Potentials under Condition of Switching over of the Programs of Manual Movements in Humans

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The objective of our research is to identify the gender-specific features of the amplitude-time characteristics of the event-related potentials (ERPs) under condition of switching over of the programs of manual movements in healthy and right-handed men (n=32) and women (n=33). The time of simple and complex visual-motor responses, latency and amplitudes of N2 and P3 components of ERPs in the response to launch and switching (dominant / subdominant arm) of the motor program of finger flexes were investigated. ERPs were analyzed in the frontal, central, and parietal lobes of the cortex. It was established that male participants had lower times indexes of simple and complex visual-motor responses than women. In addition, during the contralateral switching of motor programs of manual movements the smaller latent periods of the ERPs components in the right central and left frontal sections (component N2), in the left hemisphere lobes (component P3) among men, were observed. The amplitude of the N2 and P3 components revealed higher values in male participants at the parietal lobes. In the left hemisphere of men and women the smaller latent periods of P3 component (in the central lobe) and amplitudes of N2 and P3 components were determined comparing to the right hemisphere.

73. White matter integrity as a predictor of success in the complex real-time strategy video game

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There is an increased interest in how playing video games is associated with a wide range of cognitive processes such as perception abilities or cognitive functions. Most studies focus on genetic predispositions, personality traits, or age as factors that influence complex skill acquisition, like playing video games. Although people have the capacity to learn and perform in complex abilities, it is not clear how cognitive and neural predispositions may accompany this process. The main goal of the presented study is to identify the pretraining brain white matter (WM) characteristics that may predict the success in StarCraft2 training (real-time strategy game). Diffusion tensor imaging (DTI) scans were acquired for each participant, before starting a training session (30 hours of training). Preliminary exploratory data analysis (N=8) based on the measurement of WM integrity (fractional anisotropy, FA) revealed that the FA value of splenium of corpus callosum significantly predicted the success in the game, that was measured as a number of won matches, $F(1, 6) = 25.304$, $p = 0.002$, $\beta = 0.808$. We were not able to find any other significant predictors of the game's success, however, the process of data collection is still in progress.

74. Impact of the meaningfulness of stimuli on the diversity of brain activity differs between sensory modalitiess

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The diversity of subjective experiences is hypothesized to be reflected by the diversity of brain activity (Schartner et al., 2017a; Wang et al., 2017). Recent studies suggest that brain signal diversity is higher in response to meaningful visual stimuli and lower when stimuli is meaningless (Boly et al., 2015; Mensen et al., 2017, 2018). In the present study, we intend to replicate and reconcile the findings of Boly et al. (2015), Mensen et al. (2017, 2018) and our recent study (Bola et al., 2018). We conducted an EEG experiment to determine the relationship between the diversity of brain activity assessed by the Lempel-Ziv algorithm and the meaningfulness of the stimulus (auditory and visual). We found similar pattern of results for the temporal and spatio-temporal diversity of brain activity. We found no main effect of meaningfulness or sensory modality. However, we did find a significant interaction between meaningfulness and sensory modality. In conclusion, we replicated the results of previous studies. The analysis showed that the observed effect is dependent on sensory modality only for meaningful stimuli. Thus our study provide evidence for lack of universal dependence of diversity in brain activity in relation to meaningfulness of the stimuli.

75. The heart and mind relationship - Working memory, inhibitory control and vagal tone

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It has been shown that forebrain structures activity may impact parasympathetic regulation via vagus nerve. Thus, the positive relationship between the cognitive functions (e.g. top-down control) which are linked to the prefrontal activity and vagal tone has been postulated. The aim of the current study was to examine whether working memory (WM) and inhibitory control capacities are linked to the resting vagal tone in healthy individuals. 127 healthy

individuals (75 F; mean age = 23,90) completed both N-back (0-, 1- and 2-back with either letter or pictorial stimuli) and Stop-Signal task (SST). Then, six-minute resting electrocardiogram was measured. Behavioral accuracies for each condition were extracted from N-back task, while stop-signal delay and accuracy were extracted from SST. Time-domain heart-rate-variability (HRV) was indexed by root-mean-square-of-successive-differences (RMSSD). In line with previous research, negative linear relationship was observed between N-back condition and participants' accuracy. WM was significantly correlated with HRV only in pictorial 2-back task. In spite of our expectations, no significant relationship was observed between HRV and inhibitory control. These results may lead to conclusion that the relationship between working memory, inhibitory control and vagal tone could possibly be modulated by additional moderator variables. Moreover, WM and HRV relationship may be dependent on the modality of pictorial stimuli.

76. Does perceived social isolation impact behavioral and parasympathetic markers of emotion processing and regulation?

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Perceived social isolation (PSI; 'loneliness') was shown to impact a wide range of social cognitive processes, including emotion processing and regulation. According to the neurovisceral integration theory decreased emotion regulation may be indicated by decreased vagal flexibility, as indexed by task-related heart-rate-variability (HRV) changes. The current study aimed to test if PSI induction impacts vagal flexibility during emotion processing and regulation. 127 healthy individuals (74F; 24+/-5 yo) completed a battery of tests and were randomly given either positive (n=61; Future Belong, FB) or negative (n=66; Future Alone, FA) feedback concerning their future social relationships. Then, participants were asked to rate neutral and angry faces (OBSERVE) and then, to either increase (INCREASE) or decrease (DECREASE) their affective response to angry faces. During the experiment electrocardiogram (ECG) was recorded, including pre-feedback (BASELINE) and post-task (RECOVERY) 6-minute resting ECG. Behavioral ratings and phasic HRV changes (logHF-HRV) were analyzed. While no effects of the PSI induction on behavioral ratings were observed, a different pattern of physiological response was found in the participants subjected to FA manipulation compared to the FB group. In the FA group, change in HRV was observed only at the beginning of the task, but not during its consecutive stages. These results indicate that a transient induction of loneliness impacts parasympathetic response to social stimuli even in the absence of any overt behavioral changes during emotion regulation in lonely individuals.

77. Relationship between perceived social isolation and decreased vagal tone is mediated by maladaptive detachment

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Multiple lines of research provide evidence that prolonged perceived social isolation (PSI), commonly known as loneliness, is related to a heightened risk of coronary heart disease and increased mortality rates. However, exact mechanisms underlying the relationship have not been elucidated. Recent theoretical frameworks (i.e. neurovisceral integration theory) point towards inefficient parasympathetic regulation as indexed by decreased vagal tone (VT) as a marker of maladaptive psychophysiological processes. However, findings regarding the direct relationship between PSI and VT are inconclusive. Thus, the current study aimed at investigating the potential psychopathological mediators of this relationship. 177 participants (78M, 24+/-5y.o.) completed R-UCLA Loneliness Scale (RUCLA) and Personality Inventory for DSM-5 (PID-5) and underwent a 5-minutes resting measurement of cardiac activity. High-frequency heart rate variability (HF-HRV) was used to quantify the vagal tone. Out of five main PID-5 domains, only Detachment was linked to both loneliness ($r = .28$, $p < 0.001$) and HF-HRV ($\rho = -.17$, $p < 0.05$). Furthermore, the mediation analysis revealed that the effect of loneliness on vagal tone wss fully mediated

by Detachment. Presented findings suggest that PSI may be linked to a prolonged state of withdrawal, which can result in decreased parasympathetic regulation as measured by vagal tone.

78. Population level parcellation of the human amygdala based on Recurrence Quantification Analysis (RQA)

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Animal studies suggest that the amygdala consists of several subdivisions which play different roles in emotion-related processes. It would be advantageous to discriminate between these subdivisions in a living human brain. However, it is not possible to specify boundaries of the amygdala parts using MRI techniques because of their low spatial resolutions. The aim of this study was to develop a method of the human amygdala parcellation on the population level, based on Recurrence Quantification Analysis (RQA). The fMRI data from 74 subjects (mean age 24,6) was acquired with a 3T Trio Siemens during the 15-minute rest period (TR = 1.5 s, voxel's side = 2 mm). RQA measures were calculated for both amygdalae for all time-series voxel-wise. Clustering algorithms were used to classify voxels to given subdivisions on the basis of RQA measures. The most stable solutions were chosen on account of internal validity and were compared to already existing parcellations. Obtained result indicates that the human amygdala might be divided into two parts. Our method could be further used to study their distinct functions and connectivity. This work was supported by a grant from the National Science Centre (Poland), DEC-2014/15/B/HS6/03658.

79. Hedonic experience of music listening – an fMRI study.

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Hedonic experience is an integral part of biological reinforcers that are necessary for survival, such as food and sex. Humans can also obtain pleasure from abstract stimuli (e.g. music and artworks) and apparently the same neuronal circuits are involved in both cases. This study aimed to understand the neural basis of pleasure of music listening. Participants (n=37, 23 females, mean age 24.1 ± 3.9 years) were presented with series of 30-sec musical fragments, pleasant and neutral, in pseudorandom order. Since musical taste is highly specific to personal preferences, music individually selected for each participant was used as pleasant stimuli. The fMRI analysis comprised first five seconds of each piece. Contrast of pleasant>neutral pieces showed the largest activities in the following areas: anterior cingulate cortex (ACC), middle cingulate cortex (MCC), posterior cingulate cortex (PCC), dorsal striatum (DStr, including caudate nucleus, and putamen), globus pallidus, supplementary motor area (SMA), medial orbitofrontal cortex (mOFC) and medial prefrontal cortex (mPFC). SMA activity reflects rhythm processing and its possible relationship with subjective pleasure. The activity of mPFC and PCC, areas included in the default mode network (DMN), may indicate its role in experiencing pleasure in response to self-referential stimuli, which include a person's favorite music.

80. Superior auditory and visual rhythm discrimination in musicians is not related to cross-modal neuroplasticity in auditory cortex

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Temporal information is best processed in the auditory modality, but can be processed in other modalities as well (visual, tactile). In our recent work, Bola and colleagues (2017) showed that congenitally deaf subjects recruit their auditory cortex for visual rhythm processing. Here, examined whether similar cross-modal plasticity could be observed in expert musicians. 17 professional pianists and 20 non-musicians participated in an fMRI study during which they discriminated between sequences (rhythms) presented in visual (flashes) or auditory (beeps) modalities. In the control condition, the same flashes/beeps were presented at a constant pace. In an additional condition participants were asked to imagine rhythms. Musicians performed both visual and auditory rhythmical tasks better than non-musicians. fMRI revealed that compared to control condition, the visual task recruited the right-hemisphere auditory cortex in musicians. However, a weaker but similar activation was also observed in non-musicians for the same contrast. Comparison of the two groups revealed no significant between-group effects in the auditory cortex, only an increased activation in the right Angular Gyrus for musicians vs. non-musicians. We conclude that the musicians' superior rhythm discrimination is not related to cross-modal neuroplasticity in auditory cortex, but most likely is related to plasticity of higher cognitive functions.

81. Temporal information processing is related to manipulation but not maintenance in WM in elderly: an fMRI study

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Temporal information processing (TIP) is an essential component of human cognition, providing a neural framework for many mental functions. TIP deficits were indicated previously in normal aging. One of paradigms used to measure TIP in millisecond range is temporal-order judgment (TOJ) task. It measures temporal acuity, i.e., the ability to perceive the order of two stimuli presented in rapid succession. The study aim was to investigate whether in elderly TIP is related to the efficiency of working memory (WM), considering two WM processes: maintenance (more pure storage of information) and manipulation (updating and reorganization of the material). Healthy elderly (N=41, aged 62-78 years) performed two auditory tasks: (1) psychophysical TOJ task, and (2) verbal n-back task with 3 conditions (0-, 1- and 2-back) in the MRI scanner. The results showed that the efficiency of TIP was related to behavioral indices of WM and brain activity engaged in WM. TIP efficiency correlated with activations in insula, middle and superior frontal gyri only during WM manipulation processes (2- vs 1-back comparisons) but not during maintenance (1- vs 0-back comparisons). These results suggest that manipulation in WM is a dynamic process requiring efficient TIP. Supported by National Science Centre, Poland, grant number 2015/17/B/HS6/04182

82. Individual differences in temporal information processing on millisecond level

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Previous studies indicated that temporal information processing (TIP) is not a monolithic entity and several time ranges are essential for cognitive function. One may distinguish some tens and several hundred millisecond levels. The study goal was to test individual differences on these two levels and to verify the between-levels relations, in

particular, whether the better performance on one level is accompanied by the better skill on the other. The former level was studied using temporal order judgement task (TOJ) based on ordering of auditory stimuli, whereas the latter with tapping task performed in self-paced and maximum tempi. Participants were 29 healthy adults (mean age: 23 years). Significant correlations were found between the performance on these two temporal levels. Obtained TOJ values correlated with the performance on both tapping tasks. A novel value of our study was the indication of significant correlations between the efficiency of TIP in two studied millisecond ranges. Obtained results indicate the existence of a core mechanism controlling millisecond TIP, which may underlie the individual differences in the efficiency of cognitive function. Supported by the Polish National Science Centre grant no 2018/29/B/HS6/02038.

83. The left and right inferior frontal opercula play differential roles in encoding unpleasant facial emotions: a tDCS study.

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Neuroimaging studies suggest that the inferior frontal operculum (IFO) is part of a neuronal network involved in facial expression processing, but the causal role of this region in emotional face discrimination remain elusive. Here we used cathodal tDCS to test whether right (r-IFO) and left (l-IFO) IFO play a causal role in discriminating basic facial emotions in healthy volunteers. Specifically, we aimed to test if the two sites are selectively involved in the processing of facial expressions conveying high or low arousal emotions. Based on the Arousal Hypothesis we expected to find a modulation of high and low arousal facial emotions by delivering cathodal tDCS to the r-IFO and the l-IFO, respectively. In study 1, we validated a novel Emotional Faces Discrimination Task (EFDT). In study 2, we targeted the r-IFO and the l-IFO with cathodal (inhibitory) tDCS during facial emotions discrimination on the EFDT. Sham tDCS was used as a control condition. Overall, participants manifested the "happy face advantage" – i.e. happy faces were easier to discriminate than other expressions. Interestingly, tDCS to r-IFO enhanced discrimination of faces expressing anger (a high arousal emotion), whereas tDCS to l-IFO decreased discrimination of faces expressing sadness (a low arousal emotion). Our findings show the involvement of both r-IFO and l-IFO in the discrimination of facial expressions, revealing a differential role of the two sites in the processing of specific high and low arousal emotions. Crucially, this study suggests, for the first time, that cathodal inhibitory tDCS might reduce the neural noise triggered by specific emotions, improving discrimination of high arousal emotions but disrupting discrimination of low arousal emotions encoded in the stimulated site. These findings may offer new insight for treating the clinical population with a deficit in processing facial expressions.

84. Engagement of the Visual Word Form Area in phonological processing and its relations to the acquisition of reading.

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The region of the left ventral occipitotemporal cortex (VOTc) encompassing Visual Word Form Area is considered to host orthographic representations of words. Its involvement in spoken language is explained as automatic orthographic co-activation. This facilitates the integration of phonological and orthographic information crucial for reading. To investigate the VOTc involvement in phonological processing and its relations to reading ability we tested 80 Polish beginning readers (5.9-7.3 y.o.). In fMRI task children had to decide whether two auditorily presented words or pseudowords start with the same sound or not (phoneme matching task), or decide if they are the same (control task). Region of interest analysis showed that the activity of VOTc during phonological decisions (phoneme matching task >; control task) was positively correlated with the knowledge of letters in case of processing words. This effect was not present in processing pseudowords, where one cannot rely on orthographic whole-word representations. The activity of VOTc was not significantly related to the level of accuracy in the task nor to the general phonological awareness level. Results indicate that the increasing orthographic knowledge in beginning readers allows greater involvement of VOTc in phonological processing that enable the access to

emerging orthographic whole-word forms.

85. Chirp-evoked haptic and visual steady-state responses: exploring the a method of stimulation of sensory systems.

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Chirp-modulated signals are oscillatory signals with frequency changing monotonically in time. The aim of this study was to explore the response properties to chirp-modulated haptic and visual stimuli in 1-35 frequency range. For both types of stimulation two types of chirp modulation were used. In the linear condition stimulation frequency increased linearly, and in the logarithmic condition the increase was logarithmic. In haptic stimulation stimuli were delivered by vibrating a TL-002-14R haptuator. In the visual stimulation stimuli were delivered via a centrally positioned white LED. In all conditions subjects performed an active oddball task, and counted target stimuli (0.2 probability), consisting of constant frequency stimulation stimuli (20 Hz in visual conditions, 25 Hz in haptic conditions). EEG phase-locking factor and evoked amplitude responses were analyzed. In visual conditions we observed a robust response across all stimulation frequencies in both conditions, centered at occipital channels. Maximal response was observed around 15 Hz. In haptic condition we observed stronger responses in linear chirps condition, at parietal and frontocentral channels, with maximal response around 25 Hz. In both sensory domains we observed a significant response to chirp modulated stimulation. Different maximal response frequencies may suggest specific resonance frequencies for each stimulation modality.

86. EEG signatures of medial frontal connectivity during response conflict

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The medial frontal cortex (MFC) has been proposed to be a central hub for executive control network. Here, we examined how the MFC interact with frontal, motor, and visual regions during response conflict resolution. Ninety-one participants performed the flanker task, in which response conflict is elicited by incongruence between target and flankers. Single-trial EEG data was analyzed using a wavelet time-frequency decomposition. As the marker of conflict processing, we calculated power and trial phase-consistency (ITPC). As the markers of inter-regional connectivity, we used consistency phase angles between two electrodes (ISPC) for a given frequency band, and nonlinear phase index for cross-frequency coupling. To investigate global network characteristics, we measured cross-channels' connectivity based on graph theory. The results showed that the MFC power in theta frequency range was increased in the conflict trials, reflecting the involvement of executive control. Graph theory-based results showed an overall increase of MFC connectivity degree. The ITPC showed increased MFC phase synchronization in lower-theta. The ISPC showed increased connectivity between the MFC and disparate frontal, motor, and visual areas. In conclusion, our results provide a relatively comprehensive overview of the functional connectivity patterns underlying processing of response conflict in the flanker task.

87. The role of individual differences in relation between Real-time-strategy game proficiency and Attentional blink phenomenon

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The impact of action videogame playing on cognitive functioning is the subject of heated debate among scientists, with many studies showing superior performance of players relative to non-players on a number of cognitive tasks. However, the exact role of factors such as in-game behaviour and individual differences in the observed effects is still largely unknown. In our Event-Related Potential (ERP) study we investigate whether training in RTS video game can influence attentional skills as measured by Attentional Blink (AB) task. Forty-three participants (non-players) were recruited to the experiment. Participants were randomly assigned to either experimental or active-control group which differed only in the type of training. Trainings consisted of 30 hours of playing. Participants took part in two EEG sessions (pre- and post-training) during which they performed the AB task. Our results indicate that the experimental group improved their performance in the AB task in post-training session, while control group did not. What is more, for experimental group initial strength of neurophysiological response (the P300 ERP component) appeared to be predictive of achievements in the game environment, and, for the control group, behavior in the game environment appeared to be predictive of improvement in the AB task.

88. Cognitive resource depletion impairs emotion regulation via reappraisal, but not distraction – an ERP investigation

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This study aimed to compare the effectiveness of emotion regulation via reappraisal and distraction in a state of cognitive resource depletion. To evoke cognitive resource depletion, working memory task was used. In this task, participants had to memorize either one (low cognitive load) or four (high cognitive load) letters. In reappraisal group this was followed by the presentation of a sentence that described the forthcoming emotion-eliciting image in a more negative (no-regulation) or positive (regulation) way, while in the distraction group – by a simple equation to calculate (regulation) or a digit to remember (no-regulation). While distraction was successful in regulating emotional arousal under both high and low cognitive load – as evidenced by the reduced amplitude of the Late Positive Potential (LPP) in regulation versus no-regulation condition – reappraisal was effective under low cognitive load, but became ineffective under high cognitive load. This indicate that reappraisal may require greater amounts of available cognitive resources than other similar strategies of cognitive emotion regulation, such as distraction. We suggest that our findings may have implications for the choice of emotion regulation strategies in the context of ageing and/or various psychiatric disorders that are characterized by a decline in cognitive functioning.

89. Relationship between unbalanced diet, fatigue and cognitive performance

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Food, feeding habits, sleep quality are important factors of well-organized diet. Nutrients maintains blood-brain-barrier, improves cognitive performance or they may be the reason of deterioration of cognitive functioning due to hippocampal disruption caused by dietary factors. The diet rich in highly processed foods negatively affects the hippocampus, resulting in decline of learning and memory processes. The aim of the presented study was to examine the relation of the diet with: quality of life and fatigue measured by Fatigue Assessment Scale and cognitive functioning using The SynWin test allowing for measure multitasking abilities. Food Frequency Questionnaire was used to obtain diet quality index. Analysis (202 healthy adults) revealed that balanced diet is related to better performance in cognitive task, reflected in learning. Fatigue and lower diet quality index are reflected in decrease performance during cognitive task. We observed that the more sugar and fat in the diet the worse the cognitive task performance is, especially in memory subtest. The results of this study point towards negative relationship diet high in fat and sugar not only with our physical health but also with our cognitive abilities. The study was supported by BST grant no WP/2018/A/90.

90. Sex-related differences in resting state EEG signal complexity measured by multivariate multiscale sample entropy

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Human brain is a dynamic system producing complexive patterns of activation. Sex-related differences in spatiotemporal pattern of resting-state EEG (rsEEG) complexity is current and not fully recognized topic. In the present study we investigated sex-related differences in rsEEG in 118 healthy individuals (55 women, mean age = 26 years) who were asked to relax with eyes open for 5 min. The complexity was evaluated using Multivariate Multiscale Sample Entropy (MMSE) that quantifies changes in information richness of rsEEG in multiple data channels over different timescales. Our preliminary results showed significantly (p<;0.05) higher complexity in the frontal area on fine timescales representing local information processing, in females (mean maxslope= 0.588) compared to males (mean maxslope=0.508). MMSE measures of rsEEG, used in the present study, may be considered as potential fingerprints of various neuronal networks. This study was supported by a grant of the National Science Centre, Poland, no. 2015/18/E/HS6/00399, and a grant of the National Centre for Research and Development no. POIR-01.01.01-00-178/15.

91. How short-term language context modulates efficiency of inhibitory control: ERP investigation

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According to the Adaptive Control Hypothesis, only intense use of two languages in the same situation (called dual-language context) confers cognitive benefits in response inhibition. To test this hypothesis, we designed an innovative longitudinal study: induced specific patterns of language use experimentally and measured their cognitive after-effects. Thirty-two highly proficient Polish-English bilinguals (18 female, 22 ± 2.2 years) participated in a counterbalanced series of language games that mirrored the natural mechanisms of language use: a native language game (L1), a second language game (L2) and a dual-language game (requiring switching between L1 and L2). After each of them, they performed two inhibition tasks: the Stroop task and the stop-signal task (SST), while their ERP was recorded. We found a reduced congruency effect in the Stroop task after the L2 game, compared to the L1 game and no behavioural between-session differences in the SST. Moreover, we observed the N450 in the Stroop task and the P3 in the SST after the L1 game, but not after the L2 and the dual-language games. These findings suggest that even short-term intense use of L2 modulates some inhibitory skills in bilinguals.

92. Neural correlates of odors processing: preliminary fMRI study

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Smell –phylogenetically one of the oldest senses– has been neglected for years in neuroscience research. Although neural correlates of the smell function as well as smell disorders in several neurological and mental disorders have

been discovered, numerous aspects of this sense still remain elusive. Neuroimaging studies of smell functioning are still sparse because of the challenging methodology. The purpose of the presented fMRI research (performed with 3T Siemens PRISMA scanner) was to design an experimental procedure which effectively activates the brain areas related to smell functioning, as described in literature. We recruited 21 women and 5 men. They passively received two odorants (a pleasant flower odor and unpleasant rotten fish odor) to nostrils via the olfactometer. Data analysis (using SPM12) revealed an activation of olfactory region located in the frontal lobe, parahippocampal gyrus, insula and amygdala when stimulated by odorants, whereas the ROI analysis detected an activation of left parahippocampal gyrus when presented with the unpleasant odor (as compared to the pleasant one). The designed procedure rendered the expected results, which proves its effectiveness. It can be used in further research on smell, including studies on higher processes.

93. The role of the human amygdala subdivisions in reinforcement learning.

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Reinforcement learning is driven by the prediction error (PE) that reflects the difference between actual and expected outcomes. The sign of the PE is represented by valence which is positive when an outcome is better than expected and negative when worse than expected. Several studies have reported that the amygdala is responsive to unexpected outcomes. It remains unclear, however, whether distinct parts of the human amygdala are differentially involved in the encoding of the positive and negative valence of the PE. To address this issue, we used an fMRI method and Pavlovian learning task consisting of appetitive and aversive runs. The activity within the amygdala was localized using an in-house mask dividing the structure into dorsomedial (DM) and ventrolateral (VL) subdivisions. The results revealed that just the DM is responsive to unexpected outcomes. Specifically, the PE estimated with Rescorla-Wagner learning model is correlated with the BOLD signal in the DM in both appetitive and aversive runs, but only when the outcome is worse than expected. The result suggests that the human DM is involved in the encoding of the negative valence of the PE, regardless of the reinforcer's valence. The work supported by the National Science Center, grant no. DEC-2014/15/B/HS6/03658.

94. Motion-based stimulus-response correspondence (SRC) effect and the stimulu relative position.

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Motion-based stimulus-response correspondence (SRC) effect with congruency between stimulus motion and response movement is a phenomenon that still requires exploration and explanation. Here we investigated if motion-based SRC is influenced by the relative position when there is no spatial attention shift. To this end we presented red or green stimulus in the center of the screen or in the left or the right side of the screen. From each position stimulus could move either to the left either to the right. Participants responded to the stimulus color with leftward or rightward movements of dominant hand positioned in the body midline. We controlled with the eye-tracker if smooth pursuit eye movements occurred (no attention shift condition). Although motion-based SRC effect occurred when the stimulus was presented in the central position, this effect was larger when the stimulus was presented ipsilaterally to the response, and diminished when the stimulus was on the site contralateral to the response. The results indicate that the motion-based SRC effect is modulated by the spatial factor though it is not related to the issue of the spatial attention shift.

95. Openness to experience modulates the functional connectivity between the amygdala and the right-hemisphere affective network

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The amygdala plays a key role in emotion processing. Several recent studies have demonstrated that the pattern of its functional connectivity (FC) is modulated by personality traits such as extraversion and neuroticism, as assessed with the NEO-FFI test. However, little is known about the relationship between the amygdala FC and Openness to experience (Openness) which is associated with cognitive exploration and reward motivation. The goal of this study was to test the modulatory role of Openness on the FC between the amygdala and other brain regions. We analyzed resting-state functional magnetic resonance imaging data from 36 healthy adults. The left and right amygdalae were used as a seed in the whole-brain FC analysis. Lower Openness scores were associated with increased amygdala resting state FC mainly within the affective network in the right hemisphere including the pallidum, orbitofrontal cortex, and insula. We hypothesize that Openness could modulate the functional connectivity within the affective neural network underlying propensity to experience of negative emotions. The work supported by the National Science Centre, grant no. DEC-2014/15/B/HS6/03658.

96. An EEG study of the differential influence of valence, arousal and attention on perceptual judgments about duration

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Emotional effects on time perception are usually attributed to arousal or (selective) attention speeding up or slowing down the internal clock. This study explored how perceptual processing of emotional stimuli affect perceived duration of the time interval. ERPs were design to establish the neural basis for this effect. Forty participants took part in EEG recording while visual stimuli of varying durations were presented - temporal bisection task. Behavioral results revealed that durations of emotional stimuli were overestimated compared to neutral. The overestimation varied by the duration of the stimuli and by the type of category (evaluated on valence/arousal dimensions). The durations for high-arousal negative images were more overestimated and durations for other emotional stimuli were slightly overestimated relative to neutral images. The overestimation increased with increasing time intervals of the stimuli. ERP analysis demonstrated more pronounced amplitudes of P2, P3 and LPP potentials for high-arousal negative stimuli than other stimuli. Only in the case of N2 component, amplitude in this category was reduced. These findings indicate that emotional experiences may increase temporal estimation and suggest that attention and arousal are both involved in timing processing, but on a different degree, depending on the emotional category of the presented stimuli.

97. Early blind subjects have a thicker visual cortex. How does it relate to functional reorganization of this cortex towards new tasks such as language and reading?

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Congenitally blind subjects have a thicker visual cortex than sighted and late blind subjects (Jiang et al., 2009, structural MRI measurements). The theoretical explanation of this phenomenon ("less cortical pruning") has

remained without empirical evidence. Several functional MRI studies have also shown that the blinds' visual cortex becomes engaged in a variety of new tasks such as Braille reading or language (e.g. Rączy et al., 2019). The relationship between these two phenomena has not been investigated. Here, we tested the hypothesis that this thickness is related to the extent of functional reorganization. We extracted the increased thickness areas from 22 subjects anatomical MR scans (pericalcarine cortex, lingual gyrus and cuneus, FreeSurfer automatic parcellation) and correlated it with the strength of their fMRI activations in semantic tasks. Preliminary results show an inverse correlation between cortical thickness in the lingual gyrus (left hemispheres), and the strength of functional activations for tactile Braille words reading ($r=-.45$, $p<.05$). This suggests that sucessful reorganization for new functional tasks leads to thinner cortical gray matter in the reorganized areas. On its face, this result is consistent with the pruning hypothesis.

98. The effect of aging on learned irrelevance

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Learned irrelevance (LI) and perseveration (P) are two components that contribute to attentional set-shifting disorder, which is an integral aspect of executive function. P is the difficulty in diverting attention from the stimulus that was important in the previous stages of the task, while LI is the difficulty in shifting attention to the stimulus that was irrelevant in the previous task conditions. We investigated the influence of age on LI. An ID/ED visual discrimination learning paradigm was adopted to evaluate operationalization of the dependent variables in a more reliable way to classical neuropsychological methods (e.g. Wisconsin Card Sorting Task). Following a review of literature, hypotheses were derived suggesting P will be increased in older subjects, while LI will remain similar across groups. Older (N=28, M(age)=51,75 and younger (N=30, M(age)=25,47) subjects were recruited. LI and P levels were measured using the attentional set-shifting task by Dreisbach and Goschke (2004). The results revealed that compared to the younger adults, the older subjects have a significantly lower error rate for P conditions, with similar rates for LI. However, reaction times were longer among the older subjects for both P and LI conditions. The presented hypotheses were not equivocally confirmed.

99. Individual differences in auditory steady-state response and cognitive functions: exploratory study

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Research demonstrates potential link between gamma-band auditory steady-state response (ASSR) and cognitive functions, yet there is a gap in consistency of these results. We aim to examine the relation between the gamma-range ASSRs and cognitive functions. The data was collected from 46 subjects using 64 channels electroencephalography. Subjects underwent The Global-Local (GL), Digit span backward (DSb), Bivalent shape (BST) and Tower of London (ToL) tasks. During the recording, the auditory stimulus applied (called chirp) had changing frequency window. The peaks of the individual gamma frequency (IGF) were extracted from phase-locking index (PLI). Negative correlations were found between the PLI maximums of chirp and the performance time on the GL ($p<0.01$) and BST ($p<0.05$) tasks as well as positive correlations with the number of correct answers on the GL task ($p<0.05$). Moreover, there was a positive correlation between the peak of IGF elicited by chirp-up and move time on TOL task ($p<0.05$). The correlations shown with the GL and BST tasks suggest that lower phase synchrony might indicate slower information processing and lower number of correct answers. However, the associations found with the IGF peaks are contradictory. Study was supported by the Research Council of Lithuania (LMTLT), agreement No S-LJB-20-1.

COMPUTATIONAL POSTERS

100. Classical and exploratory ANOVA analysis of response-locked ERP

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In the classical approach, we assume that when designing the experiment in the way described in the literature, we can observe specific components of the ERP induced in specific areas of the brain with specific latencies. In order to check if the data-driven approach allows verifying the classical approach and whether it allows to better match the analysis, we compared it with the classical analysis, using data from the emotional experiment. Where we investigated the electrophysiological correlates of execution of an ambiguous task under the influence of the emotionality of words stored in the working memory. The ANOVA classical analysis of ERP was compared with an exploratory approach using GFP (Global Field Power), calculated as spatial standard deviation. The analysis of the GFP curve was used to determine the time periods in which we performed a 4-factor analysis of variance with repeated measures. In the presented case we were able to find significant effects related to the valence and origin consistent with classical analysis while maintaining control of the statistical significance. Phenomena were found to be shifted in the time domain with tilted pattern in the spatial distribution.

101. Reducing acquisition time using compressed sensing technique for diffusion microstructure imaging

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Diffusion imaging using the nuclear magnetic resonance phenomenon is a powerful diagnostic tool that enables to measure microstructural properties of the tissues, especially in the central nervous system. We can observe rapid development of technology resulting in more accurate signal acquisition and precise diffusion models. However, physical and biological restrictions cause the scan time prolongation is inevitable. To prevent this tendency new signal reconstruction techniques are developed among them the compressive sensing (CS) being a particularly interesting one. It uses incoherent sampling schemes in association with signal recovery in its sparse domain. In this work, we propose the integration of compressed sensing principles with a high angular resolution diffusion model called SHORE (Simple Harmonic Oscillator Reconstruction and Estimation). The main objective of this work is to check the quality of microstructural diffusion indices reconstructed via the CS methodology and compare to those retrieved from fully-sampled data. Diffusion measures inform about brain tissue condition like average volume, cross-sectional area and length of the white matter fiber tract within the imaging voxel. The results show that there is a significant strong correlation (Pearson's r around 0.9) between diffusion indices estimated from fully sampled and highly subsampled (even 20% of the data) images.

102. Intra-subject MR image registration

Karolina Dębowska

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Registration of images with different modalities is a helpful tool in many medical diagnoses, as it enables to detect the pathological condition in the tissue with higher accuracy. The aim of this work is to verify the accuracy of the alignment between diffusion-weighted and T2-weighted images when there is rotation and translation between them. The proposed method is based on calculating diffusion anisotropy measures from diffusion-weighted images (such as fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity) and aligning them to T2-weighted images to verify if the choice of measure has an impact on registration accuracy. Correspondence between registered images is verified using mutual information (MI). The proposed method is tested for various shifts (v = [6,6] and v = [2,2]) and rotations (5 and 7 degrees) between images on two data sets obtained from two different subjects. For the first subject, the MI value for translation v = [6,6] is 0.1 lower for fractional anisotropy than for the rest of the measures, and for the second subject, MI value is similar for all measures (around 0.45). It demonstrates that the choice of appropriate anisotropy measure differs from subject to subject and can increase registration accuracy.

103. Multi-channel Matching Pursuit algorithm as an exploratory tool for identification of event-related components

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Hypothesis-driven methods of event-related potential (ERP) analysis are the basis for searching for neural correlations of mental processes. Investigating activity changes only in components commonly known from the literature may cause some information loss by ignoring, perhaps, new effects not foreseen in the hypothesis's formation stage. An alternative approach is an exploratory, data-driven analysis. In our study, we introduce a way to adapt the multi-channel Matching Pursuit algorithm decomposition as an exploratory tool for the analyses of event-related EEG data [1]. The proposed method allows identifying components based on their time-frequency and topographic features. The properties of the technique will be presented using simulated data representing mixtures of four well-known ERP components [2]: N100, P2, P300, and LPC.

104. Corpus Callosum T1-weighted signal features and fluid intelligence

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Fluid intelligence (FI) is the potential to learn abstract relationships and apply them to novel situations irrespective of previously acquired knowledge. The relationship between brain structure and FI remains elusive. In this project, we aim to expand on the previous model proposed during the Adolescent Brain Cognitive Development (ABCD) Competition in 2019, which attempted to predict the FI using the structural brain phenotype. This study utilized the MRI features collected from 3739 ABCD subjects to predict the residual FI. We focus on using corpus callosum T1-weighted signal entropy, Kelly and Bowley skewness, and kurtosis to improve the random forest regression model. The restricted set of features model eliminated the mean and variances to highlight the effect of entropy, kurtosis, and skewness. The analysis was performed on the training and validation dataset. We observed a decrease of 0.5% in the Mean Standard Error (MSE) from the model (MSE= 67.06), on the same validation data set that was used in the ABCD-NP challenge. We achieved a small but definite improvement in explaining the FI on the validation

dataset, given the complexity that is associated with predicting a component like FI in children (9-10 y/o) based on structural brain scans.

Biological Session II

ASTROCYTES AND NEUROIMMUNOLOGY

17:00 – 18:30

chaired by: **Cleide dos Santos Souza** (Sheffield Institute for Translational Neuroscience, UK)

Astrocytes in Neurodegeneration: the influence of a bad neighbourhood

Cleide dos Santos Souza

Sheffield Institute for Translational Neuroscience, UK

Glial cells represent an important population of cells in the nervous system, yet their multiple functions remain to be fully understood. Whereas neurons generate and propagates electrical and chemical signals, glial cells assume full responsibility for modulate neuronal function and signalling and to keep the homeostasis and defence of the central nervous system (CNS). In the past, glial cells have been considered merely passive contributors to brain function. However, this view changed in the past few years and glial cells have been changing their role from support cells to protagonists. Astrocytes play a critical role in the homeostasis and function of the CNS. Astrocytes do not just provide trophic, metabolic, and structural support for neurons, but also play an active role in complex neuronal-glial communication, regulation of synapse formation, function and plasticity and regulation of blood flow. Although abnormal glial function has been described as an early pathological feature commonly observed in several neurodegenerative diseases. The role of glial cells in the pathogenesis of neurodegenerative diseases and in neurological conditions have been underestimated and these cells were considered as mere secondary responders in the pathological process. However, over the past decades, with the emergence of new technologies and model systems (cell cultures such as iPS cells and genetics), considerable progress was achieved towards our understanding of glial function, revealing a central role for these cells in the brain development, aging and progression of neural pathologies, including neurodevelopmental disorders, neurodegeneration, and demyelinating pathologies. Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterised by progressive loss of motor neurons (MNs). Although ALS is primarily an MN disease, astrocytes have an important role in its pathogenesis. A number of studies have shown that this non-cell-autonomous mechanism involves soluble factors secreted by astrocytes as the exposure to conditioned medium (CM) from ALS astrocytes is sufficient to trigger MN death. The mechanism behind astrocyte toxicity, however, remains unclear. Recent cutting-edge research has shown that endogenous DNA damage plays a key role in MN death in ALS. The aim of our study is to characterise levels, types and timing of astrocyte-induced DNA damage in MNs and identify mechanisms through which astrocytes induce DNA damage, and MNs respond to this insult. We used healthy control and ALS patient-derived astrocytes generated through a method of direct reprogramming. CM was isolated from the astrocytes and used to treat healthy human iPSC-derived motor neurons.

Uncovering novel drug therapies and targets for amyotrophic lateral sclerosis (ALS) using AI

Monika Myszczynska[1], Matthew Stopford[1], Nora Markus[1], Sophie Nyberg[1], Peter Cox[2], Peter Richardson[2], Richard Mead[1], Guillaume Hautbergue[1], Laura Ferraiuolo[1]

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Although ALS is characterised by motor neuron (MN) death, astrocytes have been implicated in the disease. There are no disease course-altering drugs available for ALS. Artificial intelligence (AI) technologies have shown a potential to uncover novel therapies for ALS in a time-efficient manner, as algorithms can identify links between diseases and repurposing candidates after a scan of scientific literature and online databases. Our aim was to determine the effect of two AI-identified drugs on MN survival and decipher their modes of action in a pathophysiologically-relevant in vitro ALS model. ALS and control induced astrocyte (iAstrocyte) lines were used in a co-culture drug screening. Protein levels of drugs' known targets were measured. Cells were assessed for hallmarks of ALS-associated TDP-43 proteinopathy: nuclear loss, fragmentation, and phosphorylation. Autophagy function assay was performed in HEK293 cells. Gefitinib and nilotinib caused a significant rescue of MN survival. Western blotting showed gefitinib to significantly reduce levels of TDP-43 fragments in patient iAstrocytes. Autophagy assay showed gefitinib to be an autophagy activator. Nilotinib had no significant effect on TDP-43 proteinopathy and autophagy, indicating that these compounds exert their therapeutic effects through different mechanisms.

Anti-inflammatory and behavioural effects of a novel formyl peptide receptor 2 agonist in two mouse models of autism spectrum disorder

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Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by abnormal social interactions, repetitive behaviors and neuroinflammation. Among lipoxins, lipoxin A4 (LXA4) is one of arachidonic acid metabolites with potent anti-inflammatory properties mediated by its receptor formyl peptide receptor 2 (FPR2). Decreased plasma levels of LXA4 were found in children with ASD, but little is known about the role of LXA4 and FPR2 in animal models of autism. Here we examined for the first time the effect of a novel ureidopropanamide based FPR2 agonist on neuroinflammatory state and on behavioural phenotype in two mouse models of ASD: the inbred strain BTBR T + tf/J mice and the murine model induced by prenatal exposure to valproic acid. Our results showed that the sub-chronic administration of this FPR2 agonist was able to increase social behavioral in different behavioral tests. Then, biological analysis revealed the important contribution of FPR2 and LXA4 in both strains. The neuroprotective effect of the FPR2 agonist was also supported both by the reduction of pro-inflammatory cytokines and by preliminary in vitro results on hippocampal neurons of BTBR mice. These findings suggest the important role for FPR2 in this disease opening a new scenario in the treatment of ASD.

Tracking vesicular gliotransmission to decoding Ca2+ signals

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The concept of "tripartite synapse" assumes that astrocytes not only support neurons metabolically but are also crucial partners in neurotransmission. Astrocytes are electrically non-excitable cells therefore, the calcium (Ca2+) signaling is considered to be a measure of their activity. However, to this day scientists have not been able to obtain a definite answer to the question: is there a biological link between the frequency of intracellular Ca2+ levels and secretion of gliotransmitters? Our aim is to try to answer this question, therefore we have designed probes to simultaneously examine exocytosis and local Ca2+ signaling in hippocampal astrocytes co-cultured with neurons. We use Synaptobrevin2 (vesicle-associated membrane protein) in fusion with pHluorine (pH-dependent form of GFP) to observe exocytosis in astrocytes. For the study of local Ca2+ signals, we tagged jRCaMP1a (genetically encoded calcium indicator) with N-terminus of Lck. We have observed both probes, previously introduced into cells via chemical transfection, using TIRFM with high axial resolution below 100 nm. Our preliminary measurements show that there is a relationship between Ca2+ levels and a rate of exocytosis. The spatio-temporal character of this process in astrocytes is poorly described, thus we plan to apply electrical stimulation for higher precision.

Cognitive Session II

Dogs (*Canis familiaris*) as a new translational model for human mental conditions

17:00 – 18:30

chaired by: **Anna Kis** (Institute of Cognitive Neuroscience and Psychology, Research Centre for Natural Sciences HAS, Budapest, Hungary)

The dog as a model for hemispatial neglect. Behavioural and psychophysiological parallels

Anna Kis, Henrietta Bolló

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The present study is a pioneer to relate human unilateral spatial neglect disorder to dogs' side-bias. Family dogs with previous history of side-bias in cognitive experiments participated in a series of two-way food choice tasks manipulating peri-and extrapersonal space and the reference of choice (egocentric vs. allocentric). Furthermore, we recorded sleep polysomnography data and compared lateralized brain activity during sleep with behavioural data.

Affective disorder-like symptoms in the dog? A sleep deprivation experiment

Henrietta Bolló[1], Krisztina Kovács[1], Radu Lefter[2], Ferenc Gombos[3], Enikő Kubinyi[4], József Topál[1], Anna Kis[1]

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It has been shown that positively versus negatively valenced dog-human social interactions substantially affect dogs' sleep structure. In the present study we manipulated dogs' sleep structure by specifically disrupting REM versus Non-REM sleep while maintaining equal sleep efficiency (monitored via non-invasive polysomnography). We show for the first time a causal link between sleep structure and inter-specific emotion-processing in the family dog.

A new translational approach to study the neurocognitive bases of autism

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Despite extensive research the pathogenesis of autism is still largely unknown. The variations in the phenotypic manifestation of autism spectrum disorder (ASD) are the final outcome of the interactions of multiple genetic and environmental factors. Regarding the proximate mechanism of the development of ASD, studies found that this disorder is related to dysfunctions of those brain regions that are specialized for early-stage processing of social information, including the amygdala, the ventral striatum, and orbitofrontal cortex. We propose that the behavioural convergences between dogs and humans make dogs especially suitable for studying ASD.

Development of a human-analogue 3-symptom domain ADHD questionnaire for dogs

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The family dog, in its natural environment, exhibits neuropsychological deficits redolent of human psychiatric disorders, including behaviours that are similar to human Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms. In humans, questionnaires are efficient tools to assess ADHD symptoms and are the basis for diagnosis. For dogs, a 13-item questionnaire has already been developed to measure two ADHD symptom dimensions (inattention and hyperactivity/impulsivity). However, owners reported some difficulties in responding and scores did not distribute symmetrically. Moreover, in modern human questionnaires, activity and impulsivity are separately measured factors. Based on standard assessment methods in humans, we aimed to (1) review the old questionnaire, (2) develop and validate a better-detailed, psychometrically improved tool to assess owners' views on relevant dog behaviours, (3) add items that allow for separate analysis of impulsivity, and (4) include questions on functional impairment. We collected data from 1168 owners for the different validation steps and also involved trainers, similarly to the human procedure, where teachers complete the questionnaires as an experienced control. Exploratory factor analysis revealed 5 factors (attention, inattention, activity, impulsivity, vocalisation) which covered all three symptom dimensions in dogs. Examination of functional impairment together with observed extreme scores can allow us to distinguish diagnosable (extreme) individuals.

PLENARY LECTURE

19:00 – 20:00

chaired by: **Anna Błasiak** (Jagiellonian University, Kraków, Poland)

Neural Mechanisms of Aggression

Dayu Lin

New York University, USA

Aggression is an innate social behavior essential for competing for resources, securing mates, defending territory and protecting the safety of oneself and family. In the last decade, significant progress has been made towards an understanding of the neural circuit underlying aggression using a set of modern neuroscience tools. Here, I will talk about the history and recent progress in the study of aggression.

TOPIC DISCUSSIONS

20:00-21:00

How drugs of abuse affect innate motivation circuits?

chaired by: **Anna Błasiak** (Jagiellonian University, Kraków, Poland)
Dayu Lin (New York University, USA)
Luigi Bellocchio (Neurocentre Magendie, Bordeaux, France)

How hippocampal inhibitory microcircuits contribute to memory?

chaired by: **Steffen Kandler** (University of Basel, Switzerland)
Pico Caroni (University of Basel, Switzerland)
Pablo Mendez (Cajal Institute, Madrid, Spain)

What is the best approach to model neurological diseases?

chaired by: **Tomasz Prószyński** (Łukasiewicz Research Network, PORT Polish Center for Technology Development, Wrocław, Poland)
Camila Esguerra (University of Oslo, Norway)
Maryam Afzali (Cardiff University, UK)
Cleide dos Santos Souza (Sheffield Institute for Translational Neuroscience, UK)

Is there anything unique about adult neurogenesis?

chaired by: **Michał Ślęzak** (Łukasiewicz Research Network, PORT Polish Center for Technology Development, Wrocław, Poland)
Alejandro Schinder (Leloir Institute, Buenos Aires, Argentina)
Martine Migaud (University of Tours, France)
Juan Manuel Encinas (Achucarro Basque Center for Neuroscience, Leioa, Spain)

DECEMBER 9, 2020 (Wednesday)

PLENARY LECTURE

11:00 – 12:00

chaired by: **Gilles van Luijtelaar** (Donders Centre for Cognition, Radboud University Nijmegen, the Netherlands)

Human defensive reactions and their role in decision making

Karin Roelofs

Radboud University, Nijmegen, the Netherlands

Psychologists often assume that automatic defensive threat reaction, while essential in explaining animal behavior, only have limited value when it comes to understand human behavior. There is, however, increasing evidence that defensive reactions, such as freezing, have an impact on subsequent approach-avoidance decisions under acute stress in humans. Understanding the mechanisms that drive such decisions is particularly relevant for patients with anxiety disorders, whose persistent avoidance is key to the maintenance of their anxiety. In recent years, computational psychiatry has made substantial progress formalizing the mechanisms through which we make (mal)adaptive decisions. However, most current models simply ignore the transient psychophysiological state of the decision maker. Here, I argue that the balance (or lack thereof) between para-sympathetic and sympathetic activity is instrumental in driving freezing behaviour, and that it influences approach-avoidance decisions under acute threat in different ways. To illustrate, I first explore the effects of freezing on different kinds of human action decisions under threat. Next, I discuss recent translational (rodent-human) work that has helped to characterize the neural mechanisms implicated in animal and human defensive freezing. Finally, through two prospective longitudinal studies, I show that individual differences in susceptibility to freezing are predictive of the development of anxiety symptoms. Overall, this work suggests that defensive threat reactions and associated psychophysiological states not only affect acute decision making, but also predict long-term symptom development. As such, these factors have great import for resilience research, and should constitute an integral part of any theory of human decision making.

Computational Session I

Computational Methods in Neuroscience

12:30-14:30

chaired by: Tomasz Pięciak (AGH University of Science and Technology, Kraków, Poland

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Quantifying Tissue Microstructure using Diffusion Magnetic Resonance Imaging

Maryam Afzali

CUBRIC, Cardiff University, UK

Diffusion-weighted magnetic resonance imaging is a non-invasive tool to investigate brain microstructure. It provides the information to estimate the compartmental diffusion parameters. Biophysical modeling in diffusion MRI tries to relate the diffusion signal to the underlying tissue microstructure. Selecting the appropriate model for the tissue microstructure and deciding about the acquisition parameters are the essential steps in extracting the features of the tissue. Robust fitting of the parameters should be validated using numerical or phantom studies. It is necessary to check the validity of the model in pathological conditions. Translating the results of research to clinical applications is one of the main parts. Each of these steps needs an appropriate strategy and has its challenges.

Heavy tails in the brain

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We study the relation between two seemingly unrelated measures in the brain that exhibit heavy tails: neuronal avalanches, i.e. bursts of activity with power-law distributions of sizes and lifetimes, and synaptic weights that are believed to be distributed according to the log-normal distribution. To this end we have developed a novel theoretical framework that abandons the prevailing Gaussian assumption. Many current models of neuronal avalanches do not rely on heavy-tailed synaptic weight distributions, suggesting that heavy tails of these two quantities may not be related. However, our recent theoretical considerations indicate that this independence no longer holds if two biologically relevant constraints are introduced, i.e., that neurons (1) receive many incoming connections and (2) do not spike if the membrane potential is below some positive threshold, e.g., in the absence of inputs. Under these assumptions we have shown that heavy tails of synaptic weights are necessary to generate biologically plausible low activity levels and associated neuronal avalanches. Moreover, our results suggest that the observed distribution of synaptic weights may play an important functional role in the brain, effectively sparsifying the network, removing the bistability, and thus enabling the network to stay close to the edge of chaos.

Local Autonomous Online Regulation of Echo State Networks

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Echo state networks (ESNs) have proven to be a powerful tool in the field of time series prediction. The spectral radius of the synaptic weight matrix provides a measure to regulate these networks into an appropriate working regime. However, for ESNs to also serve as an abstract model of biological recurrent networks, directly tuning the spectral radius is not a plausible mechanism. We show that the spectral radius can be regulated by local homeostasis, using the variance of neural activity and the variance of the membrane potential corresponding to recurrent inputs. The latter implies that our model relies on the assumption that external and recurrent input signals can be treated as two separate streams of information. We demonstrate the importance of this separation by means of the network performance, quantified by a non-linear memory recall task. The homeostatic control modulates a gain factor acting on the recurrent input and is biologically plausible in the sense that it only relies on locally available information. While theoretically it only yields precise tuning for statistically independent external driving across nodes, numerical experiments suggest that it also holds under less restrictive conditions.

Spectrums, not dichotomies. Acting as an ecological-enactive entity

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In this work I look for a common ground between ecological-enactive and representational interpretations of the free energy principle. The former stands that living organisms are the brain-body-environment dynamic systems living in an econiche which offer relevant affordances (Bruineberg et al., 2018). The latter emphasis that the generative model reflects a causal structure of the environment, but the computations take place in the model, hence - have a representational format (Hohwy, 2013; 2016; Clark, 2013; 2015; 2017). I compare this duality to a dichotomy between the model-free and the model-based accounts of behavioural control, respectively (Packard, 2008; Dolan and Dayan, 2013, Daw et al., 2005; Doya et al., 2002). Actions mediated by the model-free controller does not require higher cognitive processes and are believed to be mediated by sensorimotor parts of the brain. On the other hand, the model-based controller operates on representations by implementing action policies which

are believed to be computed in the associative structures of the brain. I stress two crucial points emerging from this comparison. First, the behavioural literature reveals, that the both controllers work together when producing behaviour. I argue that recognising this cooperation in the free-energy principle field allows for cooperation between the Helmholtzian and the ecological-enactive interpretations. Second, action automatisation is associated with a gradual transfer from DMS (dorsomedial striatum, caudate in primates) to DLS (dorsolateral striatum, putamen in primates) (Yin and Knowlton, 2006; Williams and Eskandar, 2006). Given that, I understand an emergence of the econiche as a progressive automatisation of actions performed in a given environment. In other words a shift from the model-based to the model-free controllers. This understanding implies that affordances, similarly as skills, vary in power. Thus I suggest a gradual distribution of power of the affordances; spanning from new affordances yet to be explored by the system to known signifiers (Norman, 2013, p.14) underlying performance of the habitual (automated) action in the known econiche.

Biological Session III

Endocannabinoid Modulation Of Brain Functions

12:30 – 14:30

chaired by: **Urszula Skupio** (INSERM, Neurocentre Magendie, Bordeaux France)

Cannabinoid signaling in the brain: cell type / subcellular localization underlies differential biochemical and behavioral outcomes

Luigi Bellocchio

INSERM, Neurocentre Magendie, Bordeaux France

Cannabinoid drugs (e.g. the active principle of the plant cannabis, D9-tetrahydrocannabinol, THC) exert several effects on the brain via the activation of the G protein-coupled type-1 cannabinoid receptors (CB1). On the other hand, CB1 receptors are part of a physiological system (the endocannabinoid system, or ECS), through which the particular endogenous signaling molecules (the endocannabinoids) control a plethora of brain functions. The effects of exogenous cannabinoids and the physiological roles of the ECS are only partially overlapping. This is likely due to the fact that the ECS has patterns of activation that are extremely regulated in time and space, features that are obviously overcome by massive stimulation of CB1 receptors by exogenous drugs. Dissecting the impact of CB1 receptors expressed in different brain regions, cell types or subcellular locations represent for our team a "bottom-up" approach to try addressing basic principles of brain functions. Thus, among others, CB1 receptors helped us studying in recent years the balance between neuronal excitation and inhibition in specific behaviors, the impact of astroglial signaling in memory, the role of hippocampal inhibitory transmission in the regulation of incidental associations, or the importance of bioenergetic processes in brain cellular and behavioral processes. In this lecture, I will present an excursus of our studies on the mechanisms of action of CB1 receptors in the brain, with special focus on how this approach can contribute to exploring basic principles of brain functioning.

Astroglial mitochondrial calcium dynamics determine synaptic integration

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Accumulating evidence supports a bidirectional communication between neurons and astrocytes which modulates information processing and behavior. One of the most interesting functions regarding the regulation of brain

network activity is the type-1 cannabinoid receptor (CB1)-dependent hippocampal lateral potentiation, through which astrocytes are able to enhance synaptic efficacy several tens of micrometers away from the stimulation site. However, the precise intracellular mechanisms underlying this function are currently unknown. Here we asked whether activation of astroglial mitochondrial CB1 receptors (mtCB1) might regulate intracellular calcium dynamics, thereby contributing to CB1-dependent synaptic plasticity. Using live cell imaging, two-photon and fiber photometry approaches, our results indicate that mtCB1 activation both, in vitro and in vivo, actively promotes endoplasmic reticulum-dependent calcium entry into mitochondria through a mitochondrial calcium uniporter/AKT dependent mechanism. Accordingly, electrophysiological recordings in hippocampal slices show that the deletion of mtCB1 (using a non-mitochondrial CB1 mutant receptor) or the specific astroglial mitochondrial calcium blockade drastically reduced the probability of lateral potentiation. Altogether these data reveal an unforeseen link between mitochondrial functions, astroglial activity and information processing in the brain.

Yin-Yang effects of the endocannabinoid system on panic-like behavior

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Endogenous ligands of the endocannabinoid system (eCS) are known to play a fundamental role in the regulation of fear and anxiety processes. Depending on the task, 2-arachidonyl glycerol (2-AG) and anandamide (AEA), the two main endocannabinoids, may exert opposite effects: Whereas enhanced AEA signaling showed panicolytic effects, enhanced 2-AG signaling lead to more sustained passive and active fear responses, mediated by the activation of the cannabinoid receptor 1 (CB1). Our work investigates the janus-faced role of both endocannabinoids, and the consequent involvement of CB1 in different emotional states of mice.

Adolescence – the stone(d) age of psychosis?

Tibor Štark[1,2], Alice Hartmann dos Santos[2,3], Daniel E. Heinz, Benoit Boulat[2], Michael Czisch[2], Carsten T. Wotjak[2]

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Recent global mind-shift of the general public on the perception of cannabis use with aggrandizing calling for its legalization has been creating the imperative need for a thorough understanding of its impact on health and behavior. Alarmingly, cannabis use is already on the rise among adolescents, a specifically sensitive demographic group regarding neurodevelopment. While primary research focus is mostly targeted at acute effects of cannabis and/or its constituents (e.g., THC) on cognitive and emotional domains and their correlates, temporal effect on the brain development (i.e., the period of exposure as well as the after-exposure progression over time) is not well defined. Thus, our research aimed to assess structural changes of gray and white matter of mice repeatedly exposed to THC during adolescence using longitudinal MR imaging data from PND28 until the age of 1 year, and their possible implications for behavioral traits in adulthood.

Cognitive Session III

Emotional Expression and Perception. A Functional and Evolutionary Account.

12:30 – 14:30

chaired by: **Mariska Kret** (Leiden University, the Netherlands)

Detecting attraction: deceptively simple, endlessly complicated

Iliana Samara

Leiden University, the Netherlands

To navigate our romantic environment, humans need to accurately detect cues signaling attraction. Previous research showed that participants in a dating study could not accurately detect their partners' attraction (Prochazkova et al., 2019). A likely explanation could be that since a date is a highly arousing context, detecting others' attraction cues might be more difficult. This assumption is supported by findings showing that third-observers are accurate in detecting others' attraction cues (Place et al., 2009). In the present study, we examined whether participants can accurately detect attraction between two participants who were on a date. We further examined whether direct romantic experience facilitates detection accuracy. In two studies, adults and children viewed video segments (3 sec) of participants who were on a blind date. Participants viewed either the video of the two "dating" partners simultaneously (Study 1; N = 118) or one partner in isolation (Study 2; N = 64). Our results suggest that neither adults nor children could accurately detect attraction. In this talk I will elaborate on why attraction cue detection is difficult.

The choreography of human attraction: physiological synchrony in a blind date setting

Eliska Prochazkova[1,2], Elio E. Sjak-Shie[1,2], Friederike Behrens[1,2], Daniel Lindh[3,4,5], Mariska E. Kret[1,2]

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[5]Brain and Cognition, Department of Psychology, University of Amsterdam, the Netherlands.

Humans are social animals whose mental wellbeing is shaped by the ability to attract and connect with each other. In a dating world in which success can be determined by brief interactions, apart from physical features, there is a whole choreography of movements, physical reactions and subtle expressions that drive humans' sexual attraction. To determine what drives attraction, we measured the physiological dynamics between people during real-life dating interactions outside the laboratory, where dating is most relevant. Participants wore eye-tracking glasses with embedded cameras, and devices to measure physiological signals including heart rate and skin conductance. We demonstrate that females were more expressive than males, while males looked longer at females. Crucially, visible signals that can be controlled, such as facial expressions or gaze, did not predict attraction. Instead, attraction was predicted by synchrony in heart rate and skin conductance between partners, which is unconscious and difficult to regulate. Our findings suggest that shared emotionality is vital for mutual attraction. Moreover, physiological synchrony may provide a medium for translating visible expressions into embodied emotions, which can turn into intentions via somatosensory simulation.

Emotional contagion in different interaction contexts: face-to-face vs video call

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The last few years, this year particularly, have highlighted the importance of new means of communication for interacting with other people. Although an increasingly prevalent method of communication is via video call platforms (i.e. through screens of various computer devices), little is known about the effect, if any, of this unexplored relationship involving social distance and emotional contagion. To the best of our knowledge, at the time of writing, there is no published study that has directly controlled for the medium of communication used, whilst measuring emotional contagion. The goal of this study was to investigate whether different media of communication has a direct impact on levels of emotional contagion. Using human confederate-participant dyads, the contagiousness of yawning, scratching, lip biting, and touching was tested across three different communication media: i) watching a pre-recorded video, ii) live stream (via webcams), and iii) live interaction. As priory theorizing, a main effect of communication media on levels of emotional contagion was found. Specifically, we found mimicry to be significantly higher in live interaction and live-stream compared to the pre-recorded condition. However, we didn't found a significant difference between the live interaction and live stream condition, contrary to our hypotheses. Since new media of communication are becoming incredibly crucial for our social interaction, future researches should investigate more the impact of them on the quality of our interaction.

Going beyond facial expressions: the additional value of investigating subtle emotional cues and emotional body expressions

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The investigation of nonverbal signals in human interactions has provided convincing evidence that affective information is not only communicated verbally but also less direct, via changes in physical appearance (e.g. facial expressions, pupil size, a blush). Crucially, characteristic bodily responses (e.g. arousal, mimicry) of the observer have been suggested to promote the correct interpretation of these changes. While most research so far has focused on the perception and mimicry of prototypical facial expressions, observers' reactions to other sources of information such as body postures or subtle facial cues (i.e. blushing, tears and pupil dilation) are insufficiently described. Therefore, we aimed to create a holistic picture of emotion perception by (1) using three different sources of emotional information (facial expressions, bodily expressions and subtle facial cues) and (2) measuring changes in observers' physiological reactions (facial electromyography, skin conductance, skin temperature and pupil size). Interestingly, while emotion-specific response patterns were quite similar for bodily and facial expressions in some physiological measures, we found substantive differences in others. Expressions did not have to be overt to be influential; also subtle emotional cues modulated observer's physiology. These results call for a more fine-grained description of emotional expressions and their transfer between sender and perceiver.

Emotion Processing in Homo and Pan

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Leiden University, the Netherlands

Evolution prepared group-living species, (non)human primates included, to quickly recognize and adequately respond to conspecifics' emotional expressions. Different theories propose that mimicry of emotional expressions facilitates these swift adaptive reactions. When species unconsciously mimic their companions' expressions of

emotion, they feel reflections of their emotions which informs social decisions. The majority of emotion research has focused on full-blown facial expressions of emotion in humans. However, facial muscles can sometimes be controlled; humans know when to smile, and when not to. In this talk, I therefore argue for a broader exploration of emotion signals from sources beyond the face or face muscles that are more difficult to control. More specifically, I will show that implicit sources including the whole body and subtle autonomic responses including pupil-dilation are picked up by observers and influence subsequent behavior. In my research, I take a comparative approach and investigate similarities and differences in the perception of emotions between humans and great apes. I will here discuss new, recently collected data and suggest avenues for future research that will hopefully eventually lead to a better comprehension of emotional expressions and how we come to understand each other's emotions.

POSTER SESSION I

Biological Session IV

Synaptic Plasticity

17:00 – 18:30

chaired by: **Sandra Jurado** (Institute of Neuroscience CSIC-UMH, San Juan de Alicante, Spain)

Interneuron diversity in hippocampal memory circuits

Pablo Mendez

Cajal Institute, Madrid, Spain

Activity dependent changes in synaptic strength and structure are at the basis of the remarkable adaptive capability of mammalian brain. Recent studies showed that similarly to their excitatory (glutamatergic) counterparts, also Gamma-aminobutyric acid (GABA)-releasing inhibitory synapses can undergo activity-dependent functional and structural changes. Despite substantial experimental evidence, we have only partial knowledge of the implications of this type of plasticity for the function of inhibitory synapses and the circuits they form. In my talk, I will discuss experiments directed to understand the mechanisms and functional role of this phenomenon. I will discuss the consequences of plasticity on GABAergic and glutamatergic synapses on regulating the balance between excitation and inhibition and on the memory function of hippocampal neuronal ensembles. Since GABAergic synapses originate from a very heterogeneous population composed of a stunning diversity of different subtypes, I will also discuss the possibility that plasticity of the GABAergic synapses maybe associated to equally diverse properties governing layer distribution, spatial extent and molecular composition of the different inhibitory neuron subtypes.

GABAergic tonic inhibition shows cell type-dependent plasticity in the hippocampus

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In recent years plasticity of inhibitory synapses gained a significant attention, despite being overshadowed for many years by research into the excitatory synaptic plasticity. GABA (γ-aminobutyric acid) as a main inhibitory

neurotransmitter in the adult brain, reduces a probability of action potentials generation in neurons. The majority of tonic conductance in this structure is mediated by α5-containing GABAA receptors present in extrasynaptic areas in the neuronal membrane but it is still debated whether this component of inhibition is plastic. The aim of this study is to describe whether plastic changes of tonic conductance take place in a model of chemically evoked GABAergic plasticity in specific type of neurons (PV positive interneurons and pyramidal cells in the CA1 region of mouse hippocampus). Using a whole-cell patch-clamp configuration we have recorded tonic current mediated by α5-containing GABAA receptors agonist - etomidate. Postsynaptic inhibitory long-term potentiation (iLTP) was induced by a brief applications (3min) of NMDA. We found that tonic conductance in the PV-positive interneurons is reduced after iLTP induction, however, the opposite effect is observed in pyramidal cells. We conclude that tonic inhibition is a plastic phenomenon but the direction of changes is dependent on the neuronal type. Acknowledgements: The research was supported by National Science Center (NCN) grant UMO-2018/31/B/NZ4/01998.

Medial septum directly inhibits the nucleus incertus theta phase-locked neurons - optogenetic and electrophysiological in vivo and ex vivo studies

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Hippocampal theta oscillations are correlated with locomotion and alertness. Medial septum (MS) is a key pacemaker of this rhythm. Another structure involved in theta rhythm generation is brainstem nucleus incertus (NI). MS and NI are reciprocally interconnected, however functional details of this connection remain elusive. Therefore, the aim of the current study was to determine how MS affects NI neuron activity. In vivo recordings of NI neuron activity using multi-electrode-arrays were combined with MS optogenetic stimulation. Local field potential was simultaneously recorded from the hippocampus. Ex vivo whole-cell patch-clamp recordings of the NI neurons activity were combined with optogenetic stimulation of MS-originating fibres. In vivo recordings revealed that all theta phase-locked NI neurons were inhibited and none of tonic, theta phase-independent neurons responded to MS optostimulation. Ex vivo, majority of NI neurons that were responsive to MS originating fibres photostimulation, exhibited GABAa-dependent (gabazine-sensitive) inhibitory postsynaptic currents. In individual NI neurons excitatory postsynaptic currents were observed. Direct inhibition of NI neurons by MS is possible element of the mechanism synchronizing hippocampal theta oscillations. Funding was provided by National Science Centre Poland UMO-2014/15/B/NZ4/04896 and JU-statutory-funds N18/MNS/000030.

A link between neurotransmitter identity and drug-induced behavioral alterations

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Exposure to drugs induces maladaptive brain plasticity that results in behavioral alterations. Neurotransmitter switching is an environmentally-induced form of plasticity never studied in association with drug abuse, in which activity causes a subset of neurons to stop expressing the transmitter they were expressing before and/or express a different one. Here, by combining immunohistochemistry and genetically encoded fluorescent reporters, we showed that repeated administration of the addictive drug phencyclidine (PCP) induces a subset of glutamatergic

excitatory neurons within the prelimbic cortex of adult mice to gain the inhibitory transmitter GABA and its synthetic enzyme, GAD67, both of which are still present after 18 days of abstinence. Remarkably, when we override the ability of glutamatergic neurons to gain GABA by injecting a Cre-dependent AAV expressing GAD1shRNA in the PrL of vGluT1::Cre +/- mice prior to exposure to PCP, we observe a rescue of PCP-induced cognitive deficits in the novel object recognition test, the spontaneous alternation task, and the loss of PCP-induced sensitization to the locomotor effects of the drug. This evidence establishes a causal link between the gain of GABA and PCP-induced behavioral alterations. We are now investigating less invasive strategies to prevent PCP-induced gain of GABA and rescue PCP-induced behavioral deficits.

Cognitive Session IV

Effective connectivity techniques for modelling neural functions

17:00 – 18:30

chaired by: **Balint File** (Pázmány Péter Catholic University, Budapest, Hungary)

Complete Inference of Causal Relationships in Neural Dynamical Systems

Zoltán Somogyvári, Zsigmond Benkő, Ádám Zlatniczki, Marcell Stippinger, Dániel Fabó, András Sólyom, Loránd Erőss, András Telcs

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Revealing causal interactions in the brain is of great interest, either if the origin of an epileptic seizure should be localized or the functional network behind the normal or altered information processing should be determined. The application of new causality analysis methods in neuroscience is presented here: The Cross Convergent Mapping (CCM) method for fMRI data during visuo-motor and working memory tasks and a newly developed method, the Dimensional Causality (DC) analysis method devised to detect and quantify the probability of all possible types of causal relationships between two time series observed in deterministic dynamical systems: independence, direct or circular causal connection and particularly the existence of a hidden common cause. The CCM revealed task relevant brain networks from short fMRI data series, while the DC method properly detected the increase of common cause probability between the two hemispheres during flashing light stimulation observing patients' EEG signals. During presurgical investigation the possible focus of epileptic seizure is identified; an area which drives the others. New causal analysis methods may help to understand functional networks of brain areas and their alternations either during information processing or neural diseases, while its applicability is not restricted to neuroscience.

EEG functional connectivity and network structure during memory maintenance mark vulnerable brain networks in Mild Cognitive Impairment

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Changes in functional connectivity (FC) and network topology have been reported in Alzheimer's disease, especially in the alpha frequency band. However, it is not entirely known whether these changes are able to mark cognitive decline in the early stages of the disease. FC and network structure of 17 Mild Cognitive Impairment (MCI) patients

and 20 control participants were studied with 128-channel EEG during an episodic memory task. FC was estimated with the corrected amplitude envelope correlation, while network analysis was performed by applying the Minimum Spanning Tree approach, which reconstructs the critical backbone of the original network. We did not find group differences in the mean FC in the alpha band, however, while increasing task difficulty enhanced connectivity in the control group, the MCI group showed significantly (p<;0.05) diminished FC in the highest memory load condition, which might indicate the impairment of memory maintenance. Network analysis revealed a rerouted, more centralized network in MCI with a more unequal traffic load distribution, where central hubs might become vulnerable to overload and failure. FC reflects impairment of memory retention in MCI, while changes in network topology point to the increased vulnerability of brain networks of MCI patients.

Recovering immediate and delayed brain network dynamics: Applications of convergent cross mapping

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We used convergent cross mapping (CCM)(Sugihara et al., 2012) to recover transient and delayed dynamics between brain regions from fMRI data acquired during a) transient motor responding (Diwadkar et al., 2017) and b) sustained working memory maintenance (Falco et al., 2019). Methods: Data (Siemens 3T) were acquired in 20 participants for both tasks. CCM was based on Takens' theorem (which gives the conditions under which a dynamical system can be reconstructed from a sequence of observations of the system's states). We used a time-symmetric embedding, enabling relatively precise estimation of delayed dynamics. The estimated X(t) and the original X(t) time series at different delays are compared by calculating the linear correlation coefficient between them with (potentially) asymmetric directionality. CCM detected significant (p<;.05, Bonferroni) time delayed interactions (up to 6 s lag and approximately coincident with task dynamics) during sustained working memory maintenance notably between the dlPFC and the parietal cortex. Significant dynamics (between V1, M1 and parietal cortex) for the motor task were recovered at lags of zero but not beyond. It is possible to recover dynamics and task structure from imperfect fMRI signals from a deterministic, maximally dynamic but highly "noisy" system like the brain.

Reorganization of Functional Networks During Low-Frequency Electrical Stimulation of the Cortical Surface

Balint File[1], Tibor Nánási[2], Emília Tóth[3], Virág Bokodi[1], Brigitta Tóth[2], Boglárka Hajnal[4], Zsófia Kardos[2], László Entz[5], Loránd Erőss[5], István Ulbert[2]

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Low frequency electrical stimulation (LFES) of the human brain cortical surface is a tool to investigate pre-surgery epileptic patients. Intracranial EEG data from subdural grid positions were analyzed in 16 pre-surgery epileptic patients. LFES was performed by injecting current pulses (10 mA, 0.2 ms pulse width, 0.5 Hz, 25 trials) into all adjacent electrode contacts. Dynamic functional connectivity analysis was carried out on two frequency bands (low: 1–4 Hz; high: 10–40 Hz) to investigate the early, high frequency and late, low frequency responses elicited by the stimulation. The centralization increased in early compared to late responses, suggesting a more prominent role of direct neural links between primarily activated areas and distant brain regions. Injecting the current into the seizure onset zone (SOZ) evoked a more integrated functional topology during the early (N1) period of the response,

whereas during the late (N2) period — regardless of the stimulation site — the connectedness of the SOZ was elevated compared to the non-SOZ tissue. The abnormal behavior of the epileptic sub-network during both part of the responses supports the idea of the pathogenic role of impaired inhibition and excitation mechanisms in epilepsy.

PLENARY LECTURE

19:00 – 20:00

chaired by: **Aleksandra Domagalik-Pittner** (Malopolska Centre of Biotechnology, Jagiellonian University, Kraków, Poland)

Me and my Markov blanket

Karl Friston

University College London, UK

This presentation offers a heuristic proof (and simulations of a primordial soup) suggesting that life—or biological self-organization—is an inevitable and emergent property of any random dynamical system that possesses a Markov blanket. This conclusion is based on the following arguments: if a system can be differentiated from its external milieu, then the system's internal and external states must be conditionally independent. These independencies induce a Markov blanket that separates internal and external states. This separation means that internal states will appear to minimize a free energy functional of blanket states – via a variational principle of stationary action. Crucially, this equips internal states with an information geometry, pertaining to probabilistic beliefs about something; namely external states. Interestingly, this free energy is the same quantity that is optimized in Bayesian inference and machine learning (where it is known as an evidence lower bound). In short, internal states (and their Markov blanket) will appear to model—and act on—their world to preserve their functional and structural integrity. This leads to a Bayesian mechanics, which can be neatly summarised as self-evidencing. I will use simulations to unpack these ideas in terms of predictive processing and active inference.

DECEMBER 10, 2020 (Thursday)

Biological Session V

Zebrafish in CNS and PNS Diseases Research

11:00 – 12:30

chaired by: **Kinga Aurelia Gaweł** (Centre for Molecular Medicine Norway, Oslo, Norway)**, Camilla Esguerra** (University of Oslo, Norway)

New insights into the early mechanisms of epileptogenesis in a zebrafish model of Dravet syndrome

Camilla Esguerra

University of Oslo, Norway

Dravet syndrome (DS), a severe, developmental and epileptic encephalopathy, is characterized by recurrent, intractable seizures. In 80% of cases, the disease is caused by de novo mutations in the SCN1A gene, encoding the alpha subunit of voltage-gated sodium channel Na v 1.1. Currently approved anti-seizure drugs cannabidiol and stiripentol, do not modify the disease, but rather, act to ameliorate seizures. Thus, the identification of new therapeutic treatment options as well as pathological mechanisms leading to DS is crucial. In our latest publication, we described a new zebrafish model of DS. scn1lab -/- larvae exhibit spontaneous seizures and display hallmarks of DS. Using a transgenic reporter line, we observed a 40% decrease in dendritic arborization of GABA-ergic neuron of the optic tectum in 6-day-old scn1lab -/- larvae. It was accompanied by an increase in neuronal proliferation in the same structure. Next, we assessed the activity of fenfluramine, a potent serotonin receptor agonist, to counteract the above-mentioned changes in DS mutants. Here, we observed that chronic fenfluramine treatment not only decreased the number of seizures, but also reversed the changes in GABA-ergic neurons arborization, as well as hyperproliferation. In conclusion, our study provides new evidence for (1) early DS-linked epileptogenesis mechanisms and (2) disease-modifying effects of fenfluramine in DS.

Characterization of Zebrafish Cacna1c Mutant- a Model for Schizophrenia

Nancy Saana Banono[1], Kinga Aurelia Gaweł[1,2], Wietske van der Ent[1], Tuomo Mäki-Marttunen[3], Ole A. Andreassen[4], Camila Esguerra[1,5]

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Several genes encoding voltage-dependent calcium channels have been implicated as risk genes for neuropsychiatric disorders such as schizophrenia by various genome-wide association studies (GWAS). The goal of this project was to carry out an in-depth phenotypic analysis of zebrafish larvae carrying mutations in these genes. We obtained two mutant lines generated by ENU mutagenesis (an essential splice site and nonsense mutations in the cacna1c gene) as fertilized embryos from the Zebrafish International Resource Center (Eugene, Oregon, USA) and raised to adulthood. We observed that mutations in both mutants led to developmental and behavioral abnormalities. Homozygous cacna1c mutants displayed features such as edema, hyperpigmentation, craniofacial

abnormalities, microphthalmia and microcephaly, as well as absent swim bladders. On the other hand, heterozygous cacna1c mutants were morphologically indistinguishable from their wild-type siblings, were viable and fertile. Exploration of the behavioral datasets revealed that the mutants displayed impaired locomotor and shoaling, as well as an altered pre-pulse inhibitory (PPI) response compared to wild-type controls. These findings suggest cacna1c mutants as potential genetic-models of schizophrenia, thus providing the opportunity to carry out small-molecule drug screens with the hope of identifying new drug targets capable of suppressing schizophrenia symptoms.

The role of voltage-gated potassium channels in the development of ear in zebrafish

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Voltage-gated potassium channels selectively regulate transport of K+ along electrochemical gradient in plasma membrane. They are involved in a variety of biological processes. In this study we are focused on zebrafish Kcnb1 (Kv2.1), a member of the electrically active Kv2 subfamily of Kv channels. Previously, it has been shown that it is expressed in mammalian, Xenopus laevis and zebrafish inner ear. Moreover, it is known that of all bodily fluids a fluid filling the inner ear – endolymph is the richest in K+ ions. Based on this Kv2.1 could be important for development ear, where it may be required for proper hearing and spatial orientation. Our studies for the first time show a link between a mutation in Kv2.1 and abnormal functioning of the inner ear. Ear of developing zebrafish kcnb1-/- is strongly affected and smaller in size. Moreover mutants' hair cells lost correct orientation of their kinocilia. Using qRT-PCR we checked level of expression of ear marker genes and upregulation and downregulation of some of them has been confirmed. In addition, behavioral tests showed defects in hearing and balance in kcnb1 morphants. These results support a hypothesis that Kcnb1 plays important role during development and function of zebrafish ear.

Development of a zebrafish model for nonsyndromic sensorineural hearing loss

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Hearing loss (HL) is the most common sensory impairment in human characterized by a large genetic heterogeneity. Due to evolutionary conserved features and a high accessibility for genetic manipulations zebrafish model can be used to study the role of genes involved in HL development. TBC1D24 and WFS1 genetic variants are causative for nonsyndromic sensorineural HL and different disorders with neurologic manifestations. The objective of this study was to develop genetic knock-down zebrafish models by injection of morpholino oligonucleotides to study the involvement of wfs1 and tbc1d24 genes in the development of hearing and neurological defects in zebrafish larvae. Microscopic imaging performed in wfs1 and tbc1d24 morphants revealed the negative effect gene knockdown on the size and viability of neuromasts. Both groups showed the reduction in locomotor activity and an impaired response to auditory stimuli. The tbc1d24 knock-down model also presented a probable disruption in hair cells mechanotransduction system. For wfs1 morphants a statistically significant reduction of saccular otolith size was observed, suggesting an impaired otolith formation in this group. The developed knockdowns will enable to establish a model useful for further studies on the pathogenicity of human WFS1 and TBC1D24 genetic variants.

Cognitive Session V

Modulation of Emotional Responses

11:00 – 12:30

chaired by: **Mirosław Wyczesany** (Jagiellonian University, Kraków, Poland)

The Relationship of Memory Reconsolidation and Return of Fear: Clinical and Methodological Implications of a Novel MultiCS Conditioning Paradigm

Charlene Lam, Kati Roesmann, Christian Steinberg, Angelina Höfig, Tom Barry, Tatia M.C. Lee, Markus Junghöfer

University of Hong Kong, Hong Kong

Patients with anxiety disorders frequently experience the return of fear (ROF) after receiving extinction-based psychological interventions such as exposure therapy. Classical conditioning experiments targeting memory reconsolidation suggest that reactivation of fear-memories before extinction may reduce ROF. We employed a novel MultiCS conditioning paradigm to investigate how fear memory is formed with limited contingency awareness and how ROF could be reduced using a retrieval-extinction technique. We employed a 3-day within-subject MultiCS conditioning paradigm encompassing a retrieval-extinction manipulation. On Day-1, two different aversive screams (USa and USb) were paired with different sets of 18 neutral faces (CS+a, CS+b), while another 18 neutral faces were never paired (CS-). On Day-2, USa (but not USb) was presented as a reactivation-cue 10 minutes prior to standard extinction. On Day-3 ROF was reinstated using both US. We employed MEG and fMRI methodologies to study neural responses to CS+a and CS+b compared to CS- faces, as well as corresponding pupillary responses and behavioral preferences. The successful acquisition of multiple, rather implicit CS-US associations (Day1) was reflected in preference ratings, pupil dilation and neural activity in frontal (MEG, >300ms) and limbic (fMRI) structures. Analyses further revealed a dissociation between neural and behavioral correlates of ROF and reconsolidation (Day3) after successful extinction (Day2). Overall, our findings support the potential effectiveness of MultiCS paradigms to study the neurocognitive mechanisms underpinning memory reconsolidation and ROF, and their associations with contingency awareness. As MultiCS paradigms require fewer stimulus repetitions to achieve a sufficient signal-to-noise ratio than traditional SingleCS paradigms, they are a valuable tool to investigate highly transient neural correlates underpinning these mechanisms. Translational implications of our findings regarding current models of reconsolidation and treatment-relevant mechanisms in anxiety and fear-related disorders will be discussed. Supported by the University of Hongkong, the Deutsche Forschungsgemeinschaft (DFG, Project SFB-TRR58-C08), the DAAD (Project 57390152) and the IMF of the Medical Faculty of the University of Münster, Germany (Project KE211801).

Beta band communication flow within DAN controls attentional processes

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The allocation of attention plays a role in emotional perception by gating the information conveyed for further elaboration. Endogenous allocation of spatial attention is controlled by the dorsal attention network-DAN comprised frontal (dorsal frontal eye fields-dFEF) and parietal regions (superior parietal lobe-SPL and ventral intraparietal sulcus-vIPS, which respectively showed a causal role for reorienting and maintaining attention; Capotosto et al., 2013, 2015). Our MagnetoEncephaloGraphic-MEG study examined the frequency specificity associated with the functional subdivision of the DAN. To this aim, we recorded MEG signals during task that isolates signals for maintaining or reorienting attention (Spadone et al., 2015). We examined the dynamic modulations of the Directed Transfer Function (Kaminski et al., 2001) between source activities of DAN regions obtained by a pipeline based on independent component analysis (Mantini et al., 2011). In early phase of cognitive process, reorienting versus maintaining attention induced stronger connectivity from RdFEF to RSPL in beta but not in alpha band, such directionality was subsequently reversed. In contrast, maintaining attention increased information flow between bilateral vIPS in both alpha and beta. These results suggest that beta was the spectral signature of control within DAN during attentional reorienting that was exerted by frontal to (medial) parietal region.

Implicit induction of emotional control – the role of attentional gating

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Implicit forms of emotion regulation (ER) are of growing interest and have been shown to be efficient in controlling emotional responses even though they operate without deliberate attempts or the depletion of cognitive resources. Although such forms of affective modulation are considered natural and crucial for mental health, their brain mechanisms have hardly been studied until now. In our studies, we used functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) to investigate neural responses to emotional stimuli after implicitly inducing emotion regulation goal with a scrambled sentence task. Priming participants with sentences related to ER evoked robust modulation of the middle and late-latency ERPs related to attentional processing, attenuating the N2, P3 and the Late Positive Potential (LPP) amplitudes. Moreover, decreased BOLD responses were observed in visual, attentional and emotion-related brain areas (amygdala, lingual, fusiform, and superior temporal gyrus), and increased in regions involved in top-down modulation of emotional responses (bilateral middle frontal gyrus and the right insula). These results jointly imply that implicit ER modulates early perceptual and attentional stages of unpleasant stimuli processing, and that these modulation effects originate from executive attention/cognitive control areas of the brain that have been previously associated with conscious forms of ER.

Acute aerobic exercise enhances processing of positive compared to negative pictures

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Although acute aerobic exercise (AAE) benefits different aspects of emotional functioning, it is unclear how AAE influences the processing of emotional stimuli and which brain mechanisms support this relationship. We assessed

the influence of AAE on valence biases (preferential processing of negative/ positive pictures) as revealed by source reconstructions of brain activity evoked by emotional scenes. Twenty-four healthy participants (12 women) were tested in a randomized and counter¬balanced design that consisted of three experimental protocols, each lasting 30 minutes: low-intensity exercise (Low-Int); moderate intensity exercise (Mod-Int); and seated rest condition (SRC). After each of the protocols, participants viewed negative and positive pictures, during which event-related magnetic fields were recorded. Analysis revealed a strong impact of AAE on the valence processing of emotional scenes within a widely distributed left hemispheric spatio-temporal cluster between 190 and 310 ms after picture onset. Brain activity in this cluster showed that a negativity bias at SRC (negative >; positive picture processing) diminished after Low-Int (positive = negative) and reversed to a positivity bias after Mod-Int (positive >; negative). AAE of low and moderate intensities induces a positivity bias (preferential processing of pleasant or/and attenuated processing of unpleasant material), which is reflected in early, automatic processes.

Biological Session VI

Neurobiology of Addiction

13:00 – 15:00

chaired by: **Małgorzata Frankowska & Jan Rodriguez Parkitna** (Institute of Pharmacology PAS, Krakow, Poland)

Dopamine and opioid system adaptation in alcohol addiction

Anita Hansson

Central Institute of Mental Health, Mannheim

Alcohol potently induces neuroadaptations that promote its incentive salience, escalation of its intake and aversion-resistant alcohol seeking. Such behaviors, which lead to alcohol addiction, are characterized by persistent neuroadaptations in various brain neurotransmitter systems, including the endogenous opioid-, dopamine- and other neuropeptide system, which are thought to underlie relapse. A major hypothesis in the addiction field suggests deficits in dopamine signaling during abstinence. This hypodopaminergic state is seen as a driving mechanism for the relapsing course of the disorder. Experimental support for this view comes mostly from human positron emission tomography (PET) studies that found reduced striatal D2-like receptor binding potential in alcoholics. However, the interpretation of those data is challenging as PET signals are sensitive not only to receptor but also endogenous ligand levels. Here we systematically study neuroadaptive changes in the opioid and dopamine system during the addiction cycle in alcohol dependent patients and rats. To gain insight into the time course of these neuroadaptations we compared the human data to alcohol dependent rats at several time points during abstinence and found a highly dynamic regulation of the dopamine system during three weeks of abstinence. Functional evidence is further given by electrophysiology and use of advanced transgenic animal models. In summary, we provide a new dynamic model of abstinence related changes of the striatal dopamine system in which a hyperdopaminergic state during protracted abstinence is associated with vulnerability for relapse. These findings have important implications for our understanding of the pathophysiological mechanisms underlying alcoholism and the interpretation of PET results on dopamine/opioid receptor function in general.

Binge mephedrone administration during adolescence potentiates ethanol rewarding effect in adult rats

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Mephedrone is a synthetic psychoactive drug of the cathinone class, abused particularly amongst young people. Psychostimulant use among adolescents has been shown to increase risk of drugs abuse in adulthood. Based on this research, the present study evaluated whether exposure to mephedrone during adolescence influences the rewarding effect of ethanol in young adult/adult and whether MMP-9 plays a role in this phenomenon. Wistar rats (30 PND) received saline (control) or mephedrone (10 mg/kg, i.p.), three times a day, for 7 days. Next, 2 or 14 days after mephedrone withdrawal, rats were subjected to an ethanol (0.3 – 1.0 g/kg, i.p.) -induced conditioned place preference (CPP) paradigm. The animals were then sacrificed and such brain structures as the prefrontal cortex, hippocampus and striatum were selected to assess the protein levels of MMP-9. Ethanol at the dose of 1 g/kg induced CPP rewarding effect in the mephedrone- but not saline-treated young adult (48 PND) and adult (79 PND) rats. The effect was associated with the increase of MMP-9 protein level in the hippocampus. Mephedrone abused during adolescence may lead to increased susceptibility to subsequent effect of ethanol in adulthood. Hippocampal MMP-9 is important for this phenomenon. This work was supported by Grant No. 2017/25/B/NZ7/01845 from the National Science Centre, Poland.

Why is it so hard to quit? The role of the dentate gyrus in seeking behavior of alcohol dependent mice

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Alcohol addiction is a serious health problem that also affects social and familial relationships. It is a brain disease which is driven by both genetic and environmental factors. Understanding the biological processes involved in alcohol seeking will facilitate successful treatment. In order to do that it is crucial to use animal model which refers to the diagnostic criteria of the disease in humans. The model of alcohol addiction in IntelliCages measures the pathological behaviors towards alcohol (described in DSM-V) and distinguishes animals which become "addicted" from those which control alcohol consumption. Major structure associated with context dependent cue reactivity is a dentate gyrus of the hippocampus. The growing body of evidence sheds a light on the glutamatergic system's role in the development of addiction. Here, we show the down-regulation of AMPAR and NMDAR after long-term alcohol self-administration. We also show that expression of PSD-95 is strongly associated with seeking behavior after exposure to a cue. Moreover, the levels of silent synapses in dentate gyrus depends on the addiction index of an individual. This results show the important role of the glutamatergic transmission in dentate gyrus in development of addiction.

Cholinergic modulation of dopaminergic neurons' activity- in vivo electrophysiological and pharmacological studies on NR1DATCreERT2 mice

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Functional NMDA receptors are considered to be crucial to evoke bursting activity of dopaminergic neurons, leading to increased release of dopamine in synapses. Whether other neurotransmitters can also evoke this type of activity remains an open question. Therefore, the aim of our research was to determine the effect of stimulation of cholinergic receptors on the activity of dopaminergic neurons without functional NMDA receptor. We have used genetically modified mice lacking NR1 subunit of NMDA receptor selectively on dopaminergic neurons of adult animals. Experiments were performed under urethane anaesthesia and combined extracellular recordings of midbrain dopaminergic neurons' activity and iontophoretic application of drugs. After application of non-selective

cholinergic agonist carbachol, majority of dopaminergic neurons increased their firing rate. Interestingly some of the recorded cells, both in control and mutant mice developed slow, oscillatory changes in firing rate. Neurons tested with oxotremorine application responded with an increase of firing rate and similarly to carbachol iontophoresis - some of the recorded neurons developed oscillations of firing rate. These results show that activation of cholinergic receptors alone, (i.e. without the involvement of NMDA receptors) can modulate rate as well as pattern of firing of the midbrain dopaminergic neurons. Funding: NCN, Poland, PRELUDIUM 2015/19/N/NZ4/00960.

Cognitive Session VI

Pain in the learning context

13:00 – 15:00

chaired by: **Wacław M. Adamczyk** (Jagiellonian University, Krakow, Poland).

A modified model of learning mechanisms of placebo effects in pain

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In 2011 Colloca and Miller proposed the learning model of placebo effects. In this model, placebo effects result from expectancies acquired by decoding information from the psychosocial context, including conditioned stimuli, symbolic communication, and observation. Thus, according to the model, classical conditioning, verbal suggestions, and observational learning are means by which placebo effects are induced, but expectancy is the only mechanism of the formation of placebo effects. Although the model is influential, recent findings from our lab, as well as other labs, have challenged it. First, it was found that expectancy may not always be involved in placebo effects induced by classical conditioning and that conditioning may be a distinct mechanism of placebo effects. Second, growing evidence on placebo effects induced by observational learning has been recently integrated into the separate model. Third, operant conditioning has been suggested as a new mechanism of placebo effects, and the first evidence supporting that idea was provided. In this talk, I will summarize the current state of the art in the learning mechanisms of placebo effects and propose a modified model of them.

Do you really need sensitization to elicit allodynic response?

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Pain elicitation by the non-noxious stimulus is a phenomenon called allodynia. It occurs after tissue damage as a result of peripheral and central sensitization. Hence, allodynia has been mostly viewed and described from a merely physiological perspective. However, some preliminary data suggest that allodynia might be centrally-driven omitting the cascade of neuroplastic changes at spinal laminae. In the presentation, I will show the results of our recent experiments on allodynia in healthy humans. In the first experiment, we aimed to induce pain by conditioning stimulus. In the second experiment, participants were exposed to the observational phase wherein they observe the model and learn that they may experience pain in the later phase of the study. In the end, pain acquisition by operant conditioning will be discussed in light of previous meta-analytic data and preliminary results from our laboratory. Taken together, it might be suggested that allodynia, under some circumstances, is centrally driven mechanism as a result of learning processes.

Three methodological considerations for pain and placebo research

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By definition, pain is a subjective experience. Experimental pain research, including research into placebo hypoalgesia or nocebo hyperalgesia, therefore relies on subjective reports, which are affected by various psychological factors other than treatment efficacy. Furthermore, noise introduced by unreliable protocols, or sweeping inferences not supported by the data, can impede the identification of effective treatments (or rejection of ineffective treatments). Here, I will address three lines of research aimed at increasing internal and external validity of pain research. Firstly, computer-controlled treatment delivery can facilitate standardization and blinding. Secondly, pain stimulus characteristics differ greatly between experiments, yielding different reliability depending on calibration procedures (and possibly mask effects due to floor or ceiling effects). Finally, without appropriate control conditions to account for nonspecific stimulus characteristics, inferences drawn from pain neuroimaging may be too broad, as genuinely pain-related activation is very circumscribed. The latter carries serious implications for the interpretation of treatment effects.

Pain by mistake: Investigating a link between error-related negativity and avoidance behavior

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Patients with chronic pain frequently tend to avoid activities which are thought to evoke or worsen their pain but contrary to their intention this avoidance behavior can contribute to the maintenance of pain and disability. While it is crucial to understand the factors promoting avoidance in order to be able to predict and tackle this problematic behavior, little is known about the underlying neural mechanisms. A neural marker that plays a key role in learning and the development of defensive behavior in other psychopathologies is the error-related negativity (ERN) – a negative deflection measured by electroencephalography that occurs shortly after error commission. In a series of experiments, we aimed to investigate for the first time whether the ERN is related to avoidance behavior towards painful stimuli in a novel pain-avoidance paradigm. It was hypothesized that individuals with larger ERN amplitudes would learn pain-related avoidance behavior more quickly. In contrast to the hypothesis, first results revealed slowed acquisition of avoidance behavior in error-sensitive individuals. Ongoing experiments and implications will be discussed.

POSTER SESSION II

BIOLOGICAL POSTERS

PAIN

105. What happens after chronic opioid cessation? Studies in a pain facilitatory area of the brain

Marilia Sousa[1,2], Ana Rita Costa[1,2], Isaura Tavares[1,2], Isabel Martins[1,2]

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Opioids represent the gold standard for the treatment of pain. We showed previously that chronic morphine induced hyperalgesia and shifted mu-opioid receptor (MOR) signalling in a pain facilitatory area, the Dorsal Reticular Nucleus (DRt). Here, we aim to study whether MOR signalling remains altered after opioid cessation and if this affects future treatments. Wistar rats were treated with morphine or saline for 7 days. In another group, the treatment was interrupted and the animals were tested 2 weeks later. Immunohistochemical and pharmacological studies were performed at both timings. Morphine induced pain hypersensitivity and increased MOR, pCREB and pERKs expression at the DRt. After opioid cessation, nociceptive behaviours and MOR expression normalized but not pCREB and pERKs expression. Injection of DAMGO, a MOR agonist, in the DRt induced antinociception in controls and hyperalgesia after treatment and cessation. Injection of ultra-low dose naloxone, preventing MOR signalling shift, in the DRt enhanced the antinociceptive effects of a low dose of morphine in animals with post-operative pain. Increased pCREB and pERKs, and the pronociceptive effects of DAMGO after opioid cessation indicate a maintenance of the MOR signalling switch to excitatory in the DRt. Preventing this switch enhances the analgesic effects of low morphine doses.

106. Influence of functional selectivity of CB2 agonists upon their therapeutic potential in animal model of osteoarthritis

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Osteoarthritis is a degenerative joint disease resulting in chronic pain development. Endocannabinoid system became a promising target to control both symptoms and progression of osteoarthritis. Functional selectivity upon signal transduction pathways may increase beneficial properties of drugs, while reducing side effects. The aim of the present study was to evaluate therapeutic potential of two functionally biased CB2 agonists in different treatment regimens. Osteoarthritis was induced by i.a. injection of 1mg monoiodoacetate into rear right paw of Wistar rats. Drugs (JWH133 (cAMP biased agonist) and GW833972A (beta-arrestin biased agonist)) were administered i.p. in three treatment regimens: acute or chronic from day 10 to day 28 or from day 20 to day 28 post monoiodoacetate injection. Pressure Application Measurement (PAM) and Kinetic Weight Bearing (KWB) instrument were used to assess antinociceptive effects. Both CB2 agonists exerted analgesic effects following acute administration, whereas in chronic treatment regimen, we observed tolerance following GW833972A treatment as evidenced by decline in its anti-nociceptive effects in both PAM and KWB. Results imply functional bias as a key factor in predicting clinical usefulness of drugs and significant variable in basic research. Acknowledgments: Supported by National Science Centre, Poland by grants: OPUS no. 2014/13/B/NZ7/02311 and statutory funds.

107. Effects of PZM21, a G protein-biased opioid, on stress- and anxiety-related behavior in mice

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PZM21 is a μ opioid receptor (μ-OR) agonist, proposed to be a G protein-biased compound (Manglik et al., 2016). Our previous research showed that PZM21 presents antinociceptive activity, but does not have rewarding and reinforcing effects, typical for commonly used opioids (Kudla et al., 2019). Conventional (unbiased) agonists of μ-OR, including morphine, were reported to exert beneficial effects in stress-related pathology. Thus, we aimed to investigate effects of PZM21 under stress conditions. We assessed effects of PZM21 on acute response to stress and anxiogenic environment. CD-1 mice were assigned to treatment groups: PZM21 (20, 40 mg/kg), morphine (10, 20 mg/kg) or saline. Forced swimming (FST), tail suspension (TST), light-dark box (LDB) and open field (OF) tests were performed 30 min after drug injection. The obtained results showed that treatment with morphine, but not with PZM21, resulted in decreased response to stress conditions in FST and TST. On the other hand, both morphine and PZM21 had anxiogenic effects in LDB and OF paradigms. To conclude, our data suggest that unbiased and biased opioids differently affect acute response to stress. However, compounds from both groups seem to enhance anxiety-related behavior. Support: Polish National Science Centre, grants 2019/33/N/NZ7/02378 and 2018/31/B/NZ7/03954.

108. Key genes of osteoarthritis progression in a rat model using gene expression profiling

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Osteoarthritis (OA) is a chronic degenerative joint disease, common in older adults. Recently, molecular biology has played an important role in explaining OA pathophysiology. Various stages of disease progression have been described by a complex pattern of transcriptional regulations. Based on literature, we investigated gene expression of the reported significant candidate genes. Experimental design consisted of four groups: intact animals and rats that had received intra-articular injection of 1, 2 or 3 mg of monoiodoacetate (MIA) into rear knee. After 2, 14 or 28 days post-MIA injection rats were sacrificed and nervous and joint tissue was collected. RT-qPCR was performed on RNA isolated from lumbar dorsal root ganglions (DRGs) 3–5 and cartilage. Analysis in DRGs identified unique expression patterns of inflammation-related genes (eg. IL-1β, Aif-1) as well as Cnr1 gene expression in OA in comparison with controls and according to the stage of disease. Additionally, an increase of IL-6 expression was observed at early OA stage. In cartilage, an increase in Comp gene was observed. Presented data shed new light on the understanding of OA mechanism locally in joint tissue and in nervous system. Research funded by National Science Centre, Poland OPUS no.2014/13/B/NZ7/02311, 2015-2018 and IF PAN statutory funds.

109. Kynurenic acid and Zaprinast influenced pain-related behaviour and morphine effectiveness in a mouse model of neuropathic pain

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Despite the precise guidelines and multiplicity of available drugs, conventional therapy of neuropathic pain remains inefficient. This condition significantly reduce the quality of life and have a negative impact on the physical, emotional and social aspects of human functioning, therefore new therapeutic approach is necessary. The G protein-coupled receptor 35 (GPR35) was recently suggested to be involved in nociceptive transmission. The aim of following study was to elucidate the influence of endogenous (kynurenic acid) and exogenous (zaprinast) ligands of GPR35 on pain-related behavior in mice exposed to chronic constriction injury (CCI) of the sciatic nerve. Single intrathecal administrations of kynurenic acid and zaprinast were performed on day 14th after surgery. Mechanical and thermal hypersensitivity was assessed using von Frey and cold plate tests, respectively. Experiments indicated that both, kynurenic acid and zaprinast, reduced mechanical and thermal hypersensitivity induced by CCI and what is more, significantly improved analgesic effect of morphine. In the light of obtained results, modulation of GPR35 might be a promising therapeutic target for polytherapy of neuropathic pain. Acknowledgments: Supported by National Science Centre grant-Sonata-2015/17/D/NZ4/02284 and statutory founds of the Maj Institute of Pharmacology, Polish Academy of Sciences.

110. The importance of C021 (CCR4 antagonist) in the development of pain-related behavior and opioid-induced analgesia

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Neuropathic pain is a chronic and pathological condition experienced by patients suffering from nervous system dysfunction caused by various diseases. Treatment of neuropathic pain remains clinical problems, because of poor response and undesired adverse effects of available drugs. Therefore, developing a novel more effective treatment strategy is critical in this field. Recent studies have indicated that chemokines signaling pathways are crucial in neuropathy development, however the involvement of CC chemokine receptor 4 (CCR4) has not been fully explained so far. Therefore, the aim of our research was to investigate the role of CCR4 in the development of tactile and thermal hypersensitivity and the opioids effectiveness using von Frey and cold plate test. The results of our research demonstrated that single intrathecal administration of C021, CCR4 antagonist, dose-dependently diminished neuropathic pain-related behaviors in CCI-exposed mice. Moreover pharmacological blockade of CCR4 enhances the analgesic properties of morphine and buprenorphine. Obtained data suggested that pharmacological blockade of CCR4 may be a new potential therapeutic target for neuropathic pain polytherapy. Acknowledgments: Supported by National Science Centre, Poland (OPUS 2016/21/B/NZ4/00128) and by statutory funds of the Maj Institute of Pharmacology PAS, Department of Pain Pharmacology. Joanna Bogacka acknowledges the support of InterDokMed project no. POWR.03.02.00-00-I013/16.

111. Analgesic and chondroprotective effects of CB2 receptor agonist, (E)-β-caryophyllene in osteoarthritis model

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Osteoarthritis (OA), a common disease in the elderly, is characterized by the progressive loss of articular cartilage, new bone formation, and synovial proliferation. Pain is the key complaint for OA patients and is the driving factor for visiting a primary care physician. Current pharmacological therapies are symptomatic and focus on alleviating pain, yet they are insufficient and may cause unwanted side effects or produce tolerance, therefore new solutions are sought. Cannabinoid receptor type 2 (CB2) modulators have proved their usefulness as analgesics. Targeting CB2 has promising therapeutic potential in OA since its presence is proved on chondrocytes, synoviocytes, nociceptors free end terminals, dorsal root ganglia, spinal cord, and supraspinal pain processing structures. (E)-β-

caryophyllene (BCP) is a phytocannabinoid found in relatively high concentrations in many spices and food plants. BCP exerts agonistic activity on CB2 receptors. Presented studies prove that that BCP has analgesic and chondroprotective abilities in monosodium iodoacetate (MIA) model of OA. Intrarticular (i.a.) injection of monosodium iodoacetate (MIA, 1mg) has been used to induce OA in Wistar rats. Two treatment paradigms were studied: paradigm 1) therapy following early symptomatic detection of OA (BCP treatment every second day from D10 to D28 post MIA injection) and paradigm 2) treatment paradigm reflecting patient – doctor experience in advanced stage of OA (BCP treatment every second day from D20 to D28 post MIA injection). BCP was administered i.p. at dose of 25mg/kg in both treatment paradigms, however we also studied subthreshold dose of 10mg/kg in the early-treatment paradigm. To classify if analgesic effect is mediated by cannabinoid or opioid system we combined BCP (25mg/kg) with either selective CB2 receptor antagonist AM630 (3mg/kg) or non-selective competitive opioid receptor antagonist naloxone (1mg/kg), both in late-treatment paradigm. Pain symptoms were assessed by behavioral test: kinetic weight bearing (KWB test) in D21 and D28 after OA induction. Rats were sacrificed at D28 and cartilage tissue was collected for further histological analysis. Quantification of cartilage degeneration was assessed using OARSI system scoring. We observed significant asymmetry in peak force parameter between left and right paw in in vehicle-treated OA rats at D21 and D28. This difference was not detected in any of BCP treated groups (both at D21 and D28), suggesting analgesic effect, which is mediated through CB2 and opioid receptors since it was abolished by AM630 or naloxone co-treatment. While BCP administration in paradigm 2 or its co-treatment with AM630 fails to improve OARSI scoring, abolished cartilage degeneration was observed after 10mg/kg and 25mg/kg administration of BCP compared to vehicle in paradigm 1. Thus, BCP treatment from early stages of OA may hamper disease progression. Considering its safety and efficacy in OA-related pain prevention, these results may lead to development of novel OA treatment. Acknowledgements: supported by the National Science Centre, Poland, grant OPUS UMO-2014/13/B/NZ7/02311 and IF PAS statutory funds. We wish to acknowledge PhD Jürg Gertsch (Institute of Biochemistry and Molecular Medicine, University of Bern, Switzerland) for generously providing us with BCP.

NEUROPSYCHIATRY

112. Comparison of the activation pattern of selected brain reward structures after stimulation with nicotine and caffeine.

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Structures of the brain reward system are involved in elaboration of responses induced by the action of external or internal stimuli. The source of frequently occurring activation is nicotine and caffeine. Although physiological effects initiated by administration of these two commonly used psychostimulants are well known, their effect on various structures of brain reward system is still unclear. The aim of this study was to compare activation patterns of two transcription factors pCREB and ΔFosB in selected structures of the rat's brain reward system such as nucleus accumbens (NAc), ventral tegmental area (VTA), amygdala (Amg), hippocampus (Hip), medial prefrontal cortex (mPfr) and dorsal striatum (CdP) in response to nicotine and caffeine. Activation of both factors was assessed immunohistochemically, using quantitative morphometric analysis and documented by confocal microscopy. Our results indicate: 1) different activation patterns of pCREB and ΔFosB in brain reward system after nicotine/caffeine stimulation, 2) involvement of different signaling pathways in activation of various brain reward system structures after stimulation with each psychostimulant, and 3) mutual influence of both psychostimulants on the neuronal activation pattern in selected brain reward system structures.

113. Astrocytic glucocorticoid receptor in central amygdala modulates stress-related behavior in mice

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Central amygdala (CeA) is involved in response to stressful stimuli. Stress activates hypothalamic-pituitary-adrenal axis and its final product - glucocorticoids that act by glucocorticoid receptors. Increasing evidence points to the role of astrocytes in mediating stress- and glucocorticoid-related behaviour. We aimed to evaluate impact of astrocytic glucocorticoid receptor (GR) knockdown in CeA in various aspects of stress. We knock down astrocytic GR in CeA using lentiviral vector harboring Cre-dependent shRNA expression cassette in mice expressing the Cre recombinase under aldehyde dehydrogenase 1 family promoter (Aldh1L1Cre), typical for astrocytes. After recovery we tested animals in various aspects of stress-related behaviour. Both groups did not differ in basal locomotor activity. Astrocytic GR knockdown group spend more time in central and illuminated area in open field test. Analogous tendency was also observed in light/dark box and elevated plus maze test. However, no differences was observed in tail suspension test. Knockdown group presented attenuated freezing in fear conditioning. To summarize astrocytic GR knockdown in CeA reduces anxiety, but does not influence depressive-like symptoms. Moreover, astrocytic GR in CeA modulates processes involved in stress-related learning or expression of fear. Further studies are required to understand mechanisms of those interactions. Acknowledgments: PAS statutory founds, 2013/08/A/NZ3/00848.

114. Phenotypes of reinforcement sensitivity determine motivation and anxiety of rats

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One of the most important cognitive distortions associated with affective disorders is aberrant sensitivity to negative and positive reinforcement. Under clinical conditions, this sensitivity can be measured using the Probabilistic Reversal Learning (PRL) test, which has also been recently implemented in animal studies. In this study, we took a unique opportunity to investigate how trait sensitivity to negative and positive reinforcement determines the motivation and anxiety in rats. For this, using a preclinical version of the PRL paradigm, we have identified 4 phenotypes of sensitivity to performance feedback in rats, which could represent various types of potential vulnerability to affective disorders: i) indifferent; ii) depressive; iii) manic; and iiii) hypersensitive. Subsequently, using the progressive ratio schedule of reinforcement paradigm and the light/dark box tests, we evaluated inter-phenotypic differences in basal levels of motivation and anxiety of experimental animals. We report statistically significant differences between the investigated phenotypes of reinforcement sensitivity with regard to the basal levels of appetitive motivation and anxiety. These results demonstrate for the first time that trait sensitivity to positive and negative reinforcement could interact with other measures associated with depressive like symptoms in rats. Supported by the Polish National Science Centre (grant2016/23//B/NZ4/01562).

115. Endocannabinoid-mediated mitochondrial activity regulates cognitive effects of stress

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Stress adaptation requires high cellular activity in the brain, which depends on energetic support provided by mitochondria. Growing evidence suggests that bioenergetics might be one of the mechanisms underlying behavioral and cognitive responses to stress. Recently, the endocannabinoid system has been reported to directly

regulate mitochondrial energetic activity via the type-1 cannabinoid receptors (CB1) associated to the brain mitochondria membranes. Here, we aimed to evaluate the involvement of the endocannabinoid system in the regulation of cognitive stress effects using transgenic mice and viral tools to specifically delete or re-express CB1 in different cell-populations and sub-cellular compartments. Our result show that stress or corticosterone administration induce impairment of object recognition memory in control mice, but not in mice with full deletion of the CB1 receptor, nor in mice lacking the CB1 receptor in the mitochondria. What is more, genetic deletion and rescue of CB1 receptors in specific cell types revealed that the population of CB1 receptors in GABA-ergic cells are both necessary and sufficient for corticosterone-induced impairment of memory retrieval, but CB1 receptors present in other neuronal populations are not involved. Thus, our results show previously unrecognized role of specific CB1 receptor pools in the stress-dependent regulation of memory processes.

116. A single injection of HBK-15, a 5-HT1A/5-HT7/5-HT3 receptor antagonist, rapidly reverses depressive-like behaviors and decreased BDNF level in depression model of mice

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Antidepressants are effective in only half of the patients and the therapeutic effects occur after weeks or months of the treatment. In this study, we aimed to evaluate the antidepressant-like activity of HBK-15 – a triple 5-HT1A, 5-HT7, and 5-HT3 antagonist – in the mouse depression model. To determine antidepressant-like activity, we used mouse model of the unpredictable chronic mild stress with the forced swim test, sucrose preference test and locomotor activity test as behavioral endpoints. Next, we determined the level of BDNF, p-CREB, p-CaMKIV, p-PKA and p-ERK1/2 in the prefrontal cortex using ELISA. We observed a significant increase in the immobility and reduced preference for sucrose solution in chronically stressed mice receiving saline. A single administration of HBK-15 reversed these behaviors. HBK-15 upregulated the decreased levels of BDNF p-CREB, p-CaMKIV, p-PKA, p-ERK1/2 in the prefrontal cortex of the stressed mice. We found that in the stressed mice a single administration of HBK-15 reversed depression-like behaviors and regulated decreased BDNF and p-CREB levels in the prefrontal cortex via all studied pathways. Our results suggest that the blockade of 5-HT1A, 5-HT7, and 5-HT3 receptors might accelerate antidepressant response. This study was supported by NCN (2017/01/X/NZ7/00818) and JUMC.

117. HBK-15, a triple 5-HT1A, 5-HT7, and 5-HT3 receptor antagonist, reverses intermediate- and long-term memory deficits induced by acute MK-801 administration

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Cognitive deficits are increasingly common among people suffering from depression. Interestingly, not all types of memory are equally affected. Our focus of interest is upon 1-[(2-chloro-6-methylphenoxy)ethoxyethyl]-4-(2-methoxyphenyl)piperazine hydrochloride (HBK-15), which has an antidepressant- and anxiolytic-like properties in rodents. Our research aim was to evaluate episodic-like, motor, and emotional memory in mice with MK-801-induced cognitive deficits. We used a novel object recognition test to assess intermediate- and long-term episodic-like memory, rotarod test to determine motor skill learning and passive avoidance for intermediate- and long-term

emotional memory evaluation. Mice were injected intraperitoneally (i.p.) with saline or HBK-15 at different doses 30 min before behavioral testing. After 15 min MK-801 (0,15 mg/kg) or saline was administered. We observed a significant increase in latency to entrance and novel object exploration time in mice injected with HBK-15. A single administration was enough to reverse behavioral changes in mice injected with MK-801. However, HBK-15 did not normalize MK-801-induced motor learning and memory. We found that a single administration of HBK-15 – a triple 5-HT1A, 5-HT7, and 5-HT3 antagonist – reversed intermediate- and long-term memory deficits induced by MK-801 injection. Our results suggest that the blockade of these serotonergic receptors might be crucial for memory-enhancing properties.

118. Neuropsychological and molecular mechanisms of antidepressant-like action of a 5-HT6 receptor agonist (ST1936) are similar to ketamine and distinct from venlafaxine.

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Background: A recently developed task for rats (Affective Bias Test, ABT) is a tool capable of dissociating fast-acting antidepressants (ADs, ex. ketamine) from late-onset ones (ex. venlafaxine). Ketamine reverses a negative affective bias (NAB), while venlafaxine causes a positive affective bias (PAB). We investigated the profile of AD-like action of a 5-HT6 receptor agonist in the ABT, as well as elucidated the molecular mechanisms of pharmacological modulation of PABs and NABs in the hippocampus, PFC and mPFC. Methods: Groups (n=16/group) of male Wistar rats underwent a series of ABTs, in which behavioral (psychosocial stress, heterospecific play) and pharmacological (3 mg/kg venlafaxine, 1 mg/kg ketamine) effects on PABs and NABs were validated for the first time in this strain. Next, a dose-dependency study of 0.5, 1.0 and 3.0 mg/kg of ST1936 on PAB was conducted, followed by a test of 1 mg/kg ST1936 on NAB. The drug effects on mTOR and ERK1/2 phosphorylation were subsequently studied ex vivo with AlphaLISA SureFire. Results: ST1936 did not cause a PAB, but reversed a NAB caused by psychosocial stress. All behavioral effects were accompanied by changes in mTOR phosphorylation and confined to the hippocampus and mPFC. Conclusions: 5-HT6 agonism might quickly alleviate depression symptoms.

119. Synaptic plasticity of the excitatory projection from the amygdala to the nucleus accumbens induced by natural and addictive rewards

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Drug addiction is considered an extremely durable form of appetitive learning (memory of pleasurable events). Exposure to drugs of abuse, such as cocaine, induce pathologic, virtually irreversible, addiction-related memories. Cocaine administration triggers synaptic plasticity processes such as formation of silent synapses in neurons of the brain reward system. These synapses contribute to the formation of cocaine-specific memories. In our study, we investigate the synaptic plasticity of a brain pathway between the amygdala and the nucleus accumbens (NAc) - structures strongly involved in appetitive memory formation and the execution of motivated behaviors. We use a model of appetitive learning, in which we expose mice to natural and addictive rewards - sucrose self-administration or injections of cocaine. To assess behavioral differences, we combined a self-made lickometer and a camera setup with open-source tools. Such setup enabled us to monitor two behavioural paradigms: mice preference to sweet water and the development of cocaine sensitization - increase in locomotor activity with consecutive cocaine injections. The effects of natural and addictive rewards on synaptic plasticity are evaluated by patch-clamp electrophsiological recordings from the projection.

120. Hallucinogenic compound 25I-NBOMe affects brain neurotransmission and induces anxiety in rats

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Hallucinogens are psychoactive agents which alter perception and mood but do not produce dependence and addiction. 4-Iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine (25I-NBOMe) is a N-benzylmethoxy derivative of the hallucinogen 2C family that has a high binding affinity for 5-HT2A/2C and 5-HT1A serotonin receptors. The aim of this study was to investigate the effect of 25I-NBOMe on neurotransmitter extracellular levels and rats' behavioral activity after chronic injections. The release of dopamine (DA), serotonin (5-HT) and glutamate (GLU) was studied using in vivo microdialysis. Moreover, anxiety response was measured in Light/Dark Box (LDB) test. 25I-NBOMe increased cortical DA and GLU levels in comparison to saline treated rats. Instead release of DA and 5-HT in the striatum were decreased. LDB test showed anxiogenic properties of 25I-NBOMe, reducing rats' activity and time spent in the light compartment. Release of neurotransmitters seems to be under indirect control of 5-HT2A receptors. Cortical excitatory efferent pathways innervating DA and 5-HT neurons in ventral tegmental area/substantia nigra/raphe nuclei might be responsible for changes in release from neuronal terminals. Activation of mesocortical dopamine and glutamate systems may induce anxiety-like behavioral effects. The study was supported by the National Science Centre Grant no. 2016/21/B/NZ7/01131. MH acknowledges the support of InterDokMed project no. POWR.03.02.00-00-I013/16.

121. Nasal respiration is necessary for the emergence of aberrant oscillatory activity and behavioural hyperactivity in the ketamine model of psychosis

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Nasal respiration can entrain both slow and fast rhythms in humans and rodents. Ketamine is used to model schizophrenia and is associated with the occurrence of high-frequency oscillations (HFO; 130-180 Hz) in a variety of cortical and subcortical areas. Rats were implanted with twisted wires electrodes in selected structures and thermocouples in nares. Local field potentials (LFP), thermocouple activity, and locomotion (beam breaks) were recorded. A subanesthetic dose of ketamine provoked fast sniffing in rodents which correlated with increases in HFO power in the olfactory bulb (OB). Importantly, HFO in the OB was entrained by nasal respiration on a cycle-by cycle basis and was reduced by unilateral naris blockade. Unilateral naris blockade also reduced HFO power in other regions including the ventral striatum and prefrontal cortex. Reducing naris input bilaterally, but not unilaterally, was associated with weakened ketamine-induced hyperactivity. These findings suggest that functional naris input is vital for the emergence of ketamine-induced hyperlocomotion and aberrant oscillatory activity in the OB, and that this activity can be imposed on other regions commonly associated with pathophysiology of schizophrenia.

122. The influence of a non-balanced maternal diet on the expression of AMPA receptor subunit (GluA1) in offsprings' brain.

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Recent preclinical studies indicate that a non-balanced maternal diet during pregnancy and lactation increase the risk of mental disorders - like addiction to cocaine - in offspring later in life. Long-term withdrawal from cocaine administration is accompanied by AMPA receptor subunits GluA1 overexpression/GluA2 downregulation. This changes were shown to be associated with negative affective states. Therefore, the aim of this study is to examine the influence of high-sugar and high-fat maternal diet on the expression of GluA1 in the nucleus accumbens (NAc) in the male and female offspring. In this experiment, Wistar dams were fed with a high-sugar diet (HSD), high-fat diet (HFD) or standard chow (control group) three weeks before matching, during pregnancy and lactation. The GluA1 expression in the NAc was determined in 28- and 70-day-old offspring by the Western Blot technique. The results showed that the expression of the GluA1 subunit was significantly increased in the male offspring from HSD and HFD groups. No changes were shown in females. This outcome suggests that maternal diet impacts similarly the GluA1 expression in NAc in the male offspring to the withdrawal process in the cocaine-addicted rats. Further studies are needed to discover the meaning of these changes.

123. Is a non-balanced maternal diet able to impact the expression of AMPA receptor subunit (GluA2) in offsprings' brain?

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Preclinical data show that high-sugar (HSD) or high-fat (HFD) maternal diet is associated with an increased risk of mental disorders in offspring later in life. Disturbed glutamatergic system homeostasis and structures of the brain reward system are involved in mood disorders. It was shown that one of the glutamatergic receptors expression changes - AMPA subunits GluA1 overexpression/GluA2 downregulation were associated with negative affective states. Therefore, the aim of this study is to examine the influence of HSD and HFD maternal diet on the expression of GluA2 in the nucleus accumbens (NAc) in the male and female offspring. In this experiment, Wistar dams were fed with an HSD, HFD, or standard chow (control group) three weeks before matching, during pregnancy and lactation. The GluA2 expression in the NAc was determined in 28- and 70-day-old offspring by the Western Blot technique. The results showed that the expression of the GluA2 subunit was significantly decreased in the male offspring from the HSD group, not the HFD group. No changes were shown in females. This outcome suggests that maternal HSD diminishes GluA2 expression in NAc in the male offspring. These changes are gender-specific. Further studies are needed to uncover their meaning. Supported by 2015/19/D/NZ7/00082.

124. Physiological and pathological appetitive learning – can we understand addiction by peeking inside the brain?

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The aim of the study is to elucidate how stimuli of positive valence and cues leading to addiction are processed in the whole brain perspective. To identify activated brain regions, c-Fos as a marker of neuronal responses was used. C57Bl6 wild type mice were tested in the IntelliCage training systems. For appetitive learning place preference test with sucrose as a reward was used. For acquiring alcohol addiction „Drinking in the dark" procedure with ethanol was employed. Two hours after test the mice were sacrificed, their brain were isolated and subjected to optical tissue clearing using iDisco followed by c-Fos immunostaining and the whole hemisphere imaging using light-sheet microscope. c-Fos labeled cells were imaged along tissue background. Next, these were aligned to the Allen Brain Atlas. We have developed a dedicated image computational workflow which includes robust image registration techniques and cell detection algorithms resilient to imaging artifacts. Thanks to this, we obtained three dimensional brain image and we have identified which brain regions were associated with appetitive learning and training leading to alcohol addiction. Our analysis showed the involvement of the central amygdala in appetitive learning as well as in alcohol addiction acquiring.

125. Behavioural inhibition and ADHD characteristics in dog and wolf puppies.

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The family dog, due to its unique evolutionary past, is claimed to be a powerful animal model for studying some human social behaviours including Attention-Deficit/Hyperactivity Disorder (ADHD) related characteristics, given that dogs naturally exhibit phenotypic variability with regard to its symptom domains. In humans, the nature and extent of ADHD are determined by symptoms of inattention, hyperactivity, impulsivity and characteristics of behavioural disinhibition. Our goal was to develop a behavioural test battery to measure the relationships among inhibition and ADHD characteristics at an early stage of development, when environmental effects can be considered minimal, thereby species-specific differences can be revealed. To measure inhibition and ADHD characteristics, we developed behavioural tests that allowed the use of a comparative approach to include hand-reared wolves (N=5) and dogs (N=21) at the age of 4-8 weeks. In general, wolves were less able to inhibit their behaviour compared to dogs, probably because this ability played a central role in the domestication process in dogs. Wolves were more active during the exploration phase and showed more impulsive behaviour during subtests in the age of 4 weeks. Comparison of inhibition abilities between species shed light on the role of domestication and environmental influences in shaping this ability.

126. Maternal separation affects dendritic spine head diameter of putative dopaminergic neurons in the ventral tegmental area of female rats.

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Early-life stress (ELS) disrupts brain development and results in functional and structural alterations in various brain structures. The consequences of ELS include increased risk of addiction and psychophysiological disorders in adulthood. Mesocorticolimbic dopaminergic pathways originating in the ventral tegmental area (VTA) play a crucial role in the development of these impairments but the underlying neuronal mechanisms remain obscure. The aim of this study was to reveal the influence of maternal separation (MS), an animal model of ELS, on VTA dopaminergic neurons' dendritic spine density and shape. Female rat pups were separated from dams for 3h/day from PND2 to PND14. Brain slices containing VTA were prepared from control and MS adult rats. VTA neurons were filled with biocytin and stained against tyrosine hydroxylase (TH, dopamine marker). TH-immunoreactive cells were imaged, deconvolved and their dendritic spines were counted and measured using NeuronStudio software. MS increased spine head diameter in the lateral but not medial VTA. No significant changes in spine density were observed.

Detected region-specific increase in spine head diameter may lead to augmented excitability of dopaminergic neurons and constitute an anatomical substrate of ELS induced malfunctioning of the brain reward system. Funding: NSC-Poland UMO-2016/21/B/NZ4/00204.

127. Social interactions in poly (I:C) rat model of autism: changes in ultrasonic vocalisations.

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Deficits in social communication are one of the core symptoms of the autism spectrum disorder (ASD). Those deficits are visible since early childhood and persistent throughout the whole lifespan. Recent studies provided evidence for the link between maternal infection during pregnancy and increased risk of developing ASD in the offspring. This so called maternal immune activation (MIA) can be induced by injecting a viral mimic, polyinosinic:polycytidylic acid (poly (I:C)). In this way a rodent model of ASD was made. In this study, poly (I:C) was injected intraperitoneally on GD 15 to a pregnant dam. Social Interaction Test (SI) was used on the offspring to evaluate deficits in social communication. SI test was conducted on pairs of two-month-old rats of the same sex and treatment. Next, both behaviour and ultrasonic vocalisations (USVs) of the rats were analysed. No significant changes in social behaviour were observed between the model animals and control groups. Also, no sex differences were observed. USVs analysis showed that the poly (I:C) animals emitted calls of higher peak frequency. Moreover, males emitted higher overall number of ultrasonic calls. Females' USVs were shorter but higher modulated. This study was funded by the Polish National Science Centre grant NCN 2016/23/B/NZ7/01131.

128. Trait sensitivity to positive feedback is associated with higher consumption and preference for alcohol in rats.

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Alcohol abuse is one of the leading causes of death and comorbidity worldwide, leading to social, work, and health problems. It is therefore crucial to identify factors responsible for the transition from controlled use to uncontrollable alcohol abuse. Since a growing body of evidence suggested that cognitive distortions, including abnormal sensitivity to feedback, may play a critical role in this transition, the present study has been devoted to investigating this phenomenon in an animal model. For this, initially, we tested a cohort of rats in a series of 10 probabilistic reversal learning tests, and based on this screening, we classified each animal as sensitive or insensitive to positive feedback. Subsequently, we measured the consumption of, and the preference for the alcohol in the two-bottle, free-choice paradigm. We demonstrate that the rats showing higher sensitivity to positive feedback, initially consume significantly more alcohol than their conspecifics insensitive to positive feedback. We also show that an increased sensitivity to positive feedback is associated with a higher preference for alcohol. These results show for the first time that sensitivity to positive feedback can determine vulnerability to alcohol consumption. Supported by the Polish National Science Centre (grant 2018/31/B/NZ7/03690).

129. Early life adversities affect electrophysiological properties of stress-sensitive nucleus incertus in adult male rats – implications for compulsive behaviours development.

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Early-life stress (ELS) disrupts the development and functioning of many brain structures. Its consequences include increased susceptibility to substance abuse, psychophysiological disorders and compulsive behaviours in adulthood. Recently, stress-sensitive brainstem nucleus incertus (NI) has been implicated in various behaviours including arousal and drug-seeking behaviour. NI neurons synthesize several neuropeptides, including relaxin-3 (RLN3) and cholecystokinin (CCK), however their susceptibility to stress during development has not been investigated. Therefore, this study aimed at discovering the influence of ELS on the electrophysiology of different populations of NI cells. Rat pups were submitted to maternal separation (MS; 3h/day, PND2-14), a well-established model of ELS. Whole-cell patch-clamp recordings in current and voltage clamp mode were performed to examine active and passive membrane properties of NI cells. Recorded neurons were immunostained and evaluated as RLN3+ or CCK+. MS increased excitability of NI neurons and changed their membrane capacitance. Moreover, MS decreased action potential threshold in RLN3+, but not CCK+ NI cells. Simultaneously, the time constant of NI CCK+ neurons was MS-decreased. Our results suggest that ELS increases NI neurons' excitability and changes passive membrane properties in a cell-type-specific manner. This may affect NI-governed processes and contribute to the development of compulsive behaviours caused by ELS. NSC-Poland/UMO-2017/27/N/NZ4/01545.

130. Trait sensitivity to negative feedback interacts with the effect of chronic stress on anxiety in rats

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Cognitive distortions play a pivotal role in the development of depression. One of the most important cognitive distortions associated with this disorder is aberrant sensitivity to negative feedback (NF). Under clinical conditions, this sensitivity can be measured using the Probabilistic Reversal Learning (PRL) test, which has also been recently implemented in animal studies. Although the evidence for the coexistence of depression and altered sensitivity to NF is relatively coherent, it is still unclear whether sensitivity to NF can determine vulnerability to stress and predispose to development of depression-associated symptoms such as anxiety. We tested a cohort of rats in a series of 10 PRL tests and based on this screening, we classified each animal as sensitive or insensitive to NF. Subsequently, the rats were subjected to chronic stress, and differences in the effects of stress on anxiety between NF sensitive and insensitive animals were investigated using light dark box test. We report statistically significant interaction between the sensitivity to negative feedback and stress-induced anxiety levels in rats. Trait sensitivity to negative feedback could have important implications for the resilience to stress and stress induced affective disorders. Supported by the Polish National Science Centre (grant 2016/23/B/NZ4/01562).

131. The influence of co-administration of cannabidiol and cholinesterase inhibitor, rivastigmine on scopolamine-induced memory impairments

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Memory is one of the most important brain function. There are several brain areas (mainly prefrontal cortex and hippocampus) and neurotransmitters (acetylocholine, ACh) which maintain proper cognitive processes. Disturbances in cholinergic system leads to abnormalities in memory functioning and are an essential part of clinical picture of neurodegenerative (such as Alzheimer's disease, AD). Memory loss and cognitive deficits occurring in AD is a deficiency of ACh as a result of selective loss of cholinergic neurons. Rivastigmine is a reversible cholinesterase inhibitor, used in an early pathophysiological feature of AD. Rivastigmine is enhancing cholinergic function, by increasing the concentration of ACh through reversible inhibition of its hydrolysis by cholinesterase. However, there is no effective therapy in AD and currently used drugs such as rivastigmine can cause several severe adverse effects. For that reason is necessary to search for alternative method of pharmacotherapy. One of the possible strategies for the modulation of cognitive disorders is connected with endocannabinoid system (ECS). ECS is a widespread

neuromodulatory system that plays important role in central nervous system (CNS) development, synaptic plasticity, and the response to endogenous and environmental insults. The ECS is comprised of cannabinoid receptors (CB), endogenous cannabinoids (endocannabinoids), and the enzymes responsible for the synthesis and degradation of the endocannabinoids. Cannabidiol (CBD) is a cannabinoid compound considered a multitarget drug and interacts with a diverse array of signalling system which many diverse function in the brain, e.g. neuroprotective and anti-inflammatory properties. The aim of present study was to determine the effect of co-administration of CBD and rivastigmine on the memory disorders connecting with cholinergic dysfunctions in mice. Cholinergic dysfunction in mice we provoked by using an antagonist of muscarinic cholinergic receptor - scopolamine. To assess and understand the memory-related effects in animals we used the passive avoidance (PA) test, commonly used to examine different stages of memory. Administration alone of CBD (1 mg/kg) or rivastigmine (0.5 mg/kg) significantly affect changes in scopolamine-induced disturbances in memory acquisition. Interestingly, co-administration of CBD (1mg/kg) and rivastigmine (0.5 mg/kg) also attenuated memory impairment provoked by scopolamine (1mg/kg) injection in PA test in mice. The combination therapy of these two compounds appears to be more beneficial in reducing scopolamine-induced cognitive impairment than substances administered alone. In summary, this combination of two drugs: CBD and rivastigmine seems to be favourable in pharmacotherapy of cognitive disorders, connecting with cholinergic pathways, e.g. in AD. This kind of polytherapy could increase whole therapeutic effectiveness. This study was supported by the Statutory Funds of the Medical University of Lublin, Poland (DS 21/20 M.Kruk-Slomka).

132. ATP Synthase activity of selected brain structures in morphine addiction

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Morphine exhibit an analgesic effect and is commonly used for alleviating acute and chronic pain, thereby exposing patients to risk of development of drug addiction. Long-term studies concerning proteome of CNS resulted in creating database of morphine- regulated proteins in addiction process. Most frequently repeated proteins in such research are enzymes committed to metabolic energy pathways, especially ATP Synthase. The objective of this study was to evaluate if significantly changed expression levels of ATP synthase during morphine addiction indicated by proteomic research are related to changes in its activity. Male Wistar rats were used in the experiments. Chronic morphine addiction was evoked by injections of increasing dose of morphine hydrochloride (10-40 mg/kg) for 14 days. Control rats received an equal volume of saline. The morphine- abstinence group received morphine according to the scheme and then was kept for 7 days without any injections. Animals were sacrificed through decapitation. The ATP Synthase activity was evaluated in the whole brain homogenates and selected brain structures with use of ELISA microplate immunoassay, the expression level was evaluated with Western Blotting technique. The study revealed different trends in prefrontal cortex, hippocampus and striatum regarding activity and expression level of the ATP Synthase. However there was no statistically significant differences in enzyme activity between the experimental groups in the whole brain homogenates. The correlation of acquired results was observed in analysis of complex V of striatal mitochondria – the protein level and the enzymatic activity were both diminished during morphine addiction, and restored to physiological level during abstinence. Widespread action of drugs on the neural system induce changes at molecular, biochemical, and systems levels. The mesolimbic dopaminergic system has received the most attention in this regard. Acquired results indicate differences in proteomic-indicated enzyme levels and actual activity of ATP Synthase, which may contribute to explaining the role of evaluated brain structures and better understanding of addiction mechanism. The research was supported by The Polish National Science Center, grant number: 2018/29/B/NZ4/02243.

133. The influence of co-administration of CB2 receptor agonist, JWH 133 and antipsychotic drug, haloperidol on positive symptoms of schizophrenia in mice

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Schizophrenia is a severe long-term mental health condition. The symptoms of schizophrenia are usually classified into: positive symptoms (change in behaviour or thoughts, such as hallucinations or delusions), negative symptoms (social withdrawal, anhedonia, lack of motivation) and cognitive symptoms (memory and learning impairment). The main drugs used in therapy of schizophrenia are antipsychotics. Haloperidol is a high potency first-generation (typical) antipsychotic and one of the most frequently used antipsychotic medications used worldwide. Use of haloperidol is considered highly effective for the management of the positive symptoms of schizophrenia including hallucinations, hearing voices, aggression/hostility, disorganized speech, and psychomotor agitation. However, use of this drug is limited by the development of many serious side effects (especially demonstrates a stronger disposition for causing extrapyramidal symptoms: movement disorders, such as drug-induced parkinsonism, akathisia, dystonia, tardive dyskinesia). Thus, there is intense research into developing new treatments for schizophrenia-related responses. One of the possible strategies for the modulation of positive symptoms of schizophrenia is connected with endocannabinoid system (ECS). The aim of present study was to determine the effect of co-administration of JWH 133, CB2 receptor agonist which directly modulates ECS function and haloperidol on hyperlocomotion in mice. The research was based on pharmacological glutamatergic model of schizophrenia, MK 801. MK 801 (dizocilpine) is a selective, non-competitive antagonist of the N-methyl-D-aspartate receptor in the glutamate category. Administration of MK 801 caused hyperlocomotion in mice which correlates with positive symptoms of schizophrenia in humans. We revealed that an acute administration alone of JWH 133 (2 mg/kg) or haloperidol (0.1 mg/kg, i.p) did not cause any changes in MK 801-induced (0.6 mg/kg) hyperlocomotion in mice. Whereas co-administration of JWH 133 (2 mg/kg) and haloperidol (0.1 mg/kg) decreased significantly hyperlocomotion induced by MK 801 (0.6 mg/kg). In summary, co-administration of CB2 receptor agonist, JWH 133 with antipsychotic drug, haloperidol could have a beneficial effect on the treatment positive symptoms of schizophrenia. This drug combination may give the opportunity to use lower doses of haloperidol and at the same time to reduce risk of its adverse effects, equally effectiveness of the therapy will be preserved.

NEUROPHYSIOLOGY

134. Electrophysiological properties of neurons in the rat dorsal motor nucleus of the vagus are modulated by feeding conditions

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The nervous system allows organisms to maintain homeostasis and well-being by monitoring and replying on internal as well as environmental cues. To remain in the state of homeostasis, discrete brain areas orchestrate variety of physiological functions. The dorsal motor nucleus of the vagus (DMV), structure located in a brainstem, receives information on the nutritional status and energy balance and in turn regulates the functioning of visceral organs by its projections via vagus nerve. Actions taken in accordance with neuronal instructions can reciprocally influence nervous system, what can be most notably observed in pathological states, as obesity. We argue that disrupted nutrient composition may lead to the neurophysiological dysfunctions in DMV neurons. To address this issue, we used patch clamp and multi-electrode array electrophysiological recordings to study differences between rats fed with control or high-fat diet (HFD). We observed disturbances in basic electrophysiological properties, spontaneous activity and synaptic input of DMV neurons in HFD-fed rats. Our results indicate that nutritional composition influences the nervous system on a fundamental level, what adds up to current knowledge on how improper dietary habits lead to wide-reaching health problems of the Western world. Supported by: 2018/28/C/NZ4/00099 and

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135. 25-hydroxycholesterol as a modulator of synaptic transmission in the mice neuromuscular junctions

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25-hydroxycholesterol (25HC) is a main oxysterol whose production is vastly increased during inflammatory response. Upregulation of 25HC occur at early stage of amyotrophic lateral sclerosis (ALS) associated with neuromuscular junction (NMJ) dysfunction. The significance of 25-HC for neuromuscular transmission has not been studied yet. Here, using microelectrode and optical approaches we studied the effect of 25HC on synaptic vesicle exocytosis and membrane properties in the diaphragm NMJ of mice. 25HC (1μM, 20-min application) markedly increased exocytotic neurotransmitter release at 20 Hz activity. 25HC did not modify either neurotransmitter release at 0.05 Hz or pair-pulse facilitation. In addition, spontaneous neurotransmitter release was not sensitive to 25HC. These results indicate that 25HC increases recruitment of synaptic vesicle to active zone (sites of exocytosis) rather than modulates the exocytotic machinery directly. The underlying mechanism of action can be linked with direct effect on membrane properties or via binding with the oxysterol binding receptor. 25HC had no effect on the fluorescence of lipid environment-sensitive dyes F2N12S, 22-NBD-cholesterol and bodipy C5-Ganglioside GM1 in NMJ region. The stimulatory effect of 25HC on synaptic vesicle exocytosis during 20 Hz-activity was completely suppressed by liver X receptor antagonist as well as inhibitors of Gi protein and protein kinase

136. The influence of cerebellar transcranial stimulation with constant current on maximal electroshock seizures

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The influence of transcranial direct current stimulation (TDCS) of cerebellum with different electrode polarity upon electroshock–induced seizures in Wistar rats was investigated. Seizures were induced with electric current corneal stimulation (60 Hz, 150 mA, 0,2 sec) performed at a different time from the TDCS cessation. The false corneal stimulation was performed in control rats. The shortening of tonic flexion (by 27,6%-30,3%, P<;0,05), tonic extension (by 29,6%-36,4%, P<;0,05) as well as duration of clonic seizures (by 25,0%-35,1%, P<;0,05), and stretching reflex duration shortened by two times (P<;0,05) was registered when maximal electroshock seizures were induced after TDCS with anode (600 mcA, 15,0 min). Such effects were seen during the first two hours of the poststimulative period. The analogous cerebellar stimulation with cathode also induced the shortening of tonic extension – the effect observed in 1,0 up to 10th hour from the moment of stimulation. During the early poststimulative period (up to 0,5 h from the moment of stimulation), cathode-induced effects significantly exceeded antiseizure ones induced with anode stimulation and were opposite with their sign pertained to control ones. Neurophysiological mechanisms with emphasis on different time-course of antiseizure effects of anode and cathode cerebellar TDCS are discussed.

137. Involvement of integrins in regulation of hippocampal GABAergic synaptic transmission and plasticity in the CA1 region

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It is well known that integrins which are cell adhesion receptors mediate activity dependent regulation of excitatory synaptic strength and are also involved in glycinergic transmission. However, their role in GABAergic synaptic transmission and plasticity in hippocampus is still unknown. Herein, we investigated the impact of integrins on inhibitory transmission by using patch-clamp recordings from hippocampal slices. We found that, in the presence of bath applied peptides, containing the Arg-Gly-Asp (RGD) sequence, mIPSCs amplitude recorded from pyramidal cells was reduced (GRADSP: 100±1%, n = 6; GRGDSP: 89±3%, n = 12). On the contrary, similar recordings on parvalbumin-positive interneurons led to increase of GABAergic transmission (GRADSP: 101±1%, n = 4; GRGDSP: 116±4%, n = 5). Besides the integrins involvement in inhibitory synaptic transmission we also tested how various types of integrins interfere with GABAergic synaptic plasticity. To address this issue, we induced i-LTP using NMDA application (3 min, 20μM) in control conditions (125±5%, n = 10) and in slices treated with RGD peptide or integrins activity inhibitor (cilengitide). Interestingly, we found that both compounds occlude iLTP (GRGDSP: 97±6%; cilengitide: 89±3%, n = 5). The present results provide evidence that hippocampal GABAergic transmission and plasticity strongly depend on the activity of integrins. Acknowledgements: The research was supported by National Science Center (NCN) grant UMO-2018/31/B/NZ4/01998 and by National Science Centre (Poland) grant SONA/2014/15/B/NZ4/01689. PB was supported by the Foundation for Polish Science (FNP) 2019/2020 and by Polish National Science Centre scholarship ETIUDA 2018/28/T/NZ4/00344. Equal contribution: Katarzyna Lebida, Patrycja Brzdąk.

138. High-fat diet disrupts the modulating effect of carbachol on the Dorsomedial Hypothalamus network

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The dorsomedial hypothalamus (DMH) is a brain structure strongly involved in the regulation of food intake, circadian rhythms, stress response and thermogenesis. One of the subpopulations of the DMH neurons, involved in the regulation of the feeding behavior, are the DMH cholinergic neurons which directly innervate the arcuate nucleus. It was previously shown that this specific subpopulation of the DMH neurons can respond to changes in the nutrient status (fasting condition). The effect of acetylcholine on the DMH network itself is still missing. The aim of our study was to verify if carbachol, a cholinergic receptor agonist, can modulate neuronal network of the DMH and if this modulation is disrupted during the development of obesity. Our experiments were conducted on two groups of rats: the control and fed with high-fat diet (HFD) chow. Preliminary data indicated the strong carbachol modulation of single DMH neurons both in spontaneous activity and synaptic transmission. This effect of carbachol was affected by short term intake of HFD (2-3 weeks), which suggests that even short exposure to the diet rich in fat can disrupt responsiveness to some neurotransmitters and in broader view disrupt the output information. Supported by: 2017/25/B/NZ4/01433.

139. More than 2.5 years of stable chronic recordings of single-units in the rabbit amygdala

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Stable single-unit recording is a method of recording the same neurons for more than a single day (McMahon et al., 2015). Some authors believe that observing relatively short spans of neuronal activity we ignore some brain processes taking longer time periods (Thompson, Best, 1990). The microelectrode bundles were assembled manually (Bondar et al., 2009; Kruger et al., 2010). 32 nichrome microelectrodes were implanted into amygdala of two adult rabbits under general anesthesia. The raw activity was filtered, neuronal spikes were detected by a threshold. Sorted action potentials were transferred to an automatic algorithm assessing stability of recordings (Fraser, Schwartz, 2012). Data were available for acquisition for 72 days in rabbit #1 and for 964 days in rabbit #2. In summary, there were 281 single units that were recorded for more than one day. This is the first attempt to combine chronic nichrome microelectrodes with an automatic algorithm for stable units detection. We managed to test neurons' properties in different experimental conditions presenting visual or auditory stimuli to the animals due to stable recording.

140. Identification of nucleus incertus neurons innervating medial septum – an optogenetic approach.

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Nucleus incertus (NI) is a population of GABAergic and glutamatergic neurons located just below the fourth ventricle. It contributes to the modulation of hippocampal theta oscillations via the ponto-septal pathway. However, the electrophysiological properties of NI neurons giving rise to this connection remain unknown. To fill this gap in our knowledge, electrophysiological experiments combined with optogenetics were performed. Rats were microinjected into the medial septum (MS) with retrograde viral vector pAAV-Syn-Chronos-GFP. Two weeks later in vivo multichannel recordings of NI neurons electrical activity were conducted on urethane anaesthetised rats. Hippocampal local field potential was used to determine the theta phase-preference of recorded NI neurons. The optogenetic stimulation of the observed neuronal population was used to identify the NI neurons projecting to MS. We have observed two distinct subpopulations of NI neurons: one that is theta phase-locked and second that is theta phase-independent. Only the tonic firing cells from the second group were optogenetically identified as projecting to MS. None of the theta phase-locked neurons was identified as MS projecting. Our studies have shown that regularly firing theta-phase independent neurons innervate medial septum and thus play a specific, plausibly permissive role in theta rhythm generation. Funding: NSC, Poland UMO-2014/15/B/NZ4/04896.

141. The response of ventral tegmental area and substantia nigra pars compacta neurons to optogenetic stimulation of superior colliculi.

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Midbrain dopaminergic (DA) neurons have a well-established role in the control of motor functions and reward-related behaviours. Alternation in some aspects of movements and behaviour relies on the level and pattern of dopamine release in target structures. A lower concentration of dopamine on one side of the brain, for example caused by a neurotoxic lesion of DA neurons, causes the animal to orientate in the same direction. Also superior colliculi (SC), part of the subcortical visual system, participate in object-oriented movements of eyes, head and body. DA neurons can be influenced by SC directly, as well as indirectly via their main inhibitory input - the rostromedial tegmental nucleus (RMTg). We hypothesize that this bifurcating pathway originating in SC may participate in orienting the animal toward the appetitive or salient stimuli by induction of asymmetry in the level of activity of DA neurons in the midbrain. To test this hypothesis we have injected SC of Sprague Dawley rats with AAV-DIO-CHR2-eYFP viral vector. Two weeks later we have extracellularly recorded responses of the ventral

tegmental area and substantia nigra pars compacta dopaminergic neurons to optogenetic stimulation of SC. As expected, we have observed excitatory, as well as inhibitory responses. Funding: NSC, UMO-2017/27/N/NZ4/00785.

142. Extremely low-frequency electromagnetic field exposure changes the activity of stress systems

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The influence of extremely low-frequency electromagnetic field (ELF-EMF) on human organism, especially on the nervous system, is still insufficiently described. There are many reports suggesting that ELF-EMF exposure alters stress hormone levels and thus contributes to the development of depression or anxiety. On the other hand, ELF-EMF is used in medicine. Based on various reports, we hypothesized that ELF-EMF effect on stress systems is bidirectional and it depends on its intensity. Wistar rats were divided into three groups. Animals were exposed to EMF of magnetic induction 1 mT and 7 mT 1 h/day for 1, 2 or 3 weeks. Control animals were subjected to the same experimental procedure except ELF-EMF exposure. After each exposure brain tissues were removed and the levels of main stress hormones were determined. After exposure to 1mT levels of stress hormones were initially increased, but returned to the control values with subsequent exposures. Whereas their concentrations after exposure to 7mT were elevated and remained high or even increased with subsequent exposures. We concluded that 1mT ELF-EMF may activate same adaptive mechanisms in nervous system, but the effect of 7mT ELF-EMF is permanent. The ELF-EMF of higher value can sensitize the organism to subsequent stress factors.

NEUROIMMUNOLOGY

143. The analysis of Givinostat treatment in a rat model of neonatal hypoxic-ischemic brain damage.

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Hypoxic-ischemic (HI) brain damage in neonates provokes immediate immune response, expressed primarily by the activation of microglia and release of inflammatory factors - cytokines and chemokines. Recent data show that histone deacetylase inhibitor (HDACi), Givinostat (ITF 2357), provides protection associated with reduction of inflammation in stroke model of adult rats The aim of our research was to check whether Givinostat will demonstrate the same effect in neonatal ischemic brain. Hypoxia-ischemia was produced in seven-day-old rat pups by a permanent unilateral common carotid artery ligation, followed by 60 min hypoxia (7.6% O2). Givinostat (5 and 10 mg/kg b.w.) was administered in a 5-day regime with the first injection given immediately after the onset of injury. The damage of the ipsilateral hemisphere was evaluated by immunohistochemistry 14 days after the insult. by using markers estimating pro-inflammatory (CD68/interleukin-1 beta) and anti-inflammatory (CD68/arginase-1) phenotype. The effect of Givinostat on cytokines and chemokines at 24h, 72h and 5 days after HI was assessed by Luminex assay. The anti-inflammatory action of Givinostat was only demonstrated by decrease of pro-inflammatory molecule MIP-1α, 72 h after injury. Further research are required to completely determine the action of this HDACi in brain of immature animals. Supported by ESF POWR.03.02.00-00-1028/17-00.

144. Evaluating response of glial cells in the rat in vitro model of perinatal asphyxia: in search of potential therapeutic targets

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Glial cells are extremely sensitive to a temporal limitation of oxygen and glucose, which accompanies the episodes of perinatal asphyxia and could trigger the subsequent developmental disorders. The detailed mechanisms of glial cell responses to the injury evoked by lack of trophic support remains largely unknown. To address this issue, we have established the purified monocultures of glial cells for purpose of an in vitro model of perinatal asphyxia. The primary mixed glial culture was derived from neonatal Wistar rats and then cultured for twelve days. The individual glial fractions were isolated and subjected to the oxygen-glucose deprivation (OGD). After that, the cells were cultured for 24h or 72h and collected for the subsequent molecular, biochemical and immunocytochemical analyses. As shown by the performed studies, the OGD episode affects the microglia polarization, activates astrocytes and inhibits differentiation of oligodendrocyte progenitor cells. The enumerated alterations are accompanied by the significant changes in the secretion profile of the affected cells. In conclusion, lack of oxygen and glucose triggers diversified responses of glial cells, which could contribute to the resulting neurodevelopmental disorders in children who survived perinatal asphyxia. The identified processes might be the targets of future therapeutic strategies. Supported by ESF, POWR.03.02.00-00-I028/17-00.

145. Development of New Drug-like Fpr2 Agonist With Anti-inflammatory Properties: Study in the in Vitro Model of Neuroinflammation

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Successful brain resolution of inflammation (ROI) requires the activation of endogenous pathways, which can switch from production of pro-inflammatory mediators to specialized pro-resolving mediators (SPMs). Formyl peptide receptor 2 (FPR2), a receptor modulated by endogenous SPMs, such as lipoxin A4 (LXA4) is one of the key players in the ROI. Recently we have identified a class of new non-peptidic FPR2 agonists with a ureidopropanamide scaffold, therefore in this study we perform the estimation of FPR2 agonists in terms of their protective potency in in vitro model of neuroinflammation. Primary microglia cultures were prepared from 1-2 days old Sprague-Dawley offspring. Microglia were pretreated with FPR2 agonist – AMS21 (1-5μM) and then exposed to lipopolysaccharide - immune system activator (100ng/ml). Necrotic cell death was determined by lactate dehydrogenase release, (LDH test) and the production of TNF-α was evaluated by the ELISA assay. Pre-treatment of new ureidopropanamide agonist of FPR2 receptor – AMS21 change LPS-evoked LDH and TNF-α release. Importantly, both agonists (MR-39 and AMS21) showed a long-lasting effect observed 24h after administration. We postulate that targeting the resolution of inflammation may offer new therapeutic perspectives in the treatment of chronic inflammatory diseases. Supported by the grant no. 2017/26/M/NZ7/01048, National Science Centre, Poland.

146. ICAM1 knockdown as a strategy to moderate cytotoxic T cell autoimmune response in multiple sclerosis

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Multiple sclerosis is a chronic neuroinflammatory disease that causes severe neurological dysfunction leading to disabilities. Perforins and granzymes have been known to make up cytotoxic T cell cytolytic responses and ICAM1 contributes to the cells' ability to migrate to the Blood-Brain Barrier in multiple sclerosis. miR-155 was found to be highly expressed within lymphocytes with pro-inflammatory profile in immune responses. Studies showed that miR-155 knockdown could downregulate ICAM1 expression on endothelial cells. We aim to study the knockdown of ICAM1 in cytotoxic T cells of multiple sclerosis patients and study the effect on miR-155, perforins and granzyme B; aiming to find a selective therapy for multiple sclerosis. Cytotoxic T cells from MS patients were isolated, cultured and transfected with silencers of ICAM1 and after 48 hours, expression levels of Perforin, Granzyme B and miR-155 were evaluated using RT-qPCR. The knockdown of ICAM1 caused a significant decrease in miR-155, perforin and Granzyme B with p-values of 0.0059, 0.0160 and 0.049 respectively. The knockdown of ICAM1 could be one way to maneuver around the pro-inflammatory profile of MS possibly through regulating miR-155 with its pro-inflammatory properties and the cytolytic activity of cytotoxic T cells.

NEUROGENESIS

147. Traumatic brain injury-induced changes in adult hippocampal neurogenesis

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Several important cognitive functions altered by traumatic brain injury (TBI) depend on the hippocampus, where new neurons are born throughout life in the Dentate Gyrus (DG). It has been postulated that TBI induced hyperexcitation of DG granule cells (GCs) can affect adult hippocampal neurogenesis and induce long-term changes in both neural stem cells (NSCs) and newborn neurons (newrons), and these alterations can contribute to hippocampal dysfunction. We aim to understand what particular changes TBI induces at the cellular, molecular, and electrophysiological levels in preexisting GCs, NSCs, and newrons. Observed changes in spontaneous excitatory currents (sEPSCs) frequency indicate remodeling of excitatory input, likely expressed as an increase in the number of excitatory synapses. Those changes are accompanied by a decrease in spontaneous inhibitory currents (sIPSCs) frequency, indicating a loss of GABAergic neurons. Moreover, we have observed an increase in neurogenesis up to two months after the injury. These newrons, however, present altered morphology and migration patterns. In addition, we have found that NSCs get activated in higher numbers and acquire a reactive-like phenotype. This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska– Curie grant agreement no. 799384.

148. Alginate based hydrogels as the potential carriers for stem cells in neurodegenerative disease treatment

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Intrathecal transplantation of stem cells is attractive route of cell delivery for treatment of neurodegenerative diseases. However, several obstacles remain mainly due to disruptive forces during the injection procedure that negatively influence cell survival. Thus different materials in which cells could be embedded before transplantation might be used as cell carriers and protectors. In our study alginate hydrogels (LVM) were investigated as the potential scaffolds for intrathecal stem cell delivery. The analysis of rheological properties of LVM was implemented to assess their stability. Hydrogels were supplemented with manganese ions used as tracers for T1-weighted MR imaging. Different forms of manganese i.e. free Mn2+ or manganese enclosed in compact beads was evaluated in term of long time Mn2+ labeled LVM observation in MRI after their intrathecal transplantation into SOD1 (animal model of ALS) mice. Additionally, in vitro studies were performed using human adipose-derived mesenchymal stem cells (hA-MSC) to evaluate the influence of LVM presence on cell viability, proliferation and migration. The results of our MR images revealed that alginate hydrogels supplemented with manganese are injectable and stable scaffolds that can be used in intrathecal delivery in mice. The analysis of in vitro studies of LVM on cell behavior is in progress.

149. Characterization of cells derived from heterotopic ossification

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Heterotopic ossification (HO) is a process characterized by the formation of bone within soft tissues. One of the main causes of HO development is neurological insult of which the most common are traumatic brain injury (TBI) or spinal cord injury (SCI). The presence of HO in the soft tissues causes hypoxia in the surrounding microenvironment which is thought to trigger the release of inflammatory factors that are responsible for infiltration of cells that induce new heterotopic bone formation and spreading. However, it is not entirely clear what types of cells are responsible for these pathological changes. The aim of our study was comprehensive analysis of human cells derived from HO samples obtained from patients during surgical procedures. In our studies the phenotype of cells from HO was identified using flow cytometry and immunocytochemistry. Our results have shown that cells derived from HO presented typical morphological features for mesenchymal stem cells (MSCs) and expressed CD44, CD73, CD90, CD105 markers. Isolated from HO cells showed the ability to differentiate into mesodermal cells i.e., adipocytes, chondrocytes and osteocytes. qRT-PCR and Nanostring analysis used to determine the expression pattern of genes specific for pro-inflammatory or anti-inflammatory cytokines and selected growth factors is in progress.

NEURODEGENERATION

150. Effect of unilateral intracerebral hemorrhage in the capsula interna on the degree of neurodegeneration and locomotor activity of rats.

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Hemorrhagic stroke is always accompanied by cerebral edema, dystrophic changes around the site of injury, and severe neurological deficit. Such functional disorders correlate with the level of degeneration of the white matter of the brain in the short term, but pathological processes with focal lesion, which are` delayed in time, still under debate. On a model of rats with unilateral hemorrhage in the right capsula interna, after 30 days was revealed not only the death of neurons in the cerebral cortex, corpus callosum, and progressive bilateral neurodegenerative changes in the sciatic nerve (SN), but also locomotor violations were detected. The results of electrophysiological studies showed that on the 30th and 90th day after the stroke, there was a significant decrease in the nerve conduction velocity (NCV) in the SN comparison with the control (by 62.4% and 59.8%, respectively). Moreover, there was no difference in the NCV between the left and right SN. Probably, such changes were the result of descending degeneration of nerve fibers in the fascicles, with no signs of recovery. The results of our work show locomotor disorders after a stroke are not limited to the site of damage, but cause delayed bilateral degeneration of the sciatic nerve.

151. CCL3/CCR1 signaling in mice model of traumatic brain injury

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Traumatic brain injury (TBI) is a serious worldwide health problem, due to the lack of effective recognition and treatment. Recent studies suggest that chemokine system seems to play an important role in TBI progression. Therefore we decided to study potential participation of the chemokine, CCL3 and its receptor, CCR1 in brain posttraumatic changes. In the present study, to evoke brain injury we performed controlled cortical impact (CCI) in mice. As a result of our research we have shown that CCL3 and CCR1 mRNA levels are strongly upregulated after injury in cortex, striatum, thalamus and hippocampus (1, 4, 7 days and/or 2, 5 weeks after CCI). Protein levels of mentioned chemokine and receptor were measured in the cortex and thalamus (1, 7 days post injury). Here we have observed increased level of CCL3 in cortex (in both time points) and CCR1 in thalamus (1 day after CCI). We also confirmed presence of CCR1 on micro- and astroglial cell cultures, suggesting that those glial cells are involved in TBI development. Thanks to the promising data we received, in our opinion CCL3/CCR1 signaling seems to be important target for future search for drugs. Acknowledgments: Supported by NCBiR grant ERA-NET-NEURON-COFUND/1/LEAP/15/17 and IF-PAS statutory funds.

152.CCL4/CCR5 signaling in mice model of traumatic brain injury

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Traumatic brain injury (TBI) is one of the most serious issue worldwide. We evaluated, for the first time, changes in CCL4 and its receptor (CCR5) in brain structures (cortex, striatum, thalamus, hippocampus) in a mouse model of TBI and in in vitro study presence of CCR5 in primary microglial and astroglial cells. Time-course studies revealed the up-regulation of the mRNA expression of CCL4 in all tested brain structures (mainly early stages after injury). A similar pattern of activation was observed at the protein level in the cortex and thalamus, where the strongest

activation was observed 1 day after TBI. Analyses of CCR5 demonstrated the up-regulation of the mRNA expression in all tested cerebral structures, mainly in the early phases post TBI. Protein analysis showed the up-regulation of CCR5 in the thalamus 24 h after TBI, but we did not detect any changes in the cortex. Moreover, we confirmed the presence of CCR5 in primary microglial and astroglial cell cultures. Our findings highlight that CCL4 and CCR5 offer promising targets for influencing secondary neuronal injury and improving brain injury therapy. Acknowledgments: Supported by NCBiR grant ERA-NET-NEURON-COFUND/1/LEAP/15/17 and Maj IF-PAS statutory funds.

153. The electromagnetic field changes the activity of acetylcholinesterase

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The electromagnetic field (EMF) is an important environmental factor. The increasing number of artificial sources of EMF raises the concern about its adverse effects on organisms, mainly on the nervous system function. In our experiments, we verified the hypothesis that exposure to EMF increases the activity of the nervous system. For this purpose, we assessed acetylcholinesterase (AChE) enzyme activity by modified Ellman's method on terminal abdominal ganglion of Periplaneta americana, where are cholinergic connections between sensory nerves and giant interneurons. Exposure to EMF (50 Hz, 7 mT, 24h) induced a statistically significant increase in AChE activity, changing it from 0.46 ± 0.02 μmol/mg protein in control to 0.99 ± 0.01 μmol/mg protein after exposure. Elevated AChE activity corresponds well to the increased motor activity of insects observed after the same exposure to EMF. The distance travelled by the insects during the 15-minute observation was higher after exposure to EMF by 154 % compared to the control. The results confirm our hypothesis: exposure to EMF increases activity of the nervous system. EMF has come to be seen as one factor amongst multiple interactive environmental pollutants, and probably a causative agent of nervous system disorders.

154. Adverse effect of benzophenone-3 on neurons does not result from activation of microglia cells

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Popular UV filters – benzophenone-3 (BP-3), cinnamate and camphor, are widely used in a lot of cosmetic products. Research suggests that these compounds, especially BP-3, may have an adverse effect on nerve cells. The aim of this study was to evaluate the effect of three UV filters on the viability of microglia cells in vitro and the effect of BP-3 also on microglia cells in the brain tissues of rats in vivo. Primary microglia cells were treated with tested compounds, and then lactate dehydrogenase (LDH) levels were evaluated in the culture medium. The brain tissues were isolated from rats, which were exposed to BP-3 in the prenatal period and during the 6 and 7 weeks of age. Real-Time PCR was used to determine the expression of selected markers of microglia cells activation (C1q, Cd40, Aif). UV filters (BP-3 and camphor) at concentration 10-4M increased LDH level in culture medium. However, BP-3 had no effect on mRNA expression of examined markers of microglia cells activation. The results of this study suggest that the observed harmful effects of BP-3 on neurons are caused by other neurotoxicity mechanism than damage by activation of microglia cells.

155.Impact of extremely low insecticide concentration on the nervous system of Periplaneta americana

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The nervous system plays a fundamental role in the proper functioning of the organism. It serves as a target for majority of toxic substances used in the pesticide industry. In our study we verified the hypothesis that even an extremely low concentration of insecticide can affect the functioning of the organisms, mainly the activity of nervous system. The effect of bendiocarb, a carbamate inhibitor of acetylcholinesterase (AChE) was tested on the nervous system of Periplaneta americana at a concentration 10-10 M. We measured the AChE activity (modified Ellman method), cAMP concentration (ELISA) and the phosphorylation level (pIMAGO-biotin phosphoprotein detection) in samples prepared from the last abdominal ganglion of insect nerve cord. Bendiocarb surprisingly induced a 26.5% increase in AChE activity; moreover a 40.2% decrease in phosphorylation level which corresponds well to a 40.4% decrease in cAMP level. The unusual effect of bendiocarb is probably nonspecific and may be explained by arousal in insect body induced by insecticide. Changes in phosphorylation and cAMP levels confirm changes in the functioning of the insect`s nervous system caused by an extremely low dose of insecticide. This work was supported by EU Program Knowledge, Education, Development – Poland; Project: Universitas Copernicana Thoruniensis in Futuro.

156. Method development of photothrombotic ischemic stroke and location of HuR protein in rat model

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Cerebrovascular diseases are the principal causes of mortality and disabilityworldwide. Elaborate a repeatable, well-designed model will facilitate future research on new possibilities of treatment of ischemic stroke Cellular survival and restoration of correct circulation are the goals of ischemic stroke therapy. Minocycline, by launching plethora of neuroprotective mechanisms may be beneficial as the treatement which has been confirmed in many researchmodels of acute brain damage. HuR protein, a member of ELAVL family, stabilize mRNAs by translocation to cytoplasm from nucleus. Thus, HuR is considered as a potential target for neuroprotection during stress. Aim: Testing the effect of monicycline on state of penumbra and functional outcomes after ischemic stroke with evaluation whether regulation of HuR protein is involved in this treatment.The second aim was to develop, test and select the most favorable parameters and determine the location of the HuR protein during an ischemic stroke. Photothrombotic ischemia of motor cortex was produced in 72 male Long-Evans rats. We tested different time windows: 24h, 48h and 7 days after stroke induction. Half of the experimental groups received an intravenous dose of minocycline (1 mg / 1 kgb.w / 1ml solution, 10 minutes after stroke). CatWalk XT, Grip Strength-test and elevated runway tests were performed. These functional tests were applied before andafter ischemic stroke. In groups with minocycline we observed statistically significant improvement of speed of walking, correctness of the stepping pattern and increase of grip strength. After analyzing the results, the best parameters are 15 min. exposure to light and life-time 12h-48h. These parameters made it possible to obtain a small necrosis area and a large penumbra area. Penumbra was localized by immunohistochemical techniques and we observed presence of HuR in the cytoplasm of neurons from this area. Conclusions: Minocycline improves motor function in ischemic rats. Its action also correlates with HuR protein but determining the exact relationship between minocycline and HuR protein requires in-depth studies.

157. Role of specific proteins in non-synaptic mitochondria during aging

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Mitochondrial dysfunction is evident in numerous neurodegenerative and age-related disorders. However, our current understanding of the mitochondrial changes that occur is unclear. In order to evaluate the susceptibility of cerebral non-synaptic mitochondria to aging-dependent dysfunction, male Wistar rats of 6, 15 and 27 months old were used. Basic proteomics, together with functional studies were used in order to profile the mitochondrial changes. One-dimensional gel electrophoresis revealed 25 significantly changed proteins with 10 identified as important for mitochondrial respiration and energy production. While the continuous decrease of complex I and II activity was observed during aging, complex III did not change and complex IV was affected only in a group of 15 months old. Interestingly, upregulated protein levels were detected in 15 months old mitochondria for complex I core subunits NDUS1 and NDUS2, complex II flavoprotein subunit SDHA, cytochrome b-c1 subunit 2 of complex III as well as ATP synthase subunit beta, ADP/ATP translocase, and the phosphate carrier protein. Moreover, the elimination of ROS by mitochondrial superoxide dismutase was limited during the whole aging process. Although aging is associated with oxidative stress, not all changes increase progressively with age. This work was supported by grant VEGA 1/0004/19.

158. Motor and cognitive symptoms in mice with progressive loss of dopamine neurons

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Parkinson's disease (PD) is a progressive neurodegenerative condition characterized by motor and non-motor symptoms such as anosmia, executive dysfunction, and depressive-like state. The non-motor symptoms often precede the manifestation of characteristic motor impairment and may worsen with the advancement of the disease, thus significantly decreasing quality of life of PD patients. Here, we investigated the influence of progressive loss of dopamine neurons on the PD-like symptoms in a transgenic model of progressive parkinsonism (TIF-IADATCreERT2 mice). We assessed effects of loss of dopamine neurons on motor performance and non-motor symptoms (olfactory acuity, preference for sweet taste, and executive functions). Additionally, a clustering analysis was performed to identify correlated motor and non-motor symptoms. We found that progressive loss of midbrain dopaminergic neurons was associated with alterations in motor and cognitive parameters, in particular gait parameters (paw print surface area, coordination), and increased activity in the cognitive tasks, such as greater number of total choices or rewarded choices in operant tasks.

159. Effect of the consumption of a high-fat diet together with lingonberry supplements on neuroinflammation in ApoE-/- mice

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ApoE-knockout (ApoE-/-) mice demonstrate the disturbance of lipid metabolism, atherosclerosis, and eventually, signs of neurodegeneration. We investigated the impact of lingonberries supplemented to high-fat diet (HFD) on cognition, the state of the hippocampal neurons and glia in ApoE-/- mice. 8-week-old males were divided into 4 groups and fed with low-fat (12% kcal; LF-control) and high-fat (38% kcal; HF-control) diets as well as a HFD supplemented with whole lingonberries (WhLB) and their insoluble fraction (InsLB) for 2 months. It was shown that the density of intact pyramidal neurons in the CA1 area of LF-control mice was 17±3% lower compared to other animals. The astrogliosis was observed in the hippocampus of LF-controls and WhLB. Meanwhile, the concentration of the filamentous form of GFAP was 42±8% higher in the LF-control group versus other ones. We also demonstrated enhanced microgliosis in LF-control animals, as well as increased density of Iba-1-positive cells in WhLB and their hypertrophy in HF-controls. To conclude, although the cognitive impairments did not manifest in

young adult ApoE-/- mice, the indications of neuroinflammation were observed in LF-controls and partly in WhLB. The consumption of a HFD supplemented with insoluble lingonberry fraction may protect brain tissue from neuronal loss and glia activation.

160. Role of neuroinflammation in OGD model of stroke.

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Inflammatory response plays an important role during progression of stroke. That's why, better understanding of its principles is crucial for design of new therapies which utilizes as a principle modulation of immune response. The aim of study was to find out whether modulation of receptors of particular chemokines e.g. CCL2, CXCL12 or CX3CL1 might be a alternative way of ischemic stroke treatment. As a model of ischemia, organotypic hippocampal cultures (OHC) were subjected to oxygen glucose deprivation (OGD). OGD relies on exposure of OHC medium without glucose in anaerobic condition. As assessed both by LDH assay and fluorescent imaging of propidium iodide (PI) increased mortality in OHC subjected to OGD was observed. This was followed by mechanical changes in this region of OHC measured by atomic force microscopy. Modulation of chemokines receptors lead significant changes in viability of OHC what confirm their important role in ischemia process. To sum up, OGD model allow to perform ischemic stroke mimicking experiments on complex system which contains multiple cell types which better corresponds to in vivo conditions. Investigated here chomokines were showed to play important role in OHC response to OGD and thus are promising candidates for further research on this topic.

161. Long term survival protocol and behavioral deficits in fMCAo model of ischemic stroke

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Cerebral ischemia is one of the most common causes of mortality worldwide. Stroke patients suffer from a long lasting neurological and motor deficits. In animal stroke models a high mortality is one of the factors limiting effectiveness of the long-term experiments. The aim of the present study was to evaluate a long term survival protocol of ischemic stroke. Focal middle cerebral artery (MCA) occlusion (fMCAo) in C57BL/6 mice was used. The filament was placed in the internal carotid artery (ICA) to occlude blood flow in MCA. Sham animals underwent the same surgery protocol but without ICA occlusion. During the first post-surgery week, a postoperative care protocol was applied. Weight of the animals was assessed up to 30 days post-stroke. Additionally, we performed behavioral examination with use of experimental stroke scale. After 30 days Nissl and immunofluorescence for GFAP and IBA1 stainings were performed. Weight loss in fMCAo animals was greater when compared to sham animals. fMCAo group was characterized by a slower post-stroke recovery and prominent behavioral deficits. Neurodegeneration and neuroinflammation were observed during first week post-stroke. Our study establishs an experimental protocol of post-operative care in fMCAo model of ischemic stroke and describes the long-term effects of ischemic stroke.

162. Postsynaptic SAPAP3 improves mitochondrial function in Huntington's disease.

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Huntington's disease (HD) is a neurodegenerative disorder caused by a CAG repeat expansion at the HTT gene, characterized by early psychiatric disturbances (obsessive-compulsive disorder - OCD). Mutant huntingtin affects striatal GABAergic neurons and glutamatergic cortico-striatal synapses, causing mitochondrial dysfunction. SAPAP3, a postsynaptic scaffold protein mainly located in striatum, modulates OCD and might have several mitochondrial interactors. Therefore, striatal dysfunction linked to early mitochondrial deregulation may involve changes in SAPAP3, potentially explaining HD-related disturbances. Our results show decreased SAPAP3 protein and mitochondrial levels in symptomatic YAC128 transgenic mice (expressing full-length mHTT), mature YAC128 primary neurons and HD knock-in mice-derived striatal cells, when compared to the respective controls. YAC128 primary striatal/cortical neurons single cell analysis revealed that SAPAP3 diminished levels were pronounced at distal neurites, displaying postsynaptic deregulation in HD. SAPAP3/PSD-95 colocalization demonstrated decreased puncta number, area and altered SAPAP3 levels. Of relevance, SAPAP3 modifies normal mitochondrial function, as its silencing impaired mitochondrial morphology, neurite mitochondrial movement and function, and generated higher levels of reactive oxygen species. SAPAP3 overexpression ameliorated all these mitochondrial phenotypes in HD cells. Our data indicate that SAPAP3 levels control mitochondrial function and that targeting this protein might have a neuroprotective role in HD.

163. Overexpression of neuregulin-1 in glial restricted progenitors (GRPs) – an approach to increase the functional properties of GRPs.

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Demyelination is the loss of compact myelin sheath around axons. Myelin is produced by a distinct subpopulation of glial cells – oligodendrocytes and provides electro-mechanical insulation of axons. Transplantation of oligodendrocyte-generating glial-restricted progenitors (GRPs) may restore myelin production in demyelinating disorders. Our aim is to evaluate the therapeutic potential of mice GRPs (mGRPs) overexpressing neuregulin-1 (NRG-1) transplanted into shiverer mice – an experimental model of demyelination. NRG-1 participates in oligodendrocyte proliferation, differentiation, myelin formation and thickness. Previous results reported myelinating capabilities of native mGRPs, which did not correlate with mice lifespan prolongation. Our goal is to generate mGRPs-NRG-1, with enhanced regenerative abilities. To establish an in-vitro culture of mGRPs, we isolated cells from E13-E14 mice neural tissues and performed selective culture with a bFGF-supplemented medium. We determined the phenotype of isolated cells with anti-NG2, anti-PDGFRα, anti-OLIG2, anti-GFAP, anti-MBP and anti-MAP2 antibodies-based immunocytochemistry, confirming homogeneity and progenitor status thereof. To compare the myelinating capabilities of mGRPs and mGRPs-NRG-1, we established mGPRs/mice dorsal root ganglion neuron co-culture. Finally, to overexpress NRG-1 in mGRPs, we tested two separate lentiviral systems introducing exogenous NRG-1, unfortunately with unsatisfactory results. Therefore, our new approach will include CRISPR-based lentiviral activation particles, which should induce the overexpression of endogenous NRG-1.

164. The effect of Kisspeptin-13 on spatial learning and memory in a rat model of Amyloid-beta induced neurotoxicity.

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Kisspeptin (Kp), a key regulator of the reproductive axis, might have a role in AD as well as in learning processes. Thus, the aim of this study was to investigate the effect of Kp-13 in Amyloid-beta induced neurotoxicity. 6-week-

old male and female Wistar rats were injected intracerebroventricularly with Amyloid-beta (4µg/4µl). After a recovery time, spatial memory was assessed in Morris Water Maze. Kp-13 (2µg/2µl) was injected intracerebroventricularly on the last day. Afterwards, the hippocampi were isolated and the Kp-13 (1µg/1ml) induced Glutamate release was measured via a superfusion system. Finally, the expression of Egr-1 gene levels in hippocampus and prefrontal cortex was determined by RT-PCR. Results showed a learning deficit of the AD group compared to the control group, which was blunted in females by Kp-13 treatment. Superfusion study revealed that AD hippocampal slices secreted significantly more Glutamate than control and this was antagonized by Kp-13. Finally, Kp-13 inhibited Amyloid-beta induced Egr-1 gene expression in females. Our results indicate that specifically in female rats, Kp-13 has a positive effect on Amyloid-beta induced neurotoxicity. Acknowledgements: EFOP-3.6.2-16-2017-00006.

165. The 8 amino acid long fragment of kisspeptin-13 induces anxiety-like behavior and hypolocomotion in rats.

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Kisspeptins (Kp) are RF amide neuropeptides regulating the reproductive (HPG) axis. In our previous experiments, Kp-13 activated the hypothalamic-pituitary-adrenal (HPA) axis, and induced anxiety-like behavior and hyperlocomotion in rats. We aimed to investigate whether the 8 amino acid long fragment, Kp-8 affects HPA and HPG axis activity, anxiety and locomotion. Male Wistar rats were treated intracerebroventricularly with Kp-8, then open field (OF), elevated plus maze (EPM) and marble burying (MB) tests were performed. Plasma corticosterone and luteinizing hormone (LH) concentrations were determined with ELISA. Dopamine release from the nucleus accumbens was investigated with ex vivo superfusion. Plasma corticosterone and LH concentrations were raised by Kp-8. Kp-8 reduced central ambulation (OF), and open arm time and entries (EPM), indicating anxiety-like behavior. It also suppressed locomotion and exploratory behavior, as shown by the decrease in rearing, total ambulation (OF), total arm entries (EPM) and interactions with marbles (MB). Kp-8 also stimulated dopamine release from the nucleus accumbens. Kp-8 activated the HPA axis and induced anxiety-like behavior similarly to Kp-13. However, it suppressed locomotor activity, in which the modulation of dopaminergic pathways, alterations in receptor affinity and changes in intracellular signaling could be involved. This work was supported by EFOP-3.6.2-16-2017-00006.

NEUROANATOMY

166. Superior colliculus innervates contralaterally located rostromedial tegmental nucleus – a neuroanatomical study

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Midbrain dopaminergic (DA) neurons control animals' orienting and approach towards salient and/or rewarding stimuli. Numerous brain regions influence DA neuron activity, however the sensory input is provided predominantly by the ipsilateral superior colliculus (SC). Importantly, not much is known about sensorial innervation of the rostromedial tegmental nucleus (RMTg) – the main inhibitory input to DA neurons. Therefore, the aim of this study was to describe the anatomy of the SC-RMTg circuit. To investigate connections between SC and RMTg both anterograde and retrograde tract-tracing experiments were performed. Viral vectors containing yellow fluorescent protein (YFP) genes were unilaterally injected into the SC and then RMTg was bilaterally investigated for the presence of YFP-positive fibres. In separate experiments, unilateral microinjection of FluoroGreen into the RMTg was performed and then the SC was tested bilaterally for the presence of retrogradely filled neurons. Both tract-

tracing methods revealed that SC innervates almost exclusively contralateral RMTg. Additionally, the lateral part of the intermediate SC layer is the main source of such innervation. Such brain wiring might have important implications for the lateralisation of locomotor and approach behaviours, as sensory stimuli might control DA neurons on both sides of the brain in an opposite manner. Funding: NSC, UMO-2017/27/N/NZ4/00785.

167.Early life adversities alter dendritic spine density on ventral tegmental nucleus neurons

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Early life stress has extensive and long-term consequences including increased risk of psychiatric disorders and substance abuse in adulthood. However, neuronal mechanisms underlying the observed relationship remain obscure. Potential explanation of this phenomenon might include pathological changes in the development of mesocorticolimbic dopamine system caused by traumatic events experienced in early childhood. In the following experiment we examined changes in density of dendritic spines in the ventral tegmental area (VTA) after early maternal separation, a well established rodent model of early life stress. To quantify spine density in Golgi-Cox stained VTA neurons we developed a novel machine-learning based method tailored to this specific brain area. Our results suggest that rats subjected to the early maternal separation stress have decreased density of dendritic spines on VTA neurons. Reported neuronal differences may underlie reduced excitatory input to the VTA dopaminergic neurons and subsequent detrimental behavioral changes associated with the development of addiction and psychological disorders in adulthood. Moreover, our automated method of image analysis yields results similar to the manual measurements and could potentially be adapted for other brain regions in which commonly used programs tend to underperform because of unique neuronal morphology. Funding: NSC-Poland UMO-2016/21/B/NZ4/00204.

168. Development of an in vitro model of induced instability of the dendritic arbors of mature neurons

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Loss of dendritic stability is associated with mental disorders including depression. Nevertheless, the molecular mechanisms responsible for dendritic arbor stability are still largely unknown. Therefore our study aims to develop models of induced destabilization of mature dendritic arbors of neurons cultured in vitro, which will be used for the comprehensive analysis of molecular mechanisms and processes accompanying dendritic simplification in depression. Based on the available literature, conditions that may affect the morphology of mature neurons were selected. Next, cultured rat hippocampal neurons were treated with selected compounds and the morphology of dendritic arbors was analyzed. We found that prolong gabazine and interleukin-1β treatment decreased the complexity of dendritic arbors of neurons. Additionally, gabazine treated neurons expressed a lower level of GluA1, a subunit of an AMPA receptor, and reduced frequency and amplitude of AMPA currents. On the other hand, the GluA1 level and AMPA currents remained unchanged in interleukin-1β-treated cells. These data indicate that gabazine and interleukin-1β affect mature neurons' dendritic arbor complexity through different mechanisms, allowing us to establish two different models of dendritic instability in pathology. Supported by the TEAM grant from the Foundation for Polish Science (POIR.04.04.00-00-5CBE/17-00)

169. Diversity of basal forebrain somatostatin-expressing neurons

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The basal forebrain regulates cortical activity, for instance ascending cholinergic, glutamatergic, and parvalbumin-expressing GABAergic cells have been shown to promote arousal, attention and wakefulness. However, at least one population of somatostatin-expressing GABAergic neurons is known to promote sleep through inhibiting cortically-projecting neurons. Here, using virus-mediated neuronal track-tracing techniques and immunohistochemistry, we investigated the projection patterns of the somatostatin-expressing (SOM) neurons of the basal forebrain. SOM cells were localized both to the caudo-ventral (horizontal limb of the diagonal band of Broca, substantia innominata, lateral preoptic nucleus) and rostro-dorsal (medial septum, vertical limb of the diagonal band of Broca) sub-regions of the basal forebrain. Although previous studies emphasized the role of SOM neurons in local inhibition of major ascending excitatory pathways, we found that some of them target inhibitory neurons as well. We also found that basal forebrain SOM neurons project to several cortical and subcortical areas, including the olfactory bulb, the medial and lateral habenular nuclei, the cingulate and dorsolateral entorhinal cortices as well as the hippocampal formation. Analysis of these pathways suggest that the basal forebrain harbors several different sub-populations of SOM neurons, which probably have different behavioral functions.

CIRCADIAN RHYTHMS

170. The effect of high-fat diet on the circadian rhythm of food intake and c-FOS immunoreactivity in the rat Dorsomedial Hypothalamus.

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Diet-induced obesity (DIO) is a rodent model of obesity caused by foods high in fat or sugar. We believe this type of diet changes the signaling in the brain even before the obesity is developed. Therefore, we conducted a set of experiments to find out how high-fat diet (HFD) impacts the circadian rhythm of food intake and neuronal activity of the cells located in the Dorsomedial Hypothalamus (DMH), a structure mostly affected by DIO. We discovered that after 3-4 weeks on the HFD the circadian rhythm of food intake was disrupted, with rats eating more during the day comparing to the controls. This might have been the cause of similarly changed c-FOS immunoreactivity in the DMH, as more cells were shown to be active during the second part of the day. We have also observed, that after a period of food deprivation the number of c-FOS positive cells in this structure decreases, contrary to a refeed condition, which further indicates the connection between food intake and c-FOS immunoreactivity in the DMH. These results suggest that HFD changes the behavior of the animals and activity of the DMH neurons irrespective of DIO. Supported by National Science Center grant OPUS13: 2017/25/B/NZ4/01433 and the Faculty of Biology of the Jagiellonian University: N18/MNS/000033.

171. High fat diet dysregulates circadian rhythmicity in the orexinergic fibre density in the rat locus coeruleus

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The locus coeruleus (LC) is a noradrenergic centre localised in the brainstem, critically involved in the maintenance of arousal and the regulation of wake-sleep cycle. Orexins (orexin-A and orexin-B) are neuropeptides expressed by

neurons in the lateral hypothalamus which are implicated in triggering arousal, wakefulness and regulating appetite. One of the brain structures which is strongly innervated by orexinergic neurons is the LC. Recent studies indicate that the LC can respond to metabolism cues;for instance cholecystokinin can increase cFos expression in the LC. Our aim was to evaluate possible circadian pattern of orexin fibre density in the LC in rats fed with control and high-fat diet (HFD). To aim this goal, we performed immunofluorescence labelling on brain slices prepared from rats culled at four different time points across 24h. Our results show clear circadian variability in the orexin-A-ir fibre density, which is disrupted by HFD. This disturbed circadian pattern of orexinergic innervation in the LC in HFD-fed rat may underlie our recent experiments which have shown that rats on HFD eat more during their non-active phase. We speculate that HFD causes the inappropriate level of arousal resulting in food intake during the behaviourally quiescent day. Supported by: 2017/25/B/NZ4/01433.

172. Circadian modulation of the rat pretectal area by orexinergic system

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Orexin A (OXA) is a hypothalamic neuropeptide that binds to orexin receptors 1 and 2 (OX1R, OX2R). Orexins are involved in the modulation of arousal carrying circadian information for the rest of the brain. Previous studies suggest orexinergic modulation of retinorecipient sites and place orexin receptors and fibers in the pretectal area, including the olivary pretectal nucleus (OPN) which controls the pupillary light reflex. The aim of this study was to evaluate the electrophysiological effects of OXA via identified orexin receptors and orexinergic innervation pattern of the OPN during day and night. Experiments were conducted on acute pretectal brain slices obtained from adult Sprague Dawley's rats using ex vivo electrophysiological multielectrode array (MEA) recordings. Moreover, the circadian diversity in the density of orexinergic projections across 24h in the OPN was presented by immunohistochemical staining. Here we show that OXA is a powerful modulator of the pretectal activity, including the OPN, acting predominantly via OX2R. Moreover, the density of orexinergic fibers shows clear circadian variation, with the highest values during the night. These suggest the supporting role of orexins in the function of retinorecipient sites during the behaviourally active night, when access to photic cues is limited. Supported by: 2018/28/C/NZ4/00099.

173. Circadian changes in expression and enzyme activity of the catalase, glutathione peroxidase and glutathione reductase in chicken pineal gland

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Reactive oxygen species (ROS), for example hydrogen peroxide (H2O2), are molecules containing one oxygen atom and one or more unpaired electrons. They can easily react with the cell components. The cell has developed defense mechanisms against ROS. The best known antioxidant enzymes include, catalase (CAT) glutathione peroxidase (GSH-Px) and glutathione reductase (GR). In the chicken pineal gland, the monoamine oxidase catalyse oxidative deamination of serotonin and exerts day-night changes in gene expression. The products of this reaction are: 5-hydroxyindole acetic aldehyde, ammonia and H2O2. The formed H2O2 may play a crucial metabolic and signal functions. However, accumulation of H2O2 may have a negative consequences. The aim of the project was to check whether: 1) in the chicken pineal gland there are enzymes that metabolize hydrogen peroxide: CAT, GSH-Px and GR, and 2) there is a circadian variation in their protein level and enzymatic activity. The results shows that the antioxidant enzymes are present in chicken pineal gland. Their protein level and enzymatic activity is changing between the studied time points. The study was financially supported by the Ministry of Science and Higher Education through the Faculty of Biology, University of Warsaw intramural grant DSM: 501-D114-01-1140500.

174. Sixteen shades of ultraviolet/blue light - in vivo study of the rat dorsal lateral geniculate nucleus activity

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Short-wavelength light was shown to strongly influence circadian and visual functions, in both positive and negative ways. We examined the actions of various light parameters upon neuronal activity of the rat dorsal lateral geniculate nucleus (dLGN) critical for transferring visual information from the retina to the primary visual cortex. We aimed to investigate how different dLGN neurons respond to UV, blue and filtered (cut off at 525 nm) white light applied in a wide range of intensities, and across different backgrounds, by using extracellular electrophysiological multi-channel recordings in vivo combined with ECoG registration. We report that pigmented rat dLGN responded in a comparable manner to all wavelengths from the blue light spectrum, whereas responses to UV light had a maximum peak at 380 nm. Furthermore, intensity encoding properties were disturbed by the usage of short-wavelength cut off filter, and were not identified under monochromatic UV light. Finally, we found evidence for the existence of ''spectrally opponent'' neurons in the rat dLGN. Our data shows that blue light is crucial for light intensity coding, whereas UV light for colour coding. Supported by: 2013/08/W/NZ3/00700.

175. Circadian influence of orexins upon retinorecipient neurons in the rat lateral geniculate complex

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Orexinergic system of the hypothalamus is critically involved in the modulation of arousal and feeding behaviour in the circadian fashion, with orexins acting as hands of the master clock. Despite a clear day to night difference in ambient light, the function of dense orexinergic innervation of retinorecipient brain sites is still elusive. Here we use a combination of pharmacology and ex vivo multichannel extracellular electrophysiology together with optogenetic stimulation of retinal terminals to unravel the neuronal target of orexins in the lateral geniculate complex (LGN) of adult Sprague Dawley rats. Additionally, we examine neurophysiological sensitivity to orexins, expression of their receptors (by quantitative RT-PCR) and orexinergic innervation pattern in the LGN; all across 24h. Our results prove that orexins exert powerful influence upon the activity of LGN neurons across 24h. Despite the lack of clear rhythmicity in orexin receptor expression, orexin-ir fibre density in the LGN demonstrates circadian variability peaking at night. Moreover, we establish that LGN neurons sensitive to orexins are in part directly retinorecipient. This study provides a direct link between orexinergic and visual systems. Furthermore, it suggests that orexins may prepare retinorecipient neurons for behaviourally active night, when photic cues are strongly limited. Supported by: 2018/28/C/NZ4/00099.

COGNITIVE POSTERS

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176. The relationship between EEG microstates and subjective experience

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Resting-state method is commonly applied in neuroimaging studies and refers to the intrinsic patterns of brain activity that is observable in the absence of the external task. It is well know that this activity can be modulated by various factors, including subjective experience, which can be quantified by applying The Amsterdam Resting-State Questionnaire (ARSQ). One of the options to evaluate resting-state electroencephalogram (EEG) is to apply microstate approach where the recorded oscilations are defined as „states" of the signal that evolve over time. 5 min. eyes-closed resting state 64 channels EEG were collected. After the task, participants filled in ARSQ. The last 30 seconds of EEG were subjected to Microstate analysis where topographies at Global Field Power (GFP) peaks were submitted into k-means algorithm. Duration, occurrence, contribution and transition probabilities were calculated for each of 4 microstates. Correlation coefficient of ARSQ categories scores and microstates parameters were calculated. We showed correlation between activity of microstate A and microstate B with different domains of ARSQ, suggesting that ARSQ can be used to explore the relationships between psychological and physiological variables and quantify sensory and non-sensory experience during resting- state period.

177. Three stages of 40 Hz auditory steady-state response

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40 Hz auditory steady-state response (ASSR) is increasingly used in diagnostics and monitoring on neuropsychiatric disorders. However, stimulation settings vary greatly and it is not known how different stimulus parameters might change ASSR. The influence of stimulus duration, as a factor contributing to clinically-relevant findings, has never been addressed in healthy population in detail. Our study aims to systematically evaluate how different stimulus durations influence parameters of 40 Hz ASSRs. 40 Hz ASSRs were elicited with click trains of different length (500, 1000, 1500, 2000 ms) in 14 healthy subjects. The intertrial phase coherence (ITPC) was used to evaluate ASSRs. ITPC values were averaged in four time windows: early-latency (0-100 ms); late-latency (100-500 ms); steady-state (500-1500 ms); and pre-offset (last 400 ms of stimulation) parts and compared. Our results reveal that in addition to the previously described early- and late-latency responses, in ASSRs to longer than 500 ms stimuli a third stage can be observed that potentially resembles entrainment and steady-state. This stage lasts from the late-latency response until the end of stimulation and is characterized by lower phase-locking. This research is supported by Vilnius University grant MSF-JM5/2020

178. Neurophysiological features of the brain functioning of servicemembers of the armed forces of Ukraine with traumatic brain injuries and post-traumatic stress disorders during testing of simple sensorimotor reaction

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Traumatic brain injures (TBI) in combatants in eastern Ukraine occupy the second place after bullet and fragment wounds. Most patients with TBI have no trauma-dependent abnormalities on computed tomography. At the same time, manifestations of TBI, such as cognitive deficits, headaches, anxiety, depression, and more, overlap with symptoms that are characteristics of post-traumatic stress disorders (PTSD). For research was created three groups. It was control group, veterans with PTSD and veterans with TBI. For study, we used EEG. Also, we used program for neurovisualization LORETA. For analyzing networks, we used coherent analyzing. Statistical analysis showed a significantly longer latency period in the group with TBI compared to the control group, but no difference was found between control group and the group with PTSD. In the control group during simple sensorimotor testing

the reactions was involved classic scheme of visual analyzing of information. In the PTSD group we found a shift in brain activity to the zones in the occipital area that are responsible for the primary and secondary visual information processing, In the TBI group we found decreased activity in the frontal cortex and increased activity in the parietal zone, especially in the left hemisphere.

179. Attentional differences in the front and rear space: insights from pupillometry

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There is growing evidence that each of our senses is foundational for the development of specific perceptual and cognitive capabilities. For example, visual experience may be foundational for spatial cognition, which is better in sighted vs. blind individuals, as well as within vs. outside the visual field of sighted individuals. Here we tested whether this disparity between regions of peri-personal space extends to a non-spatial skill: the ability to regulate alertness in response to non-visual events. We measured behavioral and pupillary responses to auditory odd-ball stimuli in the front or rear space (separate sessions). Participants (sighted) detected rare target sounds in a stream of repetitive standard sounds. By comparing sessions where sounds came from the rear vs. front space, we found: (1) decreased transient pupil dilation in response to target stimuli and (2) increased false alarm rates and increased steady-state baseline pupil diameter. This pattern of results is consistent with steadily increased arousal in sessions where sounds came from the rear space, implying reduced ability to single out the target stimulus. This supports the idea that even non-spatial skills, such as the ability to alert in response to unexpected events, are differentially engaged across regions of the peri-personal space.

180. Complex naturalistic stimuli maintained in working memory capture attention automatically

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Recent studies suggest that a stimulus actively maintained in working memory (WM) automatically captures visual attention when subsequently perceived. However, such a WM guidance effect has been so far observed only for stimuli defined by one simple feature. Here we investigated whether the guidance effect occurs also for complex and naturalistic stimuli, such as faces and houses.The experiment comprised two conditions – a WM condition and a mere exposure condition. After remembering or seeing a stimulus, subjects performed several trials of a dot-probe task, in which pairs of stimuli were presented laterally as distractors (remembered or seen on the one side, control stimulus on the other) and followed by a target dot, to which subjects reacted by pressing a button. We found that subjects' response was faster when the target dot followed a memorized stimulus than when it followed a control one and that the N2pc component was evoked by memory-matching stimuli. Importantly, neither RT, nor N2pc effect were observed in the mere exposure condition. In conclusion, behavioral and electrophysiological data jointly indicate that stimuli defined by multiple features are also able to attract attention automatically. The interaction between WM and attention can be thus further explored in more ecological settings.

181. How do anxiety and mood affect Subjective Cognitive Complaints and their relationship to an objective cognitive state?

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Subjective Cognitive Complaints (SCCs) are defined as a perception of cognitive decline compared to the previous period which was not objectionable. According to the DSM-V they are considered as a potential indicator of cognitive efficiency. There are psychological factors which can affect the number of generated SCCs. The aim of the study was to verify the connection between SCCs and objective cognitive functioning with control of the level of anxiety and mood. The study was attended by 50 people over 60 years of age who carried out a battery of tests: PROCOG, STAI , BDI and CANTAB with VTS. Results indicate that the subject from the group with a lower mood report significantly more problems in everyday cognitive and emotional functioning. In subgroups with lower intensity of anxiety and standard mood there was a positive relation between SCCs and measures of the attention-testing task was observed. The study confirmed the relationship between the level of anxiety or mood and the number of SCCs generated by older people. These psychological factors have also been shown to moderate the relation between SCCs and the objective cognitive state. Results show how important it is to control these variables during making a neuropsychological diagnosis.

182. Dealing with emotions and error processing in chlidren: an event-related brain potential study

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Previous research in adults revealed that error processing deficits increase with poorer stress reduction skills. The exact influence of stress and emotions on the error processing in children is not known. The present project aimed to fill this gap investigating the relationship between error processing in children and the ways their family deals with parenting and emotions. Error processing was investigated using event-related brain potentials (ERPs) that enable to monitor brain activity. The aim our research is the negative deflection in the ERP waveform peaking around 50 miliseconds after an erroneous response that is called Error Related Negaitivity (ERN). The amplitude of this component allows estimation of the brain's resources involved in error processing. EEG data was collected while the children performed the standard Go/No-Go task combined with the delivery of negative and positive reinforcements. Dealing with emotions and the parenting style was reported using questionnaire. The results received so far show the children engage more cognitive resources in error processing when receiving negative reinforcement condition, authoritative parenting style is related to less cognitive resources engaged in error processing in negative reinforcement condition, higher separation anxiety is related to less cognitive resources engaged in error processing in positive reinforcement condition.

183. Monomolecular odour recognition - effect of expertise on olfactory performance

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The perception of flavours is a multimodal sensory experience that involves particularly olfaction and taste.Although odours are ubiquitous in our environment, most people have problems with recognizing and

naming them properly.It may be expected, however, that people whose profession require them to have a good olfactory sense, should perform better in flavour recognition tests. The aim of this study was to check if professional experience really leads to better olfactory performance. 129 healthy (age:16-61) participants with no previous training participated in the experiment.The control group was naïve(n = 50), experimental included baristas and Q-graders(n = 79).The procedure was based on the psychophysical approach, participants were asked to recognize 15 odours in a given order from one of four prepared sets, correct answers were counted. Results have shown no significant overall impact of expertise on performance compared to control. However, significant differences between groups were found in the perception of two odours. With the course of the experiment, the percentage of correct responses in the control group decreases but the experimental group maintained a stable level. In summary,presented results suggest that profession have a weak influence on odour recognition, however,experienced people seem to be less prone to stress and overstimulation while testing many samples.

184. Neural correlates of executive dysfunctions in academic procrastination

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Procrastination is associated with increased impulsivity and executive dysfunctions. Our previous study demonstrated that procrastinating students present attentional lapses and error processing dysfunctions observed in both behavioral and neuronal indices (Michałowski et al., in preparation). In the present study we wanted to investigate whether these differences can be moderated by self-efficacy manipulation, as previous research has shown that low self-efficacy is one of the main causes of task completion delay (Steel, 2007) and that the type of feedback differently influence the performance depending on the individuals' procrastination level (Delaval et al., 2013). EEG was recorded in high and low procrastinating students during Go/No-go task with two levels of difficulty. After each block of trials participants received either positive or negative, false feedback regarding their performance in comparison to others. The results confirmed previous findings of increased reaction time variability and post-error slowing among high procrastinating students, who also presented smaller amplitudes of P300 and error-related negativity in comparison to low procrastinating participants. However, this effect was independent of the self-efficacy manipulation, as both groups committed more mistakes and presented increased reaction time variability along with increased error-related neuronal response in negative feedback condition.

185. Resting-state functional connectivity as an indicator of individual differences in social information processing: fMRI study

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Social cognition remains an important research topic as the alterations of effectiveness of social information processing underlie clinical and subclinical difficulties in everyday functioning. Recently, the emergence of resting-state functional connectivity (RsFC) analysis has dramatically improved our understanding of the functional architecture of the brain. However, RsFC has not been systematically studied in relation to individual differences in social cognition. Methods: 32 healthy young adults took part in rs-fMRI using a 3 T Siemens PRISMA scanner. The analysis of rs-fMRI was performed in CONN Functional Connectivity toolbox. Social functioning was assessed with the use of behavioral battery including theory of mind, empathy, social cognitive biases, participation in social relationship and autistic traits. We evaluated relationship between RsFC and individual differences in social cognition using seed-driven and ROI-ROI approach. Results: The results suggest that there is a relation between individual traits in social cognition and Rs-FC. Specifically, we found that RsFC within PCC (seed region of DMN) and frontal pole negatively correlated with social engagement; RsFC within anterior insula (seed region of salience network) and temporal gyrus negatively correlated with empathy. Conclusions: RsFC within Default Mode Network

and Salience Network remain highly sensitive indicator of social cognition.

186. Let's face it - the role of face orientation in audiovisual speech processing

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Is specialization of speech processing related to specialization of face processing in infancy? Both processes undergo dynamic changes between 5 and 9 months of age. At that time, infants become increasingly attuned to native speech. Moreover, they gradually shift from featural to configural face processing, as indexed by the face inversion effect. In an eye-tracking study, 5-, 9- and 12-months-old infants (N=215) viewed upright and inverted faces articulating syllables with congruent and incongruent auditory speech cues (McGurk stimuli). Face orientation strongly modulated attention to the mouth in 9- and 12-months-olds in congruent and incongruent conditions but only in some of them in 5-months-olds. Infants at 9- and 12- months of age preferred looking to the mouth in upright but not inverted conditions, whereas 5-month-olds were looking more to the eyes of both upright and inverted faces. This is the first study to show emerging link between specialization in audiovisual speech processing and face processing in infancy. Specifically, around the time when infants' perception specializes in native speech, they increase attention to the mouth of a talking face. Disruption of configural face processing due to face inversion affects older, but not younger infants' perception of speech cues.

187. Function of education on neuropsychological test performance (Indonesian Boston Naming Test, Verbal Fluency Test, and Token Test) among healthy adults in Indonesia

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Previous studies have shown positive effect of education on cognitive processes. Higher education may reduce risks of age-related cognitive decline or disease. Neuropsychological tests can help assess cognitive function that are linked to particular brain functions. The current research aimed at investigating demographic variables on the performance of neuropsychological-language tests. Participants were 490 adults (males = 194; females = 296), age ranged 16 to 80 years old (M = 33,17; SD = 15,21). Education were stratified into 5 levels (<; 7 years of education; 7 -9 years of education; 10 -12 years of education; 13 – 16 years of education, >; 22 years of education). Participants were administered the Indonesian BNT, Verbal Fluency Test, and Token Test. Univariate analysis was conducted to assess effects of demographic variables. Across the three neuropsychological tests, education revealed significant interactions with the Indonesian BNT, VFT, and TT (F (4,444) = 37,07, p <; 0.01, eta = .25; F (4, 444) = 17,17, p <; 0.001, eta = .13; F (4, 444) = 14, 48, p <; .001, eta = .11, respectively). These results signify the importance of education on one's cognitive processes particularly language performance.

188. BrighterTime - An App to Measure Human Performance & Ambient Light

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Ambient light intensity has been shown to impact various aspects of human physiology including alertness, mood and performance. However there is little known about these effects outside of the lab. To address this deficit we have developed a mobile phone application to measure alertness, working memory and visual cognitive performance in the field. This app – BrighterTime – uses the smartphone's camera to measure ambient light whilst presenting participants with cognitive tasks in the form of standard psychological tests and newly developed game alternatives. In addition the app gathers a plethora of personal information such as chronotype, activity levels, habits and demographic factors. We hope to use this tool to better understand ambient light's impact on human performance and how this interacts with time of day.

189. Exploratory Factor Analysis of Trail Making Test, Stroop Test, Digit Span, and Five point Test as measures of Executive Functions

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Previous study showed that Trail Making Test, Stroop Test, Digit Span, and Five Point Test were developed as measures of executive functioning. The purpose of this study was to analyze the structural model of the four tests. Participants were 490 adults (Females = 294, Males = 196), age between 16-80 years old. Years of education were stratified into 5 categories (0-6; 7-9; 10-12; 13-16; 17-22). Trail Making Test, Stroop Test, Digit Span, Five-Point Test were administered. Exploratory factor analysis was conducted to explore the constructs underlying the four tests. EFA showed that based on the variance of initial eigenvalues 4 factors are determined with a cumulative value = 69.03%. Factor 1 consisted Time-TMT A (0.839), Time-TMT B (0.743), unique responses of FPT (-0.698), and Time-Stroop Test (0.530). Factor 2 consisted DS-Backward (0.864), DS-Forward (0.776), DS-SQ (0.728). Factor 3 consisted FPT (0.931) and Error Stroop test (0.931). Factor 4 consisted Error TMT A (0.872) and Error TMT B (0.823). The current study provides four underlying constructs of the neuropsychological tests particularly executive functioning domain.

190. Positive effects of physical workout on working memory in healthy ageing

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Fourteen healthy elderly women were scanned before and after a workout program lasting 6 months. During the fMRI exam an n-back task was used. All subjects underwent also a neuropsychological examination, including fluid and crystallized intelligence, executive functioning, and visual and auditory memory. The fMRI data was processed in Freesurfer's FS-FAST surface stream with paired differences (after vs before) comparisons of contrasts of interest (1-back vs 0-back, 2-back vs 0-back, 2-back vs 1-back). The first level GLM model included additional regressors of participant's movement, and outlier timepoints (ART Toolbox based). In the second level analyses four models were tested: basic (including hours of training, participants' age and between scan time interval), IQ (basic extended with IQ scores), memory (basic extended with memory scores) and executive model (basic extended with executive functioning). There was no main effect of the scan timepoint (after workout vs before workout) in any of the comparisons, all the variance in the signal came from the variables of interest. Inclusion of neuropsychological variables changed the results significantly (especially the executive functioning), yet still a significant effect of the hours of workout was present. The analyses support beneficial role of physical workout on cognitive functioning of the elderly.

191. Processing of sad and happy autobiographical memories in healthy and depressed women - an fMRI study

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One of the central characteristics of major depressive disorder (MDD) is disrupted processing of self-referential material, including autobiographical memories. Sad memories (SM) are more arousing and salient for people with MDD, while happy memories (HM) are more important and vivid for healthy individuals. Despite some accounts of neural underpinnings for processing memories in MDD, the literature is still inconsistent. We compared neural processing of happy and sad memories in two groups. 55 MDD and 34 healthy control (HC) women provided 5 SMs and 5 HMs. They were later asked to recall the memories during an fMRI procedure. They rated their emotional state and vividness of a memory after each block. MDD group reported significantly lower emotional state during SMs than HC. Also HMs were more vivid within each group than SMs. On the neural level alone, significantly higher activation in angular and middle frontal (MFG) gyri was observed for HC during SMs - regions involved in episodic retrieval and attentional control processes. Since SMs are less self-important for HC, this result suggests that they need to be more engaged in the retrieval process and direct more attention in order to recall them, as compared to MDD.

192. Pedophilic sex offenders show reduced activation in the right DLPFC during integration of emotion and cognition – preliminary results

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The pedophilic disorder is characterized by a sexual preference for children and leads to child sexual abuse (CSA) in half of the individuals suffering from this disorder. Studies showed that pedophiles with a history of CSA (CSA+) are inferior in inhibitory control to those without (CSA-). Inhibitory control may be influenced by negative affectivity, however, it is not known if distress influences inhibitory control in CSA+ and CSA- equally. We recruited three groups of participants: healthy controls (HC), CSA+ and CSA- who performed an emotional Go-NoGo block task comprising negative and neutral pictures. We found that HC and CSA- had slower reaction time in negative compared to neutral condition (regardless of the instruction, i.e. Go or NoGo), while CSA+ did not. Consequently, HC and CSA- showed increased activation in the right dorsolateral prefrontal cortex (DLPFC) in negative compared to the neutral condition, which was not observed in CSA+. DLPFC is crucial for cognitive control, however, the activity of this region is modulated by emotional valence. Reduced engagement of DLPFC in CSA+ in negative condition (irrespectively of the task instructions), suggest that negative emotions in CSA+ disrupt also other aspects of cognitive control, rather than inhibition specifically. Supported by NCN (2016/21/B/HS6/01143).

193. Diurnal differences in brain networks organization during short-term memory task - fMRI study

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Previous studies have revealed that cognitive performance and many biological functions are under influence of internal circadian clock. Homeostatic and circadian effects are together responsible for the maintenance and control of human activity patterns. The aim of the study was to investigate the time-of-day effect on brain networks' engagement during the encoding and retrieval phases of Deese-Roediger-McDermott (DRM) paradigm. The paradigm was adjusted to study the short-term memory and abstract, visual objects were used as stimuli. Sixty-six young and healthy participants performed the short-term memory task in MR scanner during two sessions: about one hour and about ten hours after wake-up. The Independent Component Analysis (ICA) showed diurnal differences in the engagement of brain networks at the encoding but not at the recognition phase. At encoding, the DRM task induced greater activation of medial visual, parieto-occipital and dorsal attention networks as well as greater deactivation of auditory-language network in the evening, which could be explained by the compensatory processes for better performance of the task. The study broadens the knowledge of time-of-day effects on the networks organization engaged in memory processes.

194. Explicit false belief reasoning in preschool-aged children: fNIRS study

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Theory of mind (ToM), the ability to attribute mental states to others, is typically measured by false-belief tasks (FBT). In the verbal version of FBT, subjects are asked to give an explicit answer about the agent's belief. The proportion of correct answers increases significantly between the age of 3 and 5. The vast majority of previous neuroimaging studies on ToM were done with adults and participants older than 6 years old, who have already mastered FBT performance. The inclusion of children in the transitional stage would undoubtedly shed light on ToM neurodevelopmental mechanisms. The main objective of our study was to correlate behavioural results with functional brain activity, given that in this particular age group participants are expected to either pass or not to pass verbal FBT (although a short transition period might occur in between). 30 children (age range 3-5) were presented with verbal FBT. Simultaneous measurement of their brain activity was made with the use of near-infrared spectroscopy (fNIRS). The preliminary results revealed a belief-specific pattern of activation in ToM network structures. The cross-condition (false belief, true belief, no belief) comparison will be presented as well as the activation observed in FBT passers and non-passers.

195. Hypofunction of the left hemisphere as substrate of impaired conventional metaphor processing in schizophrenia – an fMRI study

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Deficits on figurative language and metaphors are commonly observed in first episode of psychosis and chronic schizophrenia individuals. In the present study we assessed 30 schizophrenia outpatients and 30 healthy controls in order to investigate this impairment by the punchline-based metaphor comprehension task and its neural substrates by fMRI. We found that clinical subjects revealing a lower level of understanding of the conventional metaphors as well as indicating absurd punchlines as more understandable, as compared to the healthy controls.

The neural substrates of this figurative language deficit were related to the hypofunction of the fronto-parietal brain regions in the left hemisphere, such as: Inferior Frontal Gyrus, Cingulate Cortex, Precuneus and Inferior Parietal Lobule. Overall, our results indicate that characteristics of impaired conventional metaphor processing in chronic schizophrenia outpatiens is related to the diminished activity of the left hemisphere when compared to the healthy controls. The study was supported by the National Science Centre, Poland (grant number 2016/23/B/HS6/00286).

196. Personality traits are associated with resting state EEG complexity

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Complexity of resting-state EEG signal (rsEEG) are considered to reflect individual differences in personality, yet, the exact association between rsEEG complexity and personality traits remains unclear. The aim of the study was to determine the relationship between personality traits measured by the revised NEO personality inventory and rsEEG signal complexity in 59 subjects (25 women, mean age: 27 years). The complexity was measured by Multivariate Multiscale Sample Entropy (MMSE), which quantifies changes in information richness of rsEEG in multiple data channels over different timescales. The difference between the right and left frontal areas in the MMSE parameter measuring the complexity over fine timescales (local information processing) was negatively correlated with neuroticism (rho=-0,325, p <; 0,05) and openness for experience (rho=-0,265, p <; 0,05) and positively with conscientiousness (rho=0,271, p <; 0,05). The proposed study might extend the current knowledge of the relationship between personality traits and the features of EEG signal in the spatiotemporal domain. This study was supported by a grant of the National Science Centre, no. 2015/18/E/HS6/00399, and by the National Centre for Research and Development grant no. POIR-01.01.01-00-178/15.

197. Higher scores on owner-rated ADHD questionnaire are associated with poorer sleep efficiency in dogs' sleep EEG

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Behavior disturbances are frequently associated with low sleep quality reflecting a disbalance of certain brain areas in humans with attention-deficit/hyperactivity disorder (ADHD). Recently, dogs have been used in non-invasive cognitive neuroscience due to their trainability without fluid/food restriction and behavior similarities with humans, such as attentional skills and impulsivity assessed by human ADHD questionnaires validated for dogs (d_ADHD). We wanted to know whether dogs' ADHD characteristics would be associated with their electroencephalogram (EEG) parameters during sleep. Thus, we assessed the EEG of 38 family dogs with their owners during a 3-hour long polysomnography and analyzed the association of their brain data and owner-reported d_ADHD data. We found that higher total d_ADHD scores were associated with lower sleep efficiency, longer periods of wakefulness after sleep onset and less sleep cycles. Regarding brain electroactivity, the high ratio of theta/beta bands during sleep was also related to higher total d_ADHD scores, which in humans is a common neural trait in individuals with ADHD. Our results are in line with studies in which the poor quality of sleep in children with ADHD is associated with specific EEG macrostructural and spectrum parameters, validating dogs as models for affective neuroscience studies.

198. Impact of personality traits on the number of cognitive complaints reported in older people

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We define subjective cognitive complaints as a belief in a decline in cognitive condition, compared to an earlier, unobjectionable period. There are reports in the literature on the relationship between the number of reported cognitive complaints and various psychological variables, including specific personality traits. The aim of the study was to test the relationship between the number of cognitive complaints reported by seniors, the objective measure of cognitive functioning and the intensity of individual personality traits. The test procedure involved 54 seniors. Each person completed questionnaires and tests to objectively assess the functioning of the attention, subjective feelings about the cognitive state and establish personality characteristics. The results of the statistical analysis revealed a correlation between the number of reported cognitive complaints and the intensity of all personality dimensions distinguished with the Big Five theory, except for openness to experience. In addition, a relationship was observed between the number of subjective cognitive complaints reported and the level of performance of tasks aimed at evaluating the functioning of the attention of the subjects. In summary, the results confirm that subjective cognitive complaints are related to psychological characteristics, which should be taken into account in the diagnosis of mild cognitive disorders.

199. The pre-supplementary motor area reflects conflict processing irrespectively of reaction times

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The medial frontal cortex has been implicated in monitoring and resolving response conflict by numerous fMRI studies. However, this brain region shows a strong positive correlation to reaction times (RT) variability, what constitutes as a major confound when contrasting brain activity for congruent and incongruent trials, which, by default, differ in RTs. Here, we investigate conflict effect under rigorous control of RTs in both Stroop and Simon tasks in simultaneous EEG-fMRI study with 37 healthy participants. Using group ICA to fMRI data, we separated the independent activity of two adjusted MFC regions, i.e. the anterior cingulate cortex (ACC) and the pre-supplementary motor area (preSMA). The former was functionally connected to the bilateral anterior insula, whereas the latter showed connectivity to bilateral intraparietal sulci and inferior frontal gyri. Activity in both networks showed a significant positive relationship with RTs, yet only the one involving preSMA dissociated between congruent and incongruent trials irrespectively of the time on task effect. These findings indicate that, in contrast to ACC, activity in preSMA reflects pure conflict. Our study highlights the necessity for controlling RT values when comparing any conditions that vary in behavioural markers.

200. How does the second language affect the word retrieval in the native language? An ERP investigation of bilingual speech production mechanisms

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Speaking in the native language (L1) after using the second language (L2) results in a word-retrieval difficulty. This phenomenon, the L2 after-effect, was be observed as a slow-down of naming in L1 or a modulation of ERPs (N300). In this study we explored whether the L2 after-effect affects the retrieval of different classes of words – nouns

and verbs – to the same extent. 29 Polish-English bilinguals completed a blocked Picture Naming task with two blocks (L1–L1) in one session and two blocks (L2–L1) in another session. The second blocks of each session were used to measure the L2 after-effect. Each block contained pictures representing actions and objects. We found that naming pictures in L1 after L2 was slowed-down for both objects and actions, and it was related to enhanced frontal positivity (250-350ms). Naming actions was slower than naming objects and however no significant modulations at the electrophysiological level nor their interaction with the word-class were found. The results suggest that even though nouns and verbs are processed differently, the previous use of L2 results in similar word-retrieval difficulty for all classes of words. While the effect of word-class was salient on both behavioural and electrophysiological level, we failed to identify the ERP component corresponding to the L1 slow-down in consequence of using the L2.

201. Listening in on consciousness. How to assess the level of consciousness with various auditory steady-state responses.

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Every night when we fall into deep sleep we appear to lose ability to consciously detect incoming acoustic stimuli. Auditory steady-state responses (ASSRs) have been proved to be sensitive to fluctuations in the level of arousal, but their relation to levels of consciousness remains unclear. In this study, we explore sensitivity of 6 Hz, 40 Hz and 80 Hz click sounds to changes in arousal during eyes-open (EO), eyes-closed (EC) conditions, and to the loss of consciousness during early deep NREM sleep (N2 and N3 stages) in the group of 25 healthy participants. We found the progressive decrease of 40 Hz ASSR phase locking-index (PLI) estimates from EO to EC, continuing gradually in N2 and N3 stages. The 80 Hz ASSR appeared unaffected by state changes, likely due to contribution of brainstem sources. For 6 Hz ASSRs we detected a decrease in N3 stage in the initial part of the response. State-related differences observed in our study strengthen the notion of gamma range ASSRs as a tool for reliable discrimination between levels of consciousness, suitable for clinical applications and support the role of cortico-thalamic part of the auditory system (dominant 40 Hz sources) in determining these variations.

202. Characterization of motor cortex spiking activity for spiking neural network model validation

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To provide a basis for the validation of balanced spiking neuronal networks and their dynamics, we characterized resting-state (no task) and task-related spiking activity of arm/hand area of macaque (pre-)motor cortex. We recorded spiking activity using a 100-electrode Utah Array (Blackrock Microsystems) during resting-state (REST) and reach-to-grasp (R2G) behavior. In REST, we defined epochs of rest (RS), sleepiness (RSS) and spontaneous movements (M); in R2G: preparatory periods (PP) and task-related movements (TM). Single units were separated into putative excitatory and inhibitory. On the level of single units, we found that ~50% of all units changed their rates significantly with behavioral epochs. Next, we characterized the network activity based on a) the dimensionality which reveals the number of principal components needed to describe the parallel spiking activity, and b) the balance between putative excitatory and inhibitory population firing (absolute difference or

instantaneous correlation). RS & PP show the highest dimensionality and the lowest instantaneous balance. Only R2G epochs show a prevalence of excitation (PP) or inhibition (TM), indicating superiority of REST for the validation of balanced network models. Support: DFG SPP1665 DE2175/2-1 & GR1753/4-2; DFG 368482240/GRK2416; EU Grants 720270 & 785907 (HBP).

203. Dynamical exploration of the repertoire of brain networks at rest is modulated by psilocybin

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Growing evidence from the dynamical analysis of functional neuroimaging data suggests that brain function can be understood as the exploration of a repertoire of metastable connectivity patterns ('functional brain networks'). The present study characterizes how the brain's dynamical exploration of resting-state networks is rapidly modulated by intravenous infusion of psilocybin, a tryptamine psychedelic found in "magic mushrooms". We employed a data-driven approach to characterize recurrent functional connectivity patterns by focusing on the leading eigenvector of BOLD phase coherence at single-TR resolution. Recurrent BOLD phase-locking patterns (PL states) were assessed and statistically compared pre- and post-infusion of psilocybin in terms of their probability of occurrence and transition profiles. Results were validated using a placebo session. Recurrent BOLD PL states revealed high spatial overlap with canonical resting-state networks. Notably, a PL state forming a frontoparietal subsystem was strongly destabilized after psilocybin injection, with a concomitant increase in the probability of occurrence of another PL state characterized by global BOLD phase coherence. These findings provide evidence of network-specific neuromodulation by psilocybin and represent one of the first attempts at bridging molecular pharmacodynamics and whole-brain network dynamics.

204. MVPA decoding of abstract tactile (Braille) numbers in the Intraparietal Sulcus of sighted Braille readers

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The IPS plays a key role in processing numbers. According to the “triple-code theory” (Dehaene, 1992), it contains a modality-independent abstract magnitude code, co-existing with modality-specific symbolic codes (visual Arabic digits, number words…). In an fMRI multi-voxel pattern analysis (MVPA) experiment, sighted Braille readers were presented with blocks of numerosities in tactile abstract (Braille), visual abstract and visual non-abstract formats. Previous studies (e.g. Bulthé et al., 2014) found that abstract visual numbers had low decoding accuracy, interpreted as symbolic numbers being mapped onto a subset of a broader population of IPS neurons tuned for corresponding non-symbolic representations. Non-symbolic numbers were assumed to be easier to decode because of their wider representation. Here, we found that tactile numbers, despite being abstract, were highly decodable in parietal regions. This suggests that low accuracy for visual abstract stimuli is due to their visual nature and/or overtraining, not to their abstract nature itself.

205. Grey matter thickness as predictor of performance enhancement in action video games training. Preliminary report

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Cognitive enhancement using video games (VG) has been in the center of brain researchers' attention for the last twenty years. Besides the significant body of literature, there is still no unanimity on the effectiveness, settings, and benefits such interventions can provide for particular subjects. One of the reasons is a limited number of studies using predictive models which also take into account various moderating and mediating factors (Bisoglio et al., 2014). In my research, I concentrated on investigating if there is a relationship between the GM surface in such ROIs as striatum, thalamic nuclei, hippocampal cortex (HC), dorsolateral prefrontal cortex (DLPFC), cerebellum and VG training scores. According to previous accounts, striatum is a key area for procedural learning which was found to play an important role for early (ventral) and late (dorsal) cognitive skills acquisition (Erickson et al., 2010). In turn, another modulator of training improvement is thalamic nuclei which is crucial for attentional and perspective processing (Momi et al., 2018). Moreover, increased plasticity was found in areas playing an important role in strategic planning, spatial navigation, working memory and motor performance (HC, DLPFC, and cerebellum) in the training group as the effect of skill acquisition (Kühn et al., 2014).

206. Implicit Learning of Hungarian Vowel Harmony

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Can Polish native speakers implicitly learn Hungarian palatal-velar vowel harmony (P-VVH)? Will they learn it better when the vowels in a word are familiar from Polish? P-VVH dictates that the suffix matches its vowel type (front or back) to the vowels in a word. In a self-paced listening task, participants heard 132 Hungarian nouns (twice). In an unexpected test they heard more nouns, and were asked to indicate if they had appeared in the training. All the new ones had a familiar stem, and a suffix that either respected or violated the P-VVH. It was hypothesized that higher erroneous endorsement of new nouns respecting P-VVH (a false memory effect) than nouns violating P-VVH, in combination with reported lack of rule awareness, would be evidence implicit learning. 32 participants took part. No one reported rule awareness. Two-way ANOVA on endorsement rates was performed with grammaticality (well-formed or not) and vowel type (Polish/non-Polish) as within subject factors. It revealed the main effect of vowel type $F(1,31) = 18{,}809$, $p < 0.001$, and an interaction between grammaticality and vowel type: $F(1,31) = 16{,}797$, $p < 0.001$. Polish participants do implicitly learn Hungarian P-VVH but only when vowels are different from their native ones.

207. Provocative advertisements containing religious element enhance brand recall

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One of the ways to attract attention of recipients and enhance effectiveness of advertisement is creation of provocative illustration that consist shocking elements. However, only the provocative aspects may attract visual attention, causing the message of the advertisement concerning a given brand being lost. The main goal of study was answer the questions on which elements of given advertisements were the recipients focusing more their visual attention, and how many information units did they memorize. The experiment used the SMI Experiment Center

program and the eye-tracker (iViewX RED500) to record the eye-movements. 41 participants were divided into two groups. Experimental group was presented with provocative (drastic, religious and erotic) advertisements while the control group was shown modified illustrations without controversial content. The study revealed that the number and mean fixation time on erotic element was significantly higher in provocative advertisements than in their non-provocative equivalents. What is more, mean fixations time on the brand was significantly greater in non-provocative advertisements than in erotic versions of these illustrations. It was found that the brand and the specific elements were better remembered in advertisements containing religious element than in their non-provocative equivalents. In contrast, the brand and the specific elements were less remembered in advertisements that contained drastic elements than in their non-provocative equivalents. This leads to the conclusion that erotic contents in advertisements attract visual attention, distracting attention from the brand. The process of memorizing the brand presented in the advertisement is enhanced by religious elements and weakened by drastic contents.

MEDICAL POSTERS

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208. Case report - sulfonylurea poisoning mimicking vertebrobasilar acute ischemic stroke

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The aim of our study was to describe the case of the man with sulfonylurea induced hypoglycemia manifesting as acute encephalopathy with focal neurological signs misdiagnosed as posterior circulation acute ischemic stroke. A 64-year-old patient treated with glimepiride for type II diabetes mellitus, after radical prostatectomy for prostate cancer, was admitted to Stroke Unit. Patient was unconscious, with upward gaze deviation, four-limb paresis, extensor response to pain, bilateral positive Babinski's sign. Head CT didn't reveal any abnormalities. Low serum glucose level (46 mg/dl) was noted and corrected with intravenous glucose infusion (80 mg/dl). Based on acute onset of focal neurological signs the initial diagnosis of AIS was made. Due to exceeding of treatment window no reperfusion therapy was performed. In further serum glucose measurements hypoglycemia was noted. For the next 72 hours repeated intravenous glucose infusions were needed to maintain it's levels above 70 mg/dl. Magnetic resonance head imaging performed in 3rd and 7th of August not reveal ischemic changes. Hypoglycemic encephalopathy due to glimepiride poisoning was diagnosed. In our case, perioperatively taken sulfonylureas resulted in prolonged hypoglycemia misdiagnosed as AIS. Prolonged insufficient brain nutrition can result in permanent brain damage.

209. Working memory in aphasia: the role of stimulus modality

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Aphasia is defined as an acquired impairment of language functions resulting from a brain lesion in language-dominant hemisphere. Aphasia is usually accompanied by deficits of non-linguistic cognitive functions, e.g., executive functions, working memory or attention which may hinder the language restitution.The aim of the present study was to investigate the efficiency of verbal and spatial working memory (WM) in aphasic subjects in the relation to particular language functions.Subjects were 33 patients aged 27-82 years suffering from post-stroke aphasia. Two tests for assessing verbal and spatial WM were administered: (1) authored receptive verbal test and, (2) the Corsi block-tapping task. Both these tests applied forward (addressing maintenance processes) and backward (addressing manipulation beside maintenance processes) conditions. Particular language functions: phonemic hearing, comprehension of words and sentences, semantic fluency and naming were measured.

For verbal WM test the performance correlated with the efficiency of all measured language functions in two conditions. In contrast, for spatial WM such correlations were significant only for the backward condition. The results indicated that the efficacy of WM in aphasic subjects depends not only on verbal competency but also on more complex processes underlying WM. Supported by National Science Centre, Poland, grant number: 2016/21/B/HS6/03775.

210. Microglial dynamics in traumatic brain injury and its modulation after cytokine/chemokine exposure

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Traumatic Brain Injury (TBI) is a significant cause of death worldwide. A crucial problem in TBI is damage due to neurotoxic behaviour of microglia (brain immune cells), whose inflammatory response has both beneficial and/or detrimental effects on neurons. We explore the basic dynamics of microglial phenotype in human TBI patients using single-cell ex vivo transcriptomics of isolated microglia. The preliminary data showing four different clusters (genotypes) of the microglial population of which we can relate the two phenotypes as, M1 (Neurotoxic) and M2 (Neuroprotective). We further investigated the microglial-cytokines responses in the in vitro system to gain some insight knowledge of the microglial behaviour after TBI. The outcome of our study will relate the cytokines/chemokines milieu after severe TBI with the microglial transcriptomic data.

211. White matter alterations and the negative symptoms in schizophrenia. The diffusion tensor imaging study.

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Schizophrenia can be explained by disconnection hypothesis as a disintegration condition of mental processes and neural circuits in the brain. In addition, MRI studies have shown that abnormal functional connections coexist with subtle changes in the structure of white matter (WM). However, the exact pathology of WM in schizophrenia is still under debate. In this study, Diffusion Tensor Imaging (DTI) was conducted on two groups: schizophrenia outpatients (n=30) and matched healthy controls. Besides between – group comparison of DTI parameters (FA, MD, RD and AD), we investigated associations between WM cytoarchitecture and psychopathology (PANSS, BNSS, MoCA scales) in clinical group. Presented results revealed widespread differences in all diffusion parameters located across the brain in schizophrenia outpatients compared to healthy controls (p<;0.001). The negative correlation was found between lower FA in the right precuneus cortex and the severity of asociality (p<;0.05). Moreover, some trends were visible: 1) association of other structures FA values with the asociality, 2) association of the right precuneus FA with anhedonia and avolition. These results indicate the presence of widespread WM abnormalities in schizophrenia and its association with the severity of the negative symptoms. The study was supported by the National Science Centre, Poland (grant number 2016/23/B/HS6/00286).

212. Is the standard neuropsychological assessment sensitive enough? Clinical examination of cognitive functioning of HIV-infected individuals on HAAR

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HIV-infected individuals on highly active antiretroviral therapy (HAART) often observe decline of the cognitive functioning. However, their cognitive deficits are not always apparent in standard pencil-and-paper neuropsychological tests which are still the most prevalent method of diagnosis in clinical examination. Aiming to find more adequate measures to detect changes in cognitive functioning, in the present study we compared the clinical sensitivity of pencil-and-paper tests and the computerized task. HIV-positive (N = 49) and HIV-negative (N = 47) subjects underwent complex neuropsychological assessment in five cognitive domains and performed computerized The Numerical Stroop Task (NST). The NST is perceived as a good measure of executive functioning.The standard assessment indicated in the HIV positive group a modest cognitive impairment in two out of five domains. It did not, however, show any signs of decline in executive functioning, which were evident in this group in a computerized version of the NST. Thus, The NST turned out to be more sensitive test to the subtle decline in executive functioning, which might underlie impairments in other domains. In conclusion, it seems that computerized versions of standard clinical tests might be more sensitive to subtle cognitive impairments than their pencil-and-paper equivalents.

213. Predicting mortality using spatial characteristics of acute intracerebral hemorrhage

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Intracerebral hemorrhage (ICH) is associated with high in-hospital mortality. The dynamics of brain damage make the development of predictive models difficult. We aimed to identify how ICH location in the brain contributes to predicting mortality during the in-hospital stay.We retrospectively analyzed a continuous sample of anonymized records of ICH patients at the Department of Neurology and Cerebrovascular Disorders for the presence of acute non-contrast head CT and status at the discharge. Brain images were manually segmented using ITK-snap software and registered to standard stereotactic brain atlas using greedy elastic registration software. Binary outcome (Survival/Death) was used as a clinical variable for the GAMMA Bayesian Voxelwise analysis. Post-hoc region of interest analysis was performed using ROCR package. We analyzed eighty-seven patient datasets. The resulting maps revealed that hemorrhagic injury of both thalami was associated with mortality. We confirmed those findings using receiver operator characteristics analysis of the lesion volume fraction in both thalami. The area under the curve was 0.78. Spatial analysis of the hemorrhage location links the thalamic injury with increased mortality. The process can be automated using a combination of existing free software image segmentation and registration methods to provide a better death risk assessment.

214. Vitamin D deficiency poses risk to cognitive health in adults aged 50+

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The prevalence of vitamin D deficiency is alarming in aging population worldwide. Only 15% of older adults reach appropriate levels of vitamin D.It is related to brain and cognitive function, yet, the findings remain inconsistent. This study examined the effects of vitamin D levels on cognitive functions in adults aged 50+. Twenty-eight adults aged 56-86 years completed the following assessments at the Istanbul University Faculty of Medicine, Istanbul, Turkey: Benton Facial Recognition Test; Boston Naming Test; Stroop Test; Verbal Fluency Test;

Clock Drawing Test; Oktem Verbal Memory Processes Test and Digit Span ; Logical Memory; Mental Control Test;Proverbs; Visual Reproduction subtests of Wechsler Memory Scale-Revised. Participants were divided into two groups, i.e., severe deficiency(≤25nmol/L, N=14) vs. insufficiency(>40-67nmol/L, N=14) of vitamin D. Hierarchical multivariate regression assessed the influence of vitamin D level after accounting for the effects of age, sex and education attainment. After correcting for demographic characteristics, adults with vitamin D insufficiency outperformed those with severe deficiency on Mental Control Test. Our data show that working memory and attention are vulnerable to the degree of lacking vitamin D in adults aged 50+.

215. Seeking Answers in Puffs of Smoke: Two Contrasting Cases of Moyamoya Disease in Poland

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Moyamoya disease is a chronic, occlusive cerebrovascular disorder characterized by progressive bilateral stenosis of the intracranial internal carotid arteries and their proximal branches with prominent arterial collateral circulation resembling "puffs of smoke". It is a rare disease and its etiology remains unknown, though higher incidence rates among the Asian population (2.3/100,000 individuals in South Korea, 0.94/100,000 in Japan vs. up to 0.09/100,000 in other regions, including North America and Europe), reported familial occurrence and advances in recent studies strongly suggest a genetic contribution. The rarity of this disorder, as well as age-related, racial and geographic differences in prevalence and presentation have limited research and the development of evidence-based management guidelines, particularly in the European population. We describe two cases in Poland that are representative of the heterogeneity of presentation and indicative of the therapeutic challenges posed by Moyamoya disease. The first patient, a 23-year-old female with no concomitant conditions, presented to our clinic with sudden facial asymmetry and left-sided hemiparesis. Central left-sided facial palsy, left-sided hypoaesthesia and left-sided hemispatial neglect were found upon neurological examination. The second patient, a 41-year-old female was admitted due to recent aggravation of chronic headaches. Neurological examination was unremarkable.

216. Mild depressive episode related changes in frontal-midline theta activity: source localization study

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Previous research suggest that depression is related to altered frontal-midline theta (fm theta) activity, although there is no general consistency on the direction of this effect (positive vs. negative relationship). Several studies (Arns et al., 2015, Jaworska et al., 2012) showed that individuals with depression have higher fm theta power than healthy participants. Some (Bailey et al., 2017, Pizzagalli et al., 2018) report that higher theta power in participants with depression is associated with better treatment response, others suggest that lower theta power is connected with better treatment outcome (Arns et al., 2015, Broadway et al., 2012). In the present study we wanted to test whether participants with mild depressive episode (MDE) have higher or lower fm theta power when compared to healthy group. We use beamforming source localization to estimate brain source of differences in theta power between groups. We found that participants with MDE have higher theta power in frontal midline regions than healthy individuals, however this effect is weak and does not appear in all analyses. Additionally, we found increased theta power in the right parietal region. Based on these results and existing literature we speculate that changes in the fm theta may reflect abnormal emotional regulation.

217. Minimum audible moving distance in mild and moderate sensorineural hearing loss

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Minimum audible movement distance (MAMD) represents measure of the auditory spatial resolution for approaching and receding sound sources localization. This ability is crucial for survival and may be affected by auditory thresholds increase and lack of compressive nonlinearity which are common for sensorineural hearing loss (SNHL). We evaluated MAMD for normally hearing subjects, for patients with mild and moderate SNHL who did not use hearing aids, and also for patients with moderate SNHL who were hearing aids users (N=4). An adaptive psychoacoustic procedure was implemented. Moving sound sources were modeled by linear counter-directional change of sound amplitude on two loudspeakers placed opposite to the subject at different distances. Average MAMD was 14 % of basic distance for normally hearing subjects, and 21 and 26 % for patients with mild and moderate SNHL, correspondingly. MAMD was significantly higher than normal only for moderate SNHL ($p<;0.05$, Mann-Whitney U-test). However, MAMD did not increase significantly for hearing aid users (21 %). Thus, moderate SNHL patients have elevated MAMD, but it can be partially compensated by hearing aids. This study was performed by means of the State assignment (AAAA-A18-118013090245-6) and supported by the Russian Foundation for Basic Research (project 18-015-00296).

218. Actigraphy in assessment of disorders of consciousness

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Diagnosis of patients with disorders of consciousness (DOC) – the clinical entity which encompasses both minimally conscious and unconscious patients – is one of the major challenges of contemporary medicine. These patients are unable to communicate, hence the standard procedure of assessment of their condition is based upon behavioral observation (e.g. Coma Recovery Scale). However, usage of more objective, physiological indices is still being discussed. One of the hallmarks of brain's functions recovery is the occurrence of circadian rhythms. While the gold standard here is polysomnography (PSG), there is a simpler approach based on actigraphy, used also in assessment of sleep disorders. However, the most popular algorithms in this field are calibrated using PSG, which is not possible for DOC patients who do not exhibit classical sleep patterns. We propose calibration-free approaches to assessment of circadian rhythms, based upon cosinor analysis, which relies on fitting sines to the actigraphic data and analysing it's properties such as amplitude or phase shift, as well as dividing signal into days and searching for similarities. We also investigate spectral properties of the signal. We present performance of these measures on example recordings from healthy volunteers and sample recordings from patients in DOC.

219. Transcutaneous Vagus Nerve Stimulation in treatment of disorders of consciousness – longitudinal case study

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Corazzol et al. (2017) reported promising results of vagus nerve stimulation on a patient in a persistent unresponsive wakefulness (vegetative state, VS). We extend this line of research to a similar patient, but utilise a non-invasive stimulator from 'tVNS Technologies©'. If transcutaneous vagus nerve stimulation (tVNS) helps restore consciousness, we hypothesise improvement in behavioural responses on a Coma Recovery Scale – Revised (CRS-R), as well as increased peak oscillations in the theta-alpha range (3-14 Hz) in resting state EEG. tVNS was applied for 4 hours daily, for 6 months. CRS-R was assessed weekly, while EEG bi-monthly. Both of these measures show signs of improvement. CRS-R scores initially ranged from 4-6 and rose to the heights of 12 and 13 in the third and fifth month, fluctuating between 7 and 12 in the final month. Peak oscillations in the theta-alpha range showed a little rise from 6.24 to 6.56 Hz. The most noteworthy finding is the re-emergence of a second, smaller peak in the alpha range in the centro-parietal regions, which was not present in a period preceding the stimulation. The location and the frequency of the second peak may suggest the return of thalamocortical network dynamics characteristic of aware subjects.

220. Facial emotional expression transfer in persons with Alzheimer's Disease

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Typical changes triggered by Alzheimer's disease (AD) are connected with the cognitive functions such as memory, attention and language. They are treated as key features of the neurodegenerative process. The patient's social interactions and its emotional content is still explored. The participants of the study were elderly persons with mild cognitive impairment (N=7), AD (N=9) and healthy elderly persons (N=9). They were shown static emotional facial expressions (POFA and pictures specially prepared by the authors). The sample set of six basic emotions plus neutral expression was introduced to the participants. The main aim of the study was to conduct the assessment of the participants facial expressions mimicking the emotions presented at the stimuli. The participant's facial expressions were recorded with Kinekt Xbox and later the set of 6000 to 74000 pictures per person were compared with the individual representative emotional facial expression. No statistically significant difference was observed in terms of frequency and adequacy of the basic emotions expression. Within AD group the negative correlation (r= -0,81; p<;0,05) between adequacy of the facial expression to positive and negative stimuli was observed. Such effect has not been observed within the rest of the groups.

Workshop: Cortivision

16:40 – 16:55

chaired by: **Dariusz Zapała** (Cortivision, Lublin, Poland)

A portable fNIRS system for measuring hemodynamic response during movement

In our short presentation, we will show how to quickly and easily measure the cerebral cortex's hemodynamic response using the new fNIRS portable system from Cortivision. We will demonstrate how to create an experimental procedure, set up the device, calibrate sensors, and export signals for analysis. We will primarily focus on measuring brain activity in movement conditions and integrating various biological signals via LSL protocol, e.g., for cognitive experiments in a VR environment. We believe that our solution will be interesting for researchers in cognitive neuroscience, movement sciences, neurorehabilitation, ergonomics, and brain-computer interfaces.

Biological Session VII

Neurogenesis

17:00 – 18:30

chaired by: **Joanna Danielewicz** (Achucarro Basque Center for Neuroscience, Leioa, Spain)

Induction of Proinflammatory Neural Reactive Stem Cells by Seizures

Juan Manuel Encinas

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Adult neurogenesis persists in the adult hippocampus of most mammals due to the presence of multipotent neural stem cells (NSCs). Hippocampal neurogenesis is involved in a range of cognitive functions and is tightly regulated by neuronal activity. NSCs respond promptly to physiological and pathological stimuli altering their neurogenic and gliogenic potential. For instance, seizures induce NSCs to convert into reactive NSCs (React-NSCs) which stop producing new neurons and become proinflammatory via interleukin 1b (IL-1b) expression. Further, we have discovered that ATP and EGFR are two signaling pathways involved in the induction of React-NSCs. Our results unveil novel properties of NSCs and provide cues for potential therapeutic strategies against epilepsy focused on preserving neurogenesis.

Time-lapse monitoring of neural changes in hippocampus during in vitro eplileptogenesis

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Several important cognitive functions altered by epilepsy depend on the hippocampus, where new neurons are born throughout life in the subgranular zone of the dentate gyrus (DG). Within the hippocampal circuitry, DG acts as "gatekeeper" of aberrant or excessive input information and filters it out from propagating further along to CA3 and CA1 areas, however DG's function is directly determined by a delicate balance between excitation and inhibition. It has been postulated, that excessive neuronal hyperexcitation, can trigger so called "aberrant neurogenesis", and aggravate the course of epileptogenesis in a spiraling cascade. In order to understand what happens in the neurogenic niche during epileptogenesis we used organotypic hippocampal cultures, which offer a unique optical access to the hippocampal circuitry over days and even weeks. We have successfully combined obtaining organotypic slices with retrospective immunolabelling of NSCs allowing us to observe neurogenesis under pathological conditions.

Coupled experimental and modeling representation of the mechanisms of epileptic discharges in rat brain slices

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Epileptic seizures and interictal discharges (IIDs) are determined by neuronal interactions and ionic dynamics. We have described the mechanisms with double-patch experiments constrained by modeling. Using the rat brain entorhinal cortex slices and applying a high potassium solution with 4-AP, we evaluated AMPA, NMDA, and GABA-A conductances for different types of IIDs, revealing either pure GABAergic or GABA-glutamatergic IIDs caused by impaired chloride gradients and synchronization of interneurons. Each IID terminates due to synaptic depression. Pure glutamatergic IIDs are observed in case of disinhibition. IIDs propagate as spontaneous waves. Ictal discharges (IDs) are clusters of IID-like events, determined by the ionic dynamics. Propagating IIDs and IDs have been reproduced in our detailed model. As a minimal model, we have designed "Epileptor-2" that reproduces IDs and IIDs. IIDs are governed by membrane depolarization and synaptic resource, whereas IDs represent bursts of bursts. Important is the role of the Na/K-. Potassium accumulation governs the onset of each ID. The sodium accumulates during ID and activates the Na/K-ATPase which terminates ID by restoring the potassium gradient and thus repolarizing the neurons. The revealed factors are to be potential targets for antiepileptic treatment. This work was supported by the Russian Science Foundation (project 16-15-10201). "Epileptor-2" model is available at https://senselab.med.yale.edu/modeldb/ShowModel?model=263074#tabs-1

Evaluation of the effects of the proneurogenic microneurotrophin BNN-20 on a Parkinsonian patient-derived cellular model and on the success rate of adult NSC transplantations in the Substantia Nigra of a preclinical mouse model of Parkinson's Disease

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Neurogenesis in the postnatal Substantia Nigra (SNpc) is poorly investigated. However, we have previously shown the existence of adult dopaminergic neurogenesis in both the wild-type and degenerated SNpc of the "weaver" mouse model of Parkinson's disease (PD) that is significantly enhanced by the pleiotropic microneurotrophin BNN-20, which partially rescues "weaver" nigrostriatal degeneration. The effects of BNN-20 have been attributed to its anti-apoptotic, anti-inflammatory and anti-oxidant properties as well as to the specific enhancement of neuronal differentiation in vivo. Moving towards a pre-clinical stage of investigation, here we report two lines of experiments: A) the investigation of the effects of BNN-20 on an induced pluripotent stem cell (iPSC)-based model derived from patients with familial PD, focusing on neuronal differentiation, but also on disease-associated phenotypes that have been described previously[1]. B) the evaluation of BNN-20's potential beneficial effect on the success rate of NSC transplantations in the "weaver" SNpc, by administering BNN-20 in recipient mice before and after grafting. The aforementioned expand our previous knowledge on BNN-20's neurogenic activity, from the preclinical "weaver" mouse model to patient-specific iPSC-based model, and are expected to provide valuable information for a potential, BNN-20-based, future cell replacement therapeutic strategy against PD. "This research is co-financed by Greece and the European Union (European Social Fund- ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning 2014-2020» in the context of the project "NeuroProPar" (MIS 5047138)."

Cognitive Session VII

Visual Perception

17:00 – 18:30

chaired by: **Łukasz Okruszek** (Institute of Psychology PAS, Warsaw, Poland)

Processing of the complex social displays in the posterior superior temporal sulcus subregions

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The posterior superior temporal sulcus (pSTS) region was shown to be implicated in a wide range of social cognitive processes, ranging from basic social perception (e.g. biological motion detiection) to complex social interactions processing. The aim of the current neuroimaging study was to examine the sensitivity of the pSTS subregions to social displays of various comlpexity. Regions-of-interest (ROI) within the pSTS were defined by using localizers presenting either biological motion (bm-pSTS), dynamic faces (f-pSTS), moving shapes (anim-pSTS) or intention attribution task (int-pSTS). Signal changes in response to dyadic point-light displays (PLDs) presenting either neutral communicative interactions (COM); emotional exchanges (EMO) and independent actions (IND), and to scrambled motion vignettes (SCR) were examined in each ROI in fifty healthy individuals (30M; 33+/-8 yrs). A similar pattern of activity, with increased response to social interactions (either neutral or emotional) compared to IND, and to PLDs compared to SCR was observed in each ROI. Furthermore, increased activity to EMO compared to COM was found in the right bm-pSTS and the right f-pSTS. These results suggest that the pSTS subregions may be activated in the linear fashion depending of the complexity of the observed social signals.

Developing a Dynamic Causal Modeling of the network governing dynamic emotional expressions

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We used Dynamic Causal Modeling (DCM) to define the functional organization of the human face perception network during the processing of dynamic emotional expressions. A novel temporal face composite paradigm was given to 24 participants undergoing fMRI while they rated the intensity of four (Anger, Happiness, Sadness, and Joyfulness) emotional facial expressions, in which the motion of internal features unfolded either globally (synchronously) and locally (asynchronously). Our DCM results suggested a direct reciprocal interaction between Inferior Occipital Gyrus (IOG) and Fusiform Gyrus (FG) across both global and local motion conditions, but the preferential engagement of the IOG and the posterior Superior Temporal Sulcus (pSTS) pathway with asynchronous expressions. DCM analysis further showed that asynchronous expression features engaged a differential information flow, centered on pSTS, which received direct input from IOG and projected to the amygdala. Moreover, pSTS and the amygdala displayed selective interactions with the ventral and dorsal Anterior Cingulate Cortex where the integration of both local and global motion cues (present in synchronous expressions) could take place. These results provide new evidence for a role of both local and global temporal dynamics in emotional expressions, extracted in partly separate brain pathways.

Recurrent processing in the visual cortex underlies (un)crowding

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In visual crowding, the presence of neighboring elements impedes the perception of a target. Increasing the number of neighboring elements can decrease crowding (uncrowding). We used a tilt discrimination task and fMRI to study the effects of (un)crowding on the BOLD response and effective connectivity in V1-V4, LOC. We used a drift-diffusion model to estimate participants' drift-rates (stimulus difficulty) in three experimental conditions: crowding, uncrowding, and no crowding. We extracted the percent BOLD signal change (PSC) for each condition in each ROI and compared models linking PSC in each of the ROIs separately with drift-rate in each condition to a null model that did not contain PSC. We found evidence for the following models: crowding – strong evidence for V2-V4 and LOC, substantial evidence for V2, V3 and LOC w.r.t. V1; uncrowding – strong evidence for all ROIs; no crowding – substantial evidence for V1-V4. We then used DCM and Bayesian model comparison to investigate whether (un)crowding modulates top-down, bottom-up, or recurrent processing. The latter model fit the data best in all three conditions. Our results suggest that crowding occurs beyond V1 while the effects of uncrowding are present throughout the visual hierarchy. Moreover, (un)crowding is mediated by recurrent processing.

ERP correlates of consciousness and attention during perception of self-related stimuli

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The P3b event-related potential (ERP) — a late brain response observed over parietal electrodes — is hipothesized to constitute a neuronal correlate of consciousness (NCC). However, recent studies show that it might be more closely related to salience and relevance of a stimulus. Considering that stimuli related to "self" capture attention and are processed preferentially we tested whether unconscious processing of such stimuli will generate the P3b component. In the conducted experiment 3 types of stimuli were presented: subject's own name, other name, or a blank (empty screen). Stimuli were displayed for 33 ms nad followed either by a blank screen (supraliminal condition) or a backward mask (subliminal condition). In separate blocks participants (N=30) were asked either to rate subjective visibility of a word, or to identify a presented name. In conscious condition robust self-preference effect - defined as greater P3b response to self- than other-name - was observed in both tasks. In the unconscious condition self-name also evoked greater P3b amplitude, but only in the identification task in which the identity of a name was task-relevant. Therefore, by demonstrating that unconscious stimuli can cause spatially widespread and temporally delayed brain activations our finding falsify P3b component as NCC.

Cognitive Session VIII

Motor Control

17:00 – 18:30

chaired by: **Rob H.J. Van der Lubbe** (University of Twente, the Netherlands; Adam Mickiewicz University, Poznan, Poland)

No support for the functional equivalence hypothesis: frontal areas are more involved during motor imagery than during motor execution/ preparation of a response sequence

Rob H.J. Van der Lubbe[1,2], Jagna Sobierajewicz, Marijtje L.A. Jongsma, Willem B. Verwey, Anna Przekoracka-Krawczyk

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Results of several neuroimaging studies support the functional equivalence hypothesis, which states that motor imagery and motor execution involve the same processes, except for the final execution component. Recently, it has been suggested that motor imagery implies the extra involvement of frontal executive processes, and/or inhibitory control. In the current study, we used a Go/NoGo version of the discrete sequence production paradigm, in which a sequence of five finger movements had to be executed, imagined, or prepared. We compared motor imagery, motor execution, and motor preparation by computing event-related (de)-synchronization in the theta, alpha, and beta bands. Results showed a major increase in frontal theta power in the case of motor imagery. At the end of the examined interval, a posterior reduction in alpha power was present during motor execution and motor preparation, but not during motor imagery. Finally, above somatosensory- and motor areas a decrease in beta power was observed that was largest in the case of motor execution. Thus, during motor imagery, there was more frontal theta activity, which may reflect increased inhibition, while the absence of reduction in posterior alpha power suggests no major involvement of visual attention. These findings do not support the functional equivalence hypothesis.

Cortical activity related to muscle relaxation of the dominant and non-dominant hand

Magdalena Siemiatycka, Joanna Mencel, Anna Jaskólska, Łukasz Kamiński, Jarosław Marusiak, Artur Jaskólski, Katarzyna Kisiel-Sajewicz

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Similar to muscle contraction, the relaxation is important for the motor control of the fine motor skills and its mechanisms are still unclear. The aim of the study was to assess the differences in cortical activity of ipsi- and contralateral hemispheres between dominant and non-dominant hand during muscle relaxation. Seventeen healthy right-handed subjects (mean age 27 ± 4) voluntarily participated in the study. They performed 40 submaximal, isometric hand-grip contractions using dominant and non-dominant hand. In each trial, subjects held the force at the target level (20% maximal voluntary contraction) for 10 s after reaching it and then relaxed the force to the baseline. EEG data was recorded using 128-channel system. Cortical signals related to relaxation were quantified by estimating amplitude of the motor related cortical potentials (MRCPs) at the time right before the muscle relaxation for electrodes located above regions related to motor control. Analysis of the MRCPs amplitudes showed significant higher ($p \leq 0.05$) cortical activity of the prefrontal, premotor and primary motor cortex of the ipsilateral

hemisphere for dominant hand and the contralateral for non-dominant hand during muscle relaxation. This work was supported by grant National Science Centre, Republic of Poland DEC-2011/03/B/NZ7/00588.

Mental replay of self-associated body movements involves activity in mirror neurons network

Mateusz Wozniak[1,2], Timo Schmidt[3], Yuan-hao Wu[3], Felix Blankenburg[3], Jakob Hohwy[2]

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Establishing arbitrary associations between the conceptual self and a diverse range of stimuli leads to facilitated perceptual processing of these stimuli. However, little is known about how creating such abstract self-associations influences various aspects of the bodily self. In order to test this issue we conducted an fMRI study in which participants were told to hold in their working memory patterns of goal-directed biological motion (displayed by point-light walkers) arbitrarily labelled as either one's own movement, or as movement performed by someone else (one of two stranger-identities). After conducting a multivariate pattern analysis we were able to decode whether a memorized movement was associated with the self or stranger from the left inferior frontal gyrus (pars opercularis), and the left middle frontal gyrus, two areas which are believed to constitute parts of the mirror neurons system. At the same time, activity in these two areas did not differentiate between two stranger-identities. Our results suggest that arbitrary association of a random movement with the self (as opposed to some other identity) leads to differential activity in the mirror neurons network.

PLENARY LECTURE

19:00 – 20:00

chaired by: **Gilles van Luijtelaar** (Donders Centre for Cognition, Radboud University Nijmegen, the Netherlands)

Remodeling of hippocampal circuits by experience and neurogenesis

Alejandro Schinder

Leloir Institute, Buenos Aires, Argentina

Brain function relies on a delicate balance between maintaining stable networks to store information bits in a long-lasting manner, and allowing plasticity of circuits that rewire to adapt to environmental changes or to improve or learn new behavioral tasks. Such plasticity allows specific brain regions to be modified in an activity-dependent manner and transform their input-output equation. The hippocampus is one of those regions undergoing intensive synaptic remodeling and, in addition, it bears the capacity to generate new neurons that build entirely new circuits that intermingle within the preexisting structures. This level of plasticity is subject to checkpoints that control generation, development, integration, and survival of new neurons. My lab investigates how integration of new neurons is regulated under different behavioral and physiological conditions in the hippocampus of adult mice, and how neurogenesis influences hippocampal processing. In my talk, I will discuss the role of parvalbumin-expressing GABAergic interneurons in controlling integration and function of adult-born neurons.

DECEMBER 11, 2020 (Friday)

PLENARY LECTURE

11:00 – 12:00

chaired by: **Aleksandra Gruszka-Gosiewska** (Jagiellonian University, Kraków, Poland)

Cognitive and mental health impact of COVID-19, insights from the Great British Intelligence Test

Adam Hampshire

Imperial College London, UK

During 2020 we have collected cognitive and mental health data from ~390,000 members of the UK public as part of a collaboration with BBC Horizon called the Great British Intelligence Test. This data spans from January, prior to the COVID-19 pandemic hitting the UK. It provides a unique set of insights into the idiosyncratic ways that people have been affected both indirectly by the pandemic and directly by illness. I will present results from this study, where multivariate and machine learning analyses are applied to determine who has been most affected, how, what can help, and whether there are unexpected benefits that we can learn from in order to improve mental health through and beyond the recovery phase.

Biological Session VIII

Neuron-Microglia Interactions In Health And Disease

12:30 – 14:30

chaired by: **Urte Neniskyte** (Vilnius University, Lithuania)

Synaptic consequences of selective microglial TDP-43 depletion

Rosa Paolicelli

University of Lausanne, Switzerland

Microglia are implicated in a variety of functions in the central nervous system, ranging from shaping neural circuits during early brain development, to surveying the brain parenchyma, and providing trophic support to neurons across the entire lifespan. Microglial phagocytic activity is important for mediating synapse elimination, clearing invading pathogens and removing protein aggregates like amyloid deposits. TDP-43, a DNA-RNA binding protein encoded by the Tardbp gene, is a critical regulator of microglial phagocytosis. Mice lacking TDP-43 selectively in microglia (cKO) exhibit drastic synapse loss and enhanced amyloid clearance in a model of Alzheimer's disease (AD). Loss of synapses in Tardbp cKO mice, however, is independent of amyloid deposition. Selective loss of TDP-43 in microglia promotes microglial engulfment of synaptic material, and is associated with decreased spine density in the motor/ somatosensory cortex. Here we show that mice lacking TDP-43 in microglia exhibit motor deficit and clasping behavior, and display altered levels of cytokines expression in the cortex and in the spinal cord. Furthermore, aberrant phagocytic microglia induced by TDP-43 depletion during early brain development leads to selective structural defects in the motor cortex, as revealed by MRI analyses. Overall, our data indicate that dysfunctional microglia significantly affect synapses, thus playing an important role in the pathogenesis of neurodegeneration.

Phosphatidylserine scrambling is required for developmental axon pruning

Urte Neniskyte[1,2], Auguste Vadisiute[1,2,3], Kristina Jevdokimenko[1], Ludovico Coletta[1], Daiva Dabkeviciene[1], Emerald Perlas[2], Ugne Kuliesiute[1], Bernadette Basilico[3], Alessandro Gozzi[4], Davide Ragozzino[3], Cornelius T. Gross[2]

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The mature brain connectome emerges through synaptic pruning of superfluous connections in developing brain. The signal that labels synapses for elimination has not yet been identified. Here we investigated the role of phosphatidylserine scrambling in synaptic pruning. We found that phosphatidylserine was preferentially exposed on synaptic structures and promoted microglia-synapse interaction. Phosphatidylserine exposure was developmentally upregulated and required the activity of Xkr8 – a major phospholipid scramblase, which was expressed throughout the brain and was developmentally upregulated after birth. Conditional Xkr8 knock-out in excitatory neurons diminished axonal bouton trogocytosis and caused insufficient elimination of excitatory synapses. Furthermore, Xkr8 cKO brains had significantly higher axonal density in corticospinal tracts of pyramidal neurons, indicating reduced elimination of the whole axons. These morphological aberrations were followed by abnormal electrophysiological profiles of Xkr8-deficient neurons that exhibited increased spontaneous activity and the failure of functional synaptic maturation. Finally, Xkr8 deficiency led to increased global connectivity of the brain that was maintained into adulthood, as measured by functional MRI. This is the first evidence that mammalian synaptic pruning requires developmental phosphatidylserine exposure via scramblase activity, identifying the first „eat-me" signal that is exposed on unnecessary synapses for their developmental removal.

Phagocytic microglia actively regulates adult hippocampal neurogenesis

Jorge Valero[1,2,3], Irune Díaz-Aparicio[1,2], Iñaki Paris[1,2], Virgina Sierra-Torre[1,2], Ainhoa Plaza-Zabala[1], Noelia Rodríguez-Iglesias[1,2], Mar Márquez-Ropero[1,2], Sol Beccari[1,2], Paloma Huguet[1,2], Ohiane Abiega[1,2], Elena Alberdi[1,2], Carlos Matute[1,2], Irantzu Bernales[2], Angela Schulz[4], Lilla Otrokoscsi[5], Beata Sperlagh[5], Kaisa E. Happonen[6], Greg Lemke[6], Mirjana Maletic-Savatic[7,8], Amanda Sierra[1,2,3]

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During adult hippocampal neurogenesis, the majority of newborn cells die by apoptosis and are rapidly phagocytosed by resident microglia to avoid disturbing the surrounding neurons. Here, we propose that phagocytic microglia is not merely removing corpses but have an active role in regulating adult hippocampal neurogenesis. First, we found that neurogenesis was disrupted in mice chronically deficient for two microglial phagocytosis pathways (P2Y12, MerTK/Axl), but was transiently increased in mice in which MerTK expression was conditionally downregulated. We then followed an in vitro approach to perform a transcriptomic analysis of microglial phagocytosis and identified genes involved in metabolism, chromatin remodeling, and neurogenesis-related functions. Finally, we determined that the phagocytic microglia secretome limits the production of new neurons both in vivo and in vitro. Our data suggest that reprogrammed phagocytic microglia acts as a sensor of local cell death, modulating the balance between cell proliferation and cell survival in the neurogenic niche, supporting the long-term maintenance of adult hippocampal neurogenesis. This work was supported by the Spanish Ministry of Economy and Competitiveness with FEDER funds to AS (BFU2012-32089 and RYC-2013-12817), to AS and JV (BFU2015-66689); a Leonardo Award from the BBVA Foundation to AS; a Basque Government project (PI_2016_1_0011).

The microglial P2Y6 receptor mediates microglial phagocytosis of neurons in multiple models of neurodegeneration

Mar Puigdellivol[1], Stefan Milde[1], Anna Vilalta[1], David H. Allendorf[1], Francesca W. van Tartwijk[1], Jeff Lee[1], Miguel A. Burguillos[1], Jacob M. Dundee[1], Katryna Pampuščenko[2], Vilmante Borutaite[2], Hugh N. Nuthall[3], Jack H. Brelstaff[4], Maria Grazia Spillantini[4], Guy C. Brown[1]

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The mechanisms of neuronal death during neurodegeneration are unclear, but one potential mechanism is microglial phagocytosis of stressed-but-viable neurons and synapses. We show here that the microglial P2Y6 receptor is required for microglial engulfment of live neurons and synapses (neurophagy), but not dead neurons and debris. Injection of Aβ into brain induced uptake of neuronal cell bodies into microglia, prevented by P2Y6 receptor knockout. P2Y6 receptor knockout also prevented neuronal loss in: i) inflamed glial-neuronal cultures, ii) an inflammatory model of Parkinson's disease, iii) an amyloid model of Alzheimer's disease, and iv) a tau model of Alzheimer's disease and frontotemporal dementia. Furthermore, memory deficits were prevented by P2Y6 receptor knockout in the amyloid and tau models. These findings indicate that excessive microglial phagocytosis causes neuronal loss during neurodegeneration, and that blocking the P2Y6 receptor may prevent neuronal and memory loss in such brain pathologies.

Cognitive Session IX

Crossmodal Brain Plasticity In Humans

12:30 – 14:30

chaired by: **Katarzyna Cieśla** (The Baruch Ivcher Brain, Cognition and Technology institute, Interdisciplinary Center Herzliya - IDC, Israel; World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw, Poland).

Improvement of speech-in-noise perception by audio to tactile sensory substitution

Katarzyna Cieśla[1,2], Tomasz Wolak[2], Artur Lorens[2], Benedetta Heimler[1], Henryk Skarżyński[2], Amir Amedi[2]
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The number of patients with hearing loss is growing. Many of them, including users of hearing aids/cochlear implants, struggle with understanding speech in presence of competing speakers. We developed an audio-to-tactile sensory substitution device (SSD) and a supporting set-up to present auditory sentences with accompanying low-frequency speech-extracted signals as tactile vibrations on two fingertips. Twelve and 20 non-native English speakers participated in two preliminary studies, respectively. They were asked to repeat sentences in background noise that were earlier vocoded to resemble stimulation delivered via a cochlear implant system. In our first behavioral study we found an immediate improvement of 6 dB (mean,group) for the audio-tactile vs audio only condition, without any prior training. In the second study we applied a ~45 min training of understanding speech in noise with congruent tactile vibration and found that performanceimproved even further. The results of the study support the inverse effectiveness law saying that multisensory enhancement is largest when the SNR between senses in lowest. The findings are relevant for development of SSDs and rehabilitation programs for the hearing impaired. The developed audio-to-tactile SSD is 3T MR compatible.

Functional selectivity to facial expression sounds in the fusiform gyrus of congenitally blind individuals

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The human ventral occipitotemporal cortex (VOTC) contains areas responding preferentially to stimuli from either the animate or the inanimate domain. Recent studies have revealed a domain by sensory modality interaction in this region – preference for inanimate objects is observed independently of stimulation modality (visual/auditory/tactile) and subjects' visual experience (sighted/blind individuals), whereas preference for animate

entities is robust only in the visual modality, in sighted subjects. This observation has prompted a conjecture that non-visual information activates the VOTC representation of stimulus shape only when it systematically maps onto action system computations (as in the inanimate objects' case). To test this conjecture, we studied fMRI activation in 20 blind and 22 sighted subjects while they listened to animal, object and human sounds. Critically, the human sound category included facial expression sounds, for which the face-shape-to-action mapping is systematic and stable. We found functional selectivity to the facial expression sounds in the fusiform face area (FFA) in the blind group. Furthermore, based on FFA activation, we were able to distinguish facial expression sounds from other sounds in both groups. We conclude that auditory stimulation activates VOTC representations of either animate or inanimate objects if their shape systematically maps onto the action system.

Letter and speech sound association in early blind children and adults

Joanna Plewko[1], Gabriela Dzięgiel-Fivet[1], Marcin Szczerbiński[2], Artur Marchewka,[3] Marcin Szwed[4], Katarzyna Jednoróg[1]

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The first and critical step for reading development is learning letter-speech sound (LS) association. In sighted adults and children LS integration is related to left superior temporal cortex activity (e.g. Blau et. al. 2009). Where the LS integration takes place in the blind and how similar this process is to the sighted population is unknown. Pishnamazi et. al. (2016) suggested that blind adults do not integrate audio-tactile syllables due to mal-development of multisensory mechanisms, but small sample and lack of sighted controls greatly limits these findings. To better understand LS integration we tested 40 early blind children and adults and compared their brain activity for letters, speech sounds, and congruent and incongruent LS pairs to a matched population of sighted controls. Behaviorally, the blind showed enhanced verbal abilities compared to the sighted and similarly accurate but slower reading. No differences between the groups were found in accuracy or reaction times for bimodal LS stimuli. We will present both within group comparisons between congruent and incongruent LS pairs as well as argue that audio-tactile LS integration takes place in blind subjects' brain, though not exactly in the same areas as in the sighted.

Neural network for tactile reading – similarities and differences to print reading

Gabriela Dzięgiel-Fivet[1], Joanna Plewko[1], Marcin Szczerbiński[2], Karolina Domańska[3], Artur Marchewka[4], Marcin Szwed[5], Katarzyna Jednoróg[1]

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Neural networks for print reading are generally script invariant and show convergence with the speech processing network in the perisylvian areas. Polish blind readers use the Braille system essentially identical, in terms of grapheme-phoneme correspondences to Polish orthography, but in the tactile modality. Here we examine the alterations in the neural reading network due to visual deprivation and changed modality used for reading. A group of early blind and sighted adults (n=25 per group) were presented with words, pseudowords and non-linguistic control stimuli in two modalities: tactile (blind) or visual (sighted) and auditory during an fMRI session. During reading, word-specific (real words vs control stimuli) activations in the blind group were very similar to activity during pseudoword reading in the sighted. Regions where speech processing and reading-related activations overlapped were different between the two groups. In the blind subjects, the main site of the reading-speech processing convergence was bilateral ventral occipitotemporal cortex, whereas in the sighted the convergence appeared in the left middle and superior temporal gyri. Our results indicate that despite some astonishing similarities between tactile and visual reading networks, sensory experience influences the functional organization of the language network in a significant way.

Medical Session I

Psychiatry and Alzheimer's Disease

12:30 – 14:30

chaired by: **Witold Libionka** (WSS Gdańsk, Poland)

Using noninvasive neurostimulation to target frontostriatal brain circuits: Implications for treatment of negative symptoms in schizophrenia

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Noninvasive brain stimulation (NIBS) using electromagnetic fields is increasingly used to treat depression, but is also tested experimentally for schizophrenia. Negative symptoms refer to a reduction in goal-directed behavior and are the most disabling aspect of schizophrenia pathology. Here we report neural effects of such rTMS and the results of a clinical trial of theta-burst repetitive transcranial magnetic stimulation (rTMS) targeting the dorsolateral prefrontal cortex (dLPFC) to reduce negative symptoms in patients with schizophrenia. The location of stimulation was based on theoretical models of the functional neuroanatomy of goal-directed behavior. We tested iTBS (intermittent theta-burst TMS) over the right DLPC for improving negative symptoms (especially apathy) in patients with schizophrenia. In addition, we investigated the neural effects of a single bout of this brain stimulation in healthy participants by measuring fMRI before and after stimulation. The randomized clinical trial using iTBS (as yet unpublished), did not reveal any significant improvement after real versus sham treatment (both groups improved somewhat). Notwithstanding, we did observe effects on brain activation as measured with fMRI in healthy subjects, in frontostriatal circuits and areas associated with the default-mode network. Methodological aspects of NIBS will be discussued, that may need adaptation to maximize effects. Results of optimized parameters may not only have clinical implications but will also inform neuroanatomical hypotheses. Quantification of neural effects is important to further aid the development of novel treatment strategies.

Time-frequency dynamics of resting state in euthymic bipolar disorder patients

Anna Maria Sobczak[1], Adrian Andrzej Chrobak[2], Bartosz Bohaterewicz[1], Anna Tereszko[3], Anna Krupa[4], Anna Ewa Ceglarek[1], Magdalena Fafrowicz[1], Amira Bryll[5], Tadeusz Marek[1], Marcin Siwek[6], Dominika Dudek[2]

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The goal of the study was to investigate the baseline brain activity in euthymic bipolar disorder (BD) patients by comparing it to healthy controls (HC) with the use of temporal dynamics resting state fMRI analyses such as Amplitude of Low Frequency Fluctuations (ALFF) and fractional ALFF (f/ALFF). We hypothesize that temporal dynamics techniques will differentiate BD from HC indicating on dissimilarities within different brain structures. Total of 37 participants divided into two groups of euthymic BD patients (n=19) and HC (n=18) underwent rs-fMRI evaluation. Typical band ALFF, as well as subdivided frequency bands: slow-4, slow-5, f/ALFF was calculated based on 390 data time-points. As opposed to HC, BD patients revealed increased ALFF in left insula; increased slow-5 in left middle temporal pole; increased f/ALFF in left superior frontal gyrus, left superior temporal gyrus, left middle occipital gyrus, right putamen and bilateral thalamus. There were no significant differences between BD and HC groups in slow-4 band. To our best knowledge this is the first rs-fMRI study combining ALFF, f/ALFF and subdivided frequency bands in euthymic BD patients. The results obtained with above methods enable to identify group-specific brain structures; no overlap between the brain regions was detected.

Blood plasma lipid alterations in psychiatric disorders

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Blood plasma lipidomics is an emerging field providing opportunities for the discovery of novel blood-based markers of psychiatric disorders. For this study, we quantified lipid abundances in the blood plasma of 476 schizophrenia patients, 333 bipolar disorder patients, 256 major depressive disorder patients, and 529 control individuals representing three independent cohorts collected in Germany, China and Russia. Analysis of 1361 lipid features revealed significant differences in lipid abundances between schizophrenia patients and control individuals that were reproducible across all three sample cohorts. Among these differences, the abundance levels of phospholipid plasmalogens and acylcarnitines were reduced in schizophrenia patients, while ceramides were consistently increased. Moreover, logistic regression classifier demonstrated that schizophrenia patients could be distinguished from control individuals with good accuracy based on blood lipid abundances. Comparison of lipid alterations observed in schizophrenia patients with the differences found in bipolar and major depression disorders further revealed extensive similarity of disease-related lipidome alterations among three disorders. This work is supported by the Russian Science Foundation under grant 19-74-00151.

The cerebrospinal fluid postsynaptic protein concentration in Alzheimer's Disease

Maciej Dulewicz, Agnieszka Kulczyńska-Przybik, Aleksandra Klimkowicz-Mrowiec, Joanna Pera, Agnieszka Słowik, Barbara Mroczko

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Recent studies have shown that synaptic proteins are involved in neurodegenerative diseases, such as AD. Early deficits of memory and other cognitive signs have neural and molecular background closely related to synaptic plasticity and their dysfunctions. Neurogranin (Ng), is a type of postsynaptic substrate for protein kinase C, mainly located in dendrites and spines in brain structures like the hippocampus. Ng plays an essential role in synaptic transmission and modulation of memory processes, and it seems that it can be a novel biomarker of synaptic injury. Considering the above facts, the purposes of our investigation were the quantitive assessment of Ng levels in the CSF and evaluation of the potential usefulness of this protein in the diagnosis of AD patients. The study included 15 patients with AD and 15 non-demented controls. The CSF levels of neurogranin and classical AD biomarkers, such as Aβ-42, Aβ-42/Aβ-40, hTau and pTau181 were assessed by immunoenzyme assays. We showed that the concentration of Ng was significantly higher in the CSF of AD patients compared to non-demented controls and positively correlated with pTau181 and hTau. Our results suggest that Ng is a promising biomarker for AD.

Circulating miRNA biomarkers for Alzheimer's disease (AD) diagnostics

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Alzheimer's disease (AD) is the most common cause of age-related dementia and number of people suffering from this neurodegenerative disorder is increasing. Clinical diagnosis of AD is based on neuropsychological tests and can be supported by biomarkers in brain imaging and in cerebrospinal fluid. However, these methods require expensive equipment or are invasive and not adjusted for screening of many patients. For these reasons diagnostic biomarkers in blood are urgently needed. One of promising approaches is profiling of blood microRNA (miRNA), a group of non-coding, short RNA molecules involved in regulation of translation. Our research aims at development of a new diagnostic method based on dysregulated miRNAs in human plasma. Previously we identified 6 miRNAs as the best potential biomarkers. Here we applied RT-qPCR for verification of these miRNA in plasma from new groups of subjects: 40 AD patients and 20 healthy individuals. The obtained data showed significant differences for all investigated miRNAs in AD patients versus control subjects confirming chosen miRNAs as non-invasive diagnostic biomarkers for AD. Research supported by the European Union's H2020 FETOPEN grant no 737390 (ArrestAD) and NCN grant OPUS 2018/29/B/NZ7/02757.

POSTER SESSION II

PLENARY LECTURE: FUTURE OF NEUROSCIENCE

17:00 – 19:00

chaired by: **Michał Ślęzak** (Łukasiewicz Research Network, PORT Polish Center for Technology Development, Wrocław, Poland)

Translational neuroscience: from network theory to personalized medicine

Viktor Jirsa

Aix-Marseille University, France

Over the past decade we have demonstrated that the fusion of subject-specific structural information of the human brain with mathematical dynamic models allows building biologically realistic brain network models, which have a predictive value, beyond the explanatory power of each approach independently. The network nodes hold neural population models, which are derived using mean field techniques from statistical physics expressing ensemble activity via collective variables. Our hybrid approach fuses data-driven with forward-modeling-based techniques and has been successfully applied to explain healthy brain function and clinical translation including stroke and epilepsy. Here we illustrate the workflow along the example of epilepsy: we reconstruct personalized connectivity matrices of human epileptic patients using Diffusion Tensor weighted Imaging (DTI). Subsets of brain regions generating seizures in patients with refractory partial epilepsy are referred to as the epileptogenic zone (EZ). During a seizure, paroxysmal activity is not restricted to the EZ, but may recruit other healthy brain regions and propagate activity through large brain networks. The identification of the EZ is crucial for the success of neurosurgery and presents one of the historically difficult questions in clinical neuroscience. The application of latest techniques in Bayesian inference and model inversion, in particular Hamiltonian Monte Carlo, allows the estimation of the EZ, including estimates of confidence and diagnostics of performance of the inference. The example of epilepsy nicely underwrites the predictive value of personalized large-scale brain network models. The workflow of end-to-end modeling is an integral part of the European neuroinformatics platform EBRAINS and enables neuroscientists worldwide to build and estimate personalized virtual brains.

Active dendrites and their role in neuronal and circuit computations

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The goal of this presentation is to provide a set of predictions generated by biophysical and/or abstract mathematical models regarding the role of dendrites in information processing, learning and memory across different brain regions. I will present modelling studies from our lab –along with supporting experimental evidence- that investigate how dendrites may be used to facilitate the learning and coding of both spatial and temporal information at the single cell, the microcircuit and the neuronal network level. I will present the main findings of a number of projects in lab dealing with dendritic nonlinearities in PV interneurons and their consequences on memory encoding, the role of dendrites in solving nonlinear problems in human neurons and microcircuit contributions to place cell dynamics in the CA1.

Developing a new generation of human brain disease models using CRISPR editing and iPS cells

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Molecular human brain research heavily depends on model systems recapitulating key aspects of brain physiology and disease pathology. Most current knowledge about mechanisms organising brain function and dysfunction comes from primary or immortalized cell cultures, as well as rodent models, especially mice. However, these models have drawbacks, including species differences and incomplete phenotypes, impeding research on impactful neurodegenerative and neurovascular disorders. Furthermore, it is also conceivable that shortcomings of current models contribute to failures of model-tested drugs in clinical trials. Human models derived from induced pluripotent stem cells (iPSCs) have great potential to complement existing disease models, as they allow directly studying affected human cell types, have the genetic configuration of patients and display crucial cell biological features also found in human brain. In addition, recent development in genome editing using the CRISPR/Cas system have revolutionized the way we can study our genome and reveal the impact of genetic alterations on disease formation. In principle, the combination of genome editing with iPSC technology allows studying most genetic alterations in most cell types of our body, yielding a highly versatile system for disease research. The work in my lab focusses on advancing these technologies to generate a new generation of iPSC-based disease models for human brain diseases, such as Alzheimer's disease (AD) and stroke, with 3 major aims:

(1) We have improved CRISPR editing in many ways to increase specificity, efficiency and reliability of genome editing in iPSCs. In our most recent work, we describe the widespread occurrence of deleterious on-target effects after CRISPR editing in iPSCs and show how these can negatively affect formation of disease phenotypes. We developed simple and broadly accessible technologies to detect these OnTEs, which will help the field to identify and remove erroneous cell lines from research projects, and thus lead to more faithful disease modelling in iPSC-based models.

(2) We are optimizing iPSC differentiation protocols to generate highly pure, homogeneous and well- characterized cultures of major disease-relevant human brain cell types, including cortical neurons, astrocytes, oligodendrocytes, microglia, endothelial cells, smooth muscle cells and pericytes. Based on these cells, we are developing 3D co-culture and tissue engineering technology of these brain cells, to generate self-organizing brain-like tissues with typical cell biological features.

(3) Combining these two approaches we generate genetic disease models of AD and stroke by introducing disease-causing mutations/risk SNPs etc. with our efficient CRISPR platform, to accelerate naturally occurring disease processes and promote pathology.

In my talk, I will present our recent progress in these research areas. We expect that our models will form the basis for studies elucidating novel, potentially human-specific pathomechanisms and provide a human framework for translational and screening approaches.

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