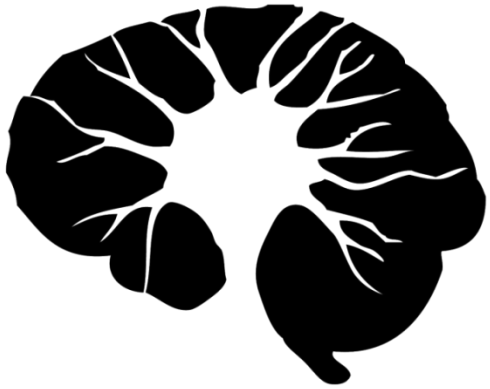

NEURONUS 2018

IBRO NEUROSCIENCE FORUM

APRIL 20–22 2018, KRAKOW, POLAND

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Student Interest Group of Neurology
Jagiellonian University Medical College

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APRIL 20, 2018 (Friday)

9:00	Registration opens
10:00 – 10:15	Large Aula A **Opening Ceremony** Prorector of the Jagiellonian University prof. dr hab. Dorota Malec
10:15 – 12:30	Large Aula A **DRUGS THAT HEAL, DRUGS THAT KILL:** **Tribute to Professors Jerzy Vetulani and Krzysztof Wędzony** co-organized with the Institute of Pharmacology, Polish Academy of Sciences chaired by: **Irena Nalepa** (Institute of Pharmacology PAS, Krakow, Poland) & **Michał Ślęzak** (BioMed X Innovation Center, Heidelberg, Germany) **Phil Skolnick** (CSO Opiant Pharmaceuticals, Santa Monica, USA): Rescue By Naloxone: On the Front Lines Of The Opioid Epidemic **Johannes G. Ramaekers** (Maastricht University, the Netherlands): Cannabinoids, Friends or enemies? **Eero Castrén** (University of Helsinki, Finland): Neuronal plasticity and the antidepressant action
12:30 – 13:30	Lunch

13:30 – 14:30	Large Aula A **Plenary Lecture:** **<u>Emma Robinson</u>** (University of Bristol, UK): How new methods to study emotional behaviour in rodents have provide insights into the neurobiology of mood disorders and their treatment
14:30 – 15:30	Large Aula A **FlashTalks**
15:30 – 17:00	**Oral Sessions:**
	Large Aula A **LEARNING AND MEMORY** chaired by: **Jan Rodriguez Parkitna** (Institute of Pharmacology PAS, Krakow, Poland) & **Szymon Wichary** (SWPS, Wrocław, Poland) **<u>Mark Walton</u>** (University of Oxford, UK): Rapid dopamine release during decision making: waiting, acting, choosing? **<u>Przemysław Eligiusz Cieślak</u>** (Institute of Pharmacology PAS, Krakow, Poland): A role of NMDA receptor-dependent burst firing of midbrain dopamine neurons in adaptive decision-making **<u>Diana Legutko</u>** (Nencki Institute of Experimental Biology, Warsaw, Poland): Where does the brain store its memories? – Comparison between appetitive and aversive experience **<u>Kacper Kondrakiewicz</u>** (Nencki Institute of Experimental Biology, Warsaw, Poland): Central amygdala regulates social transfer of fear

15:30 – 17:00	Medium Aula **DEVELOPMENTAL AFFECTIVE NEUROSCIENCE** chaired by: **Jiska S. Peper** (Leiden University, The Netherlands) **Jiska S. Peper** (Leiden University, The Netherlands): Neuro-endocrinological correlates of adolescent risk-taking and impulsivity: a longitudinal study **Anna Tyborowska** (Radboud University Nijmegen, The Netherlands): Pubertal testosterone shifts neural social emotional action control during adolescence **Corinna Laube** (Max Planck Institute for Human Development, Germany): Teens, Testosterone and Time: Endocrinological and neural correlates of adolescent impatience **Jeroen Van Dessel** (KU Leuven, Belgium): Developmental changes in neural response towards certain and conditional monetary loss anticipation in attention-deficit/hyperactivity disorder
	Seminar Room **MEDICAL SESSION I** chaired by: **Witold Libionka** (WSS Gdańsk, Poland) **Witold Libionka** (WSS Gdańsk, Poland): Neurostimulation of the CNS – from mechanisms to clinical applications **Aleksandra Gałwa** (Poznań University of Medical Sciences, Poland): Clinical analysis of patients treated for lymphoma of central nervous system **Marta Grzywacz** (College of Medicine, National University of Ireland, Galway, Ireland): Progression of Thalamic and Third Ventricular Volume in First Episode Psychosis: A Three-year Follow Up Study **Karol Wdowiński** (Poznan University of Medical Sciences, Poland): Endovascular treatment of basilar artery occlusion – case series presentation
17:00 – 17:30	Coffee Break
17:30 – 18:30	Exhibition Room **Poster Session I**

18:30 – 19:30	Large Aula A **Plenary Lecture:** **Markus Ullsperger** (Oto von Guericke University Magdeburg, Germany): Neuronal Mechanisms of Performance Monitoring and Adaptive Control
19:30	Welcome Reception

APRIL 21, 2018 (Saturday)

8:30	Registration opens
9:00 – 10:00	Large Aula A **Plenary Lecture:** **Ole Jensen** (University of Birmingham, UK): On the role of alpha and gamma oscillations for routing and prioritizing information in the working brain
10:00 – 11:30	**Oral Sessions:**
	Large Aula A **BRAIN STATE DEPENDENT OSCILLATIONS** chaired by: **Mehrnoush Zobeiri** (Westfälische Wilhelms-Universität, Münster, Germany) **Magor László Lőrincz** (University of Szeged, Hungary): Brain state dependent modulation of physiological and pathological thalamic activity **Mehrnoush Zobeiri** (Westfälische Wilhelms-Universität, Germany): Oscillations and brain connectivity in thalamocortical dysrhythmia **Máté Pethő** (Eötvös Loránd University, Budapest, Hungary): Region-specific adenosinergic modulation of the slow cortical rhythm in urethane-anesthetized and freely moving rats **Jagoda Jeczmien-Lazur** (Jagiellonian University in Krakow, Poland): Silencing visual cortex does not influence light responsiveness in the rat dorsal lateral geniculate nucleus

10:00 – 11:30	Medium Aula A **DECISION MAKING** chaired by: **Adrian Fischer** (Otto von Guericke University Magdeburg, Germany) **Wouter Rys** (Trinity College Dublin, Ireland): Exploring the neural basis of metacognition in decision-making **Ewa Beldzik** (Jagiellonian University in Krakow, Poland): When three is greater than five: EEG and fMRI signatures of erroneous decisions **Mikołaj Magnuski** (University of Social Sciences and Humanities, Warsaw, Poland): Advanced EEG statistics in studies of decision making **Adrian Fischer** (Otto von Guericke University Magdeburg, Germany): Beta power reveals the dynamics of human choice formation
	Medium Aula B **PAIN IN MULTISENSORY SPACE** chaired by: **Valery Legrain** (Université catholique de Louvain, Belgium) **Janet Bultitude** (University of Bath, UK): Impaired sensorimotor interaction and spatial perception in pathological pain **Monika Halicka** (University of Bath, UK): Altered spatial representations in pathological pain and how they could be targeted for treatment **Camille Vanderclausen** (Université catholique de Louvain, Belgium): Danger in the dark! Localization of nociceptive stimuli in normally sighted and congenitally blind people **Axel Vittersø** (University of Exeter, UK): Updating peripersonal space and body representation during acute pain
	Seminar Room **MEDICAL SESSION II** chaired by: **Roberto Furlan** (INSpe, Milan, Italy) **Roberto Furlan** (INSpe, Milan, Italy): Intrathecal cytokine delivery for the treatment of experimental neuroinflammation **Paula Chlebanowska** (Jagiellonian University Medical College in Krakow, Poland): Comparative derivation of 3D human midbrain-like organoids from human induced pluripotent stem cell (iPS) lines of single donor origin **Rafał Skowronek** (Medical University of Silesia, Poland): Time-related morphometric studies of CD34 antigen expression in vessels in brain contusions **Joanna Wójcik** (World Hearing Center in Warsaw/Kajetany, Poland): Levels of glutamine and glutamate in tinnitus patients assessed with proton magnetic resonance spectroscopy

11:30–12:00	Coffee Break
12:00 – 13:30	**Oral Sessions:**
	Large Aula A **NEUROPEPTIDES** chaired by: **Christoph Schwarzer** (Medical University of Innsbruck, Austria) **Christoph Schwarzer** (Medical University of Innsbruck, Austria): Neuropeptides - Functional Role and Therapeutic Options in Epilepsy **Iwona Kmieć** (Medical University of Innsbruck, Austria): Functional neuroanatomy of prodynorphin **Zofia Harda** (Institute of Pharmacology PAS, Krakow, Poland): The role of opioid modulation of D1 dopaminoceptive cells in social contact initiation **Alan Kania** (Jagiellonian University in Krakow, Poland): Searching for neuronal mechanism of neuropeptide's orexigenic action - relaxin-3 signalling in paraventricular nucleus of hypothalamus
	Medium Aula A **CANINE MODELS OF HUMAN NEUROCOGNITION** chaired by: **Attila Andics** (Eötvös Loránd University, Budapest, Hungary) **Attila Andics** (Eötvös Loránd University, Budapest, Hungary): Imaging the awake dog brain **Anna Kis** (Hungarian Academy of Sciences, Hungary): Investigation of canine brain activity during sleep using noninvasive polysomnography **Ivaylo Iotchev** (Eötvös Loránd University, Budapest, Hungary): The dog as a model animal for studying sleep spindles – emerging evidence for an analogy regarding function and age-related changes between dogs and humans **Laura V. Cuaya** (Institute of Neurobiology, National Autonomous University of Mexico, Maxico): Cerebral activity in dogs related to perception of human faces **Raúl Hernández-Pérez** (Institute of Neurobiology, National Autonomous University of Mexico, Mexico): Decoding human emotional faces in the dog's brain

<table>
<tr><td>12:00 – 13:30</td><td colspan="2">Medium Aula B
AUDITORY NEUROSCIENCE
chaired by: Inga Griskova-Bulanova (Vilnius University, Lithuania)

<u>Inga Griskova-Bulanova</u> (Vilnius University, Lithuania): Processing of periodic sounds in the brain: importance and practical applications of auditory steady-state responses
<u>Marek Binder</u> (Jagiellonian University in Krakow, Poland): How the level of consciousness can affect auditory steady-state responses
<u>Martin Andermann</u> (University Hospital Heidelberg, Germany): Assessing auditory steady state responses by means of magnetoencephalography
<u>Anna Samsel</u> (KU Leuven, Belgium): Auditory steady state responses in cochlear implant users
<u>Cecile Pacoret</u> (University of Geneva, Switzerland): Implication of synchronous spiking to the auditory steady-state response interpretation: an EEG study</td></tr>
<tr><td>13:30 – 14:15</td><td colspan="2">Lunch</td></tr>
<tr><td>14:15 – 15:15</td><td>Exhibition Room
Poster Session II</td><td rowspan="3">Exhibition Room

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<tr><td>15:15 – 16:00</td><td>Large Aula A
Panel Discussion:
Industry Meets Academia - What are Career Options?</td></tr>
<tr><td>16:00 – 16:45</td><td>Exhibition Room
Coffee Break / Meet the Speaker over Coffee</td></tr>
</table>

	Oral Sessions:
16:45 – 18:15	Large Aula A **SYSTEMS NEUROSCIENCE** chaired by: **Marcin Szczot** (NIH/NCCIH, Bethesda, USA) **Alexander Chesler** (NIH, Bethesda, USA): Under Your Skin: Molecules and Cells for Touch and Pain **Agata Staszelis** (University of Lodz, Poland): Immunohistochemical classification of neurons in layer V of the medial entorhinal cortex with proven convergent input from the subiculum and the retrosplenial cortex **Weronika Szadzinska** (Nencki Institute of Experimental Biology, Warsaw, Poland): Prefrontal cortex neuronal activity underlying fear extinction **Katarzyna Zajda** (Jagiellonian University in Krakow, Poland): Prefrontal cortex catecholaminergic activity regulates cue-induced cocaine craving
	Medium Aula A **NEUROSCIENCE OF LANGUAGE** chaired by: **Marcin Szwed** (Jagiellonian University in Krakow, Poland) **Agnieszka Dębska** (Nencki Institute of Experimental Biology, Warsaw, Poland): Neural signatures of reading and spelling deficits in children **Magdalena Łuniewska** (Nencki Institute of Experimental Biology, Warsaw, Poland): Phonological awareness in children developing dyslexia - a longitudinal fMRI study **Agnieszka Kacprzak** (Nencki Institute of Experimental Biology, Warsaw, Poland): Voxel and surface based morphometry in elementary school late talking children with and without developmental dyslexia **Clara Kuper** (Free University Berlin, Germany): Functional changes during the acquisition of spoken and written Greek

16:45 – 18:15	Medium Aula B **EMOTIONAL MODULATION OF ATTENTION AND PERCEPTION** chaired by: **Hadas Okon-Singer** (University of Haifa, Israel) **Hadas Okon-Singer** (University of Haifa, Israel): Neural Modulation of Emotional Reactions: Focus on Attention and Personality **Ruben Azevedo** (University of London, UK): Truth from within: physiological responses to emotionally charged photos of real-life events predicts judgments of photo authenticity **Maria Lojowska** (Radboud University Nijmegen, The Netherlands): Freezing modulates early visuocortical activity in humans **Manon Mulckhuyse** (Radboud University Nijmegen, The Netherlands): The role of the right posterior parietal cortex (PPC) in emotional attention **Antonio Schettino** (Ghent University, Belgium): Independent vs. interactive effects of emotion and basic visual features during word reading
18:15 - 19:15	Large Aula A **Plenary Lecture:** **Yves de Koninck** (Université Laval and CERVO Brain Research Centre, Québec, Canada): Gating pain; from normal to pathological transmission
	Social Events

APRIL 22, 2018 (Sunday)

9:30 – 10:30	Large Aula A **Plenary Lecture:** **Thomas Kuner** (University of Heidelberg, Germany): Imaging cell biology at work in the awake mouse brain
10:30 – 11:00	Coffee Break
11:00 – 12:30	**Oral Sessions:**
	Large Aula A **SYNAPTIC PLASTICITY** chaired by: **Anna Błasiak** (Jagiellonian University in Krakow, Poland) **Jeremy Henley** (University of Bristol, UK): Mechanisms and consequences of kainate receptor regulation for synaptic plasticity, health and disease **Agata Nowacka** (Nencki Institute of Experimental Biology, Warsaw, Poland): Activity-dependent trafficking of PSD-95 after LTP and LTD **Łukasz Bijoch** (Nencki Institute of Experimental Biology, Warsaw, Poland): Synaptic plasticity of natural and addictive rewards **Zahra Fayyaz** (Sharif University of Technology, Iran): A multi-fractal approach for studying neuronal activity

11:00 – 12:30	Medium Aula A **MOTOR ACTIVITY** chaired by: **Rob van der Lubbe** (University of Twente, The Netherlands) **Rob van der Lubbe** (University of Twente, The Netherlands): How to demonstrate a normal contralateral organization of hand-motor areas at an individual level for children affected by Cerebral Palsy? **Dalina Delfing** (Radboud University Nijmegen, The Netherlands): Examining the motor observation and motor imagery capacity of typically developing children and children with unilateral cerebral palsy – an EEG study **Mikołaj Buchwald** (Adam Mickiewicz University in Poznań, Poland): Decoding functional grasps of tools from brain activity: An fMRI Multi-Voxel Pattern Analysis study **Maciej Raś** (Adam Mickiewicz University in Poznań, Poland): Neural underpinnings of actions involving complex tools: an fMRI study
	Medium Aula B **FACTORS AFFECTING EMOTIONAL PROCESSING** chaired by: **Mirek Wyczesany** (Jagiellonian University in Krakow, Poland) **Johanna Kissler** (Bielefeld University, Germany): A social brain: How attributed social context modulates verbal emotional feedback processing **Constantin Winker** (University of Münster, Germany): Noninvasive stimulation of the ventromedial prefrontal cortex enhances pleasant scene and face processing **Markus Junghöfer** (University of Münster, Germany): On the impact of ventromedial PFC stimulation on emotional picture processing in major depression: Magnetoencephalographic correlates **Tomasz Ligeza** (Jagiellonian University in Krakow, Poland): How much reappraisal is in reappraisal? The role of unspecific factors in attenuating emotional response **Agnieszka Adamczyk** (Jagiellonian University in Krakow, Poland): Uninstructed emotional regulation: implicit reappraisal attenuates emotional processing
12:30 – 13:15	Lunch
13:15 – 14:30	Exhibition Room **Poster Session III**

14:30 – 16:00	**Oral Sessions:**
	Large Aula A **NEUROPATHOLOGY** chaired by: **Dagmar Ehrnhöfer** (BioMed X Innovation Center, Heidelberg, Germany) **Dagmar Ehrnhöfer** (BioMed X Innovation Center, Germany): Modeling Alzheimer's disease-related tau pathology - from human brain dysfunction to in vitro models and back again **Annika Behrendt** (BioMed X Innovation Center, Germany): Asparagine endopeptidase cleaves tau at a novel cleavage site in vivo **Maciej Winiarski** (Nencki Institute of Experimental Biology, Warsaw, Poland): Ultrastructural rescue effects of matrix metalloproteinase 9 inhibition in Fragile X Syndrome mouse model **Dennis van der Meer** (Norwegian Centre of Mental Disorders Research, University of Oslo, Norway): Genetic architecture of hippocampal subfield volumes: shared and specific influences
	Medium Aula A **MOTIVATIONAL NEUROSCIENCE** chaired by: **Marek Wypych** (Nencki Institute of Experimental Biology, Warsaw, Poland) **Marek Wypych** (Nencki Institute of Experimental Biology, Warsaw, Poland): Attenuated brain activity during error processing and punishment anticipation in procrastination – monetary Go/No-go fMRI study **Bertille Somon** (ONERA The French Aerospace Lab, France): Out-of-the-loop pilots: Study of an applied phenomenon through performance-monitoring EEG measures **Magdalena Matyjek** (Berlin School of Mind and Brain, Humboldt University of Berlin, Germany): The Role of Autistic Traits in Reward Anticipation **Michał Szczepanik** (Nencki Institute of Experimental Biology, Warsaw, Poland): Observational fear learning in humans – toward greater ecological validity **Rashmi Gupta** (Indian Institute of Technology, Bombay, India): Learned-predictiveness but not valence modulates unconscious neural activity in early visual cortex

14:30 – 16:00	Medium Aula B **CORTICAL PLASTICITY AND REORGANISATION** chaired by: **Katarzyna Cieśla** (World Hearing Center, Warsaw/Kajetany, Poland) **Katarzyna Cieśla** (World Hearing Center, Warsaw/Kajetany, Poland): Tonotopic organisation of auditory cortex in sensorineural hearing loss **Maksymilian Korczyk** (Jagiellonian University in Krakow, Poland): Auditory cortex recruitment for visual rhythms in musicians **Łukasz Bola** (Jagiellonian University in Krakow, Poland): Functional hierarchy for tactile processing in the visual cortex of sighted Braille readers **Mathias Valstad** (Norwegian Centre for Mental Disorders Research, University of Oslo, Norway): Visual evoked potential plasticity and gamma power in the EEG of healthy participants
16:00 – 17:00	Large Aula A **Closing Lecture:** **Amir Amedi** (Hebrew University of Jerusalem, Israel): How experience shapes brain specializations
17:00	Large Aula A **Closing Remarks** (with awards for the best oral and poster presentations)

Scientific Committee would like to kindly thank Dr Ewa Beldzik, Dr Marek Binder, Mr Ivaylo Iotchev, Mr Przemysław Kac, Professor Valéry Legrain, Ms Maria Lojowska, Dr Jan Rodriguez Parkitna, Dr Christoph Schwarzer, Ms Anna Tyborowska, Professor Tineke van Rijn, Dr Szymon Wichary, Dr Miroslaw Wyczesany, and Dr Mehrnoush Zobeiri for their help with symposia organization.

You can find the Index of Presenting Authors at the end of the booklet.

APRIL 20, 2018 (Friday)

DRUGS THAT HEAL, DRUGS THAT KILL: TRIBUTE TO PROFESSORS JERZY VETULANI AND KRZYSZTOF WĘDZONY

10.15 – 12.30

chaired by: **Irena Nalepa** (Institute of Pharmacology PAS, Krakow, Poland) & **Michał Ślęzak** (BioMed X Innovation Center, Heidelberg, Germany)

Rescue By Naloxone: On the Front Lines Of The Opioid Epidemic

Phil Skolnick

CSO Opiant Pharmaceuticals, Santa Monica, USA

The magnitude of the current opioid epidemic is startling: it has been estimated that more than 4% of the adult population (>10 million Americans) currently misuse opioids. Perhaps the most visible manifestation of the opioid epidemic is an increasing number of overdose deaths, estimated at more than 50,000 in 2016. The epidemic is dynamic: in less than 5 years, there has been a dramatic shift in the opioids responsible for these overdoses. Thus, from 2000-2010, prescription opioids were responsible for the majority of overdose deaths. Beginning in 2010, perhaps coincident with the introduction of abuse deterrent formulations of oxycodone, there was a dramatic rise in fatalities due to heroin and more recently, synthetic opioids like fentanyl. Fentanyl, which is ~50-fold more potent than heroin, is now responsible for more overdose deaths (>20,000) than either heroin or prescription opioids. The opioid antagonist naloxone remains first line treatment for suspected or confirmed opioid overdose. While parenteral naloxone has been approved to treat opioid overdose for over 45 years, beginning in the late 1990s, the harm reduction community led efforts to distribute improvised intranasal naloxone "kits" to first responders, including potential bystanders. While successful rescues have been reported with these improvised kits, assembly and administration require training, and both the peer-reviewed and patent literature suggest plasma concentrations produced by these kits are well below levels attained using the minimum recommended (0.4 mg) parenteral dose. In this presentation, I will describe the pharmacokinetic properties and human use characteristics of a recently approved intranasal naloxone product developed by the National Institute on Drug Abuse in collaboration with the pharmaceutical sector. Intranasal administration of this naloxone formulation produces plasma concentrations as rapidly as an intramuscular injection. This product has become quickly become the 'gold standard' used by first responders such as police and emergency medical services. Nonetheless, the ready availability of powerful, long acting synthetics like fentanyl and carfentanil has led to a call for "second generation" rescue agents. I will describe current efforts aimed at developing potent, long duration opioid antagonists that can be used by first responders.

Cannabinoids, Friends or enemies?

Johannes G. Ramaekers

Dept of Neuropsychology and Psychopharmacology, Faculty of Psychology and Neuroscience,
Maastricht University, The Netherlands

Cannabis is the most widely used illicit drug in the world. Population data suggests that 4% of the global population uses cannabis and that one out of ten users develops daily use patterns. A solid volume of epidemiological and clinical research has established that recreational cannabis use can produce adverse effects on cognitive function and mental health that may persist beyond the acute intoxication phase. The prevalence of cannabis use is expected to increase following recent legalization of medical and recreational use in several countries worldwide and the introduction of a legal cannabis industry. Cannabis and cannabinoid drugs are increasingly being used to treat disease or alleviate symptoms, but their efficacy for specific indications is not always clear. There is evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. Evidence suggesting that cannabinoids are associated with improvements in nausea and vomiting due to chemotherapy, sleep disorders, and Tourette syndrome is less convincing. Medical treatment with cannabinoids is likewise associated with an increased risk of short-term adverse

events, such as impairment of psychomotor and cognitive function. Possibly, the impairing effects of cannabis might decrease after repeated use, due to tolerance. Neurobiological and imaging studies of cannabinoid induced impairment may reveal mechanisms underlying neuroadaptation to cannabinoid use.

Neuronal plasticity and the antidepressant action

Eero Castrén

University of Helsinki, Finland

Neuronal networks are tuned to optimally represent external and internal milieu through neuronal plasticity during critical periods of juvenile life. After the closure of the critical periods, plasticity is considered to be much more limited. We have shown that critical period-like plasticity can be reactivated in the adult mammalian brain by pharmacological treatment with the antidepressant fluoxetine. We have further demonstrated that antidepressant drug treatment also activates critical period-like plasticity in mood-related networks, suggesting that induced plasticity is involved in the mood alleviating effects of these drugs. Neurotrophin BDNF, serotonergic system and reduced inhibition are among the mechanisms that mediate induced plasticity, but how these systems work together it open adult plasticity is unclear. These studies establish a new principle, induced juvenile-like plasticity (iPlasticity). For optimal results, iPlasticity should be combined with physical or psychological rehabilitation, which guide the plastic networks and together allow better adaptation towards changing environment. iPlasticity may facilitate functional recovery after brain injury and underlie the enhanced efficacy of combined antidepressant treatment and psychotherapy.

PLENARY LECTURE:
13.30 – 14:30

How new methods to study emotional behaviour in rodents have provide insights into the neurobiology of mood disorders and their treatment

Emma Robinson

University of Bristol, UK

Rodent models for psychiatry research have come under criticism due to their limited translational validity. We have tried to address this in the field of depression research by developing new methods which test how emotions impact on cognitive processes, termed affective biases. This approach uses behavioural methods designed to recapitulate in animals similar neuropsychological processes to those being tested in patients. In this talk, I will present our findings from two different tasks which investigate how either positive or negative affective states impact on decision-making behaviour and reward learning and memory. This includes extensive pharmacological validation as well as our initial findings into the relevant neural circuits. I will also discuss how results from different antidepressant treatments have enabled us to generate and test new hypotheses about the mechanisms of action of these drugs and particular the rate of onset of action. This has revealed new evidence suggesting that neuropsychological mechanisms may play a key role in the rapid onset of action of drugs such as ketamine and could also explain why conventional antidepressants require chronic treatment before their clinical benefits develop.

FLASHTALKS:

14:30 – 15.30

chaired by: **Michał Ślęzak** (BioMed X Innovation Center, Heidelberg, Germany) & **Wioleta Walentowska** (Psychophysiology Laboratory of the Jagiellonian University in Krakow, Poland & Cognitive and Affective Psychophysiology Laboratory, Ghent University, Belgium)

1) Jaroslav Rokicki - PS I - 17
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3) Michał Wilczkowski - PS I - 31
4) Ewelina Bartoszek - PS I - 34
5) Magdalena Zygmunt - PS II - 2
6) Lucja Kudla - PS II - 5
7) Alina Zawiślak - PS II - 28
8) Kaja Kasper - PS II - 37
9) Aleksandra Stępniak - PS III - 3
10) Joanna Borowska - PS III - 6
11) Levan Bokeria - PS III - 8
12) Anna Kustron - PS III - 21
13) Gytis Baranauskas - PS III - 32
14) Anastasiya Lado - PS II - 53
15) Krzysztof Gociewicz - PS I - 37
16) Mikolaj Szulczewski - PS I - 45
17) Sara Boccadoro - PS I - 57
18) Mikolaj Compa - PS I - 64
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21) Louise Manfron - PS III - 68

LEARNING AND MEMORY

15.30 – 17.00

chaired by: **Jan Rodriguez Parkitna** (Institute of Pharmacology PAS, Krakow, Poland) & **Szymon Wichary** (SWPS, Wrocław, Poland)

Rapid dopamine release during decision making: waiting, acting, choosing?

Mark Walton

University of Oxford, UK

Dopamine is the neuromodulator about which we know most and have the most precise theories. For instance, it is now widely accepted that the activity of many dopamine neurons and dopamine release in parts of the striatum represent predictions of future rewards. But in spite of this precision, the content and function of these dopamine signals during reward-guided behaviours remains a matter of great controversy. I'll discuss voltammetric data that demonstrate such predictive mesolimbic dopamine signals may play a surprisingly limited role in guiding economic decisions between options. Instead, rapid dopamine release, particularly in the nucleus accumbens, may be critical to shape decisions about whether or not to act.

A role of NMDA receptor-dependent burst firing of midbrain dopamine neurons in adaptive decision-making

Przemysław Eligiusz Cieślak, Jan Rodriguez Parkitna

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Burst firing of midbrain dopamine (DA) neurons is crucial for certain aspects of adaptive behavior, particularly action selection and action initiation. Transition to high-frequency burst firing in DA neurons is driven by N-methyl- D-aspartate receptors (NMDARs). Here, we sought to determine the effects of disrupted NMDAR-dependent burst firing in midbrain DA neurons on performance in an adaptive decision-making task. We used a genetically modified mice (the NR1DATCreERT2 strain) with cell-type specific ablation of NMDARs in DA neurons. Animals were trained in a task, in which they had to learn to choose an alternative with higher reward probability and adapt their choices to the

reward contingency reversal. Disruption of NMDAR-dependent signaling in DA neurons, caused an initial impairment in error-driven learning and reduced the likelihood of selecting more often rewarded alternative. Moreover, loss of NMDARs in DA neurons, decreased the likelihood of repeating previously rewarded actions and caused a delay in action initiation. Our results suggest that NMDAR-dependent signaling in midbrain DA neurons is necessary for quick and adaptive decision-making.

Where does the brain store its memories? – Comparison between appetitive and aversive experience

Diana Legutko[1], Klaudia Kogut[1], Sylwia Bednarek[2], Marzena Stefaniuk[1], Monika Pawłowska[1], Leszek Kaczmarek[1]

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Brain structures involved in information processing are different depending on the kind of experience that we undergo. Amygdala is one of the well-described structures engaged in processing of emotional information. While, lateral part of the basolateral amygdala is mainly involved in fear learning, during the pleasure experience we observe neuronal activation in the central nucleus of the amygdala. However other brain regions involved in memory formation of different kind of experience are still elusive. To define those regions we decided to perform whole brain clearing. For this, we applied iDisco+ tissue clearing technique combined with immunolabeling for c-Fos (Renier et al., 2016). Next, we performed imaging using home-built light-sheet microscope. This approach allowed us to achieve the cellular level of detection for c-Fos in the entire mouse brain. Our aim was to track functional activation of neuronal circuits involved in different kind of behavioural training. Mice underwent either aversive or appetitive training. Data obtained from experimental brains were analysed with a ClearMap software (Renier et al., 2016). Particular brain regions were compared according to the number of c-Fos- positive cells. The results helped us to define brain areas involved in learning of information of positive and negative valence.

Central amygdala regulates social transfer of fear

Kacper Kondrakiewicz, Karolina Rokosz, Karolina Ziegart-Sadowska, Ewelina Knapska

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In order to study how rodents communicate information about danger, we developed a model of observational transmission of fear. In our paradigm one of the rats (observer) directly watched its cage-mate (demonstrator) undergoing contextual fear conditioning. This type of stimulation elicited robust freezing in both rats as well as increased number of 22-kHz (aversive) vocalizations. Since the central nucleus of the amygdala (CeA) is critical in regulation of single-subject defensive responses, we hypothesized that it controls also observational fear. To test this, viral vectors carrying either channelrhodopsin 2 (ChR2) or halorhodopsin (NpHR) were injected into the CeA of the observer rats. Both opsins were placed under c-fos promoter to ensure that they would be expressed only in the population of cells activated by the task. After 2-3 weeks, observational transfer of fear was performed to trigger the construct expression. 24 hours later, the animals were subjected to a modified version of open field test, during which we optogenetically either stimulated or inhibited the CeA circuit. The results were increase or decrease in avoidance behaviours, respectively. We can conclude that CeA contains a population of neurons which is activated by social transmission of fear and regulates anxiety.

DEVELOPMENTAL AFFECTIVE NEUROSCIENCE

15.30-17.00

chaired by: **Jiska S. Peper** (Leiden University, The Netherlands)

Neuro-endocrinological correlates of adolescent risk-taking and impulsivity: a longitudinal study

Jiska S. Peper, Lara Wierenga, Anne-Lise Goddings, Eveline Crone

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Leiden University, The Netherlands

Adolescence is an important time of change occurring between childhood and adulthood. With the relatively recent discovery that changes in brain structure and function stretch into adulthood, the interest in adolescent brain development has grown. Brain changes in adolescence are not only driven by age-related change, but there is increasing evidence that major changes in brain structure and connectivity are driven by pubertal hormones, such as testosterone and estradiol. These changes on the neural level may have implications for behavioural changes observed during adolescence and related to puberty, such as increased risk-taking and reward sensitivity. In my talk, I will present insights from developmental neuroscience (structural MRI and DTI) and endocrinology (gonadal hormones) to predict adolescent impulsivity and risk-taking across adolescence. The data are derived from a longitudinal study ('Braintime') with three time points, separated by 2 years, in participants aged 8-29 years (670 observations).

Pubertal testosterone shifts neural social emotional action control during adolescence

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Increased occurrence of reward- and sensation-seeking behaviors during adolescence is often attributed to the relative imbalance in prefrontal– subcortical/limbic maturation. Previously, we have shown that pubertal maturation (indexed by testosterone levels) shifts executive control of emotions from subcortical to prefrontal regions during mid-adolescence (Age 14). The present study builds on these findings and assesses the neuro-developmental trajectories of emotional control and how they relate to the changing role of pubertal testosterone. To this end, the same participants are re-tested during late adolescence (Age 17). Three main findings point to the changing role of testosterone in the maturation of the prefrontal-amygdala circuit and its role in down-regulating emotion-driven activity. First, prefrontal control becomes less dependent on testosterone from mid-to-late adolescence. Second, amygdala activity concurrently decreases during this time. Third, prefrontal-amygdala connectivity changes as a function of maturation and gender. Namely, an adult-like pattern of negative prefrontal-amygdala connectivity becomes apparent in 17-year-old girls. Taken together, these findings suggest the emergence of mature adult-like patterns of neural control by late adolescence. The relevance of these findings will be discussed in light of current neurobiological models of pubertal development and linked to alterations in emotion control observed in affective disorders peaking during this time.

Teens, Testosterone and Time: Endocrinological and neural correlates of adolescent impatience

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Adolescence describes the developmental phase between childhood and adulthood and is characterized by rapid

changes in physiology, hormones and behavior. Typical adolescent behavioral tendencies such as impulsivity are thought to evolve from a major biological reorganization of the adolescent brain. However, it remains unclear how these large-scale biological changes impact specific processes that result in increases in impulsive behavior in adolescence. I will present findings of two empirical studies focusing on the relationship between pubertal testosterone and impatient decision-making assessed by an intertemporal choice task. In the first study, we found that testosterone but not age is associated with increased sensitivity to immediate rewards. To gain further insight into these mechanisms, we designed a follow-up fMRI study, in which we investigated the neural mechanisms underlying the relationship between pubertal testosterone and impatient decision-making. Here, results indicated that testosterone specifically impacts the dorsal, but not the ventral striatum, which in turn lead to behavior that was biased towards choosing smaller sooner rewards. I will then discuss how these results may provide first insights into the role of pubertal hormones for adolescent plasticity and learning, and outline new research directions.

Developmental changes in neural response towards certain and conditional monetary loss anticipation in attention-deficit/hyperactivity disorder

Jeroen Van Dessel[1], Matthijs Moerkerke[1], Emund Sonuga-Barke[2,3], Saskia Van der Oord[4,5], Jurgen Lemiere[1], Marina Danckaerts[1]

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The neural response towards cues signalling monetary gain and loss has been extensively studied through the Monetary Incentive Delay (MID) task. Anticipation of loss is often directly compared against anticipation of gain to represent the trade-off between positive and negative outcomes. In daily life situations, these events occur independently from each other and one can often avoid money loss. We used an adaptation of the MID functional Magnetic Resonance Imaging task to investigate the differential brain activity to cues signalling certain, conditional and no monetary loss. Developmental changes in neural response were compared between children (n=20) and adolescents (n=19) with attention-deficit/hyperactivity disorder and typically developing controls (n=34). We provide some of the first evidence of a distinctive brain pattern between conditional and certain monetary loss anticipation across the development. The identification of such contingencies can provide more insight in how children and adolescents respond to monetary loss in daily life.

MEDICAL SESSION I

15.30 – 17.00

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

Neurostimulation of the CNS – from mechanisms to clinical applications

Witold Libionka

WSS Gdańsk, Poland

Surgical interference of the human mind has since ever been intriguing method, raising ethical concerns. Functional neurosurgery offers the possibility of altering somatic and – to certain degree – vegetative functions. Apart from these, a surgeon is enabled to affect higher CNS functions, such as the memory or mood, which falls under psycho-neurosurgery. Neurostimulation is a dynamically developing method enabling safe and reversible manipulation of the CNS function. Therapeutic effects usually occur immediately after the onset of the stimulation, while the cessation of the treatment leads to reappearance of symptoms. Recent progress in understanding of physiology and pathophysiology of brain regions controlling pain, hunger or psychiatric disorders revealed new anatomical targets for functional neurosurgery. Neurostimulation of identified areas resulted in spectacular effects in treatment of movement disorders (Parkinson's disease, tremor, dystonia, Huntington's disease), pharmacoresistant chronic pain, epilepsy, psychiatric diseases (obsessive-compulsive disorder, pharmacoresistant depression), Alzheimer's disease, memory disorders, and even helped patients with disturbance of consciousness resulting from brain trauma. In my talk, I will provide an update on neurostimulation and present an outlook for future development of this promising method.

Clinical analysis of patients treated for lymphoma of central nervous system

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Poznan University of Medical Sciences, Poland

Primary central nervous system lymphomas represent 4% of intracranial tumours with poor prognosis. Clinical course is similar to glioblastoma multiforme. In the course of the diagnostic procedure CT, MRI and stereotactic biopsy are routinely performed. Extended laboratory tests and histopathology (H&E stain, immunohistopathology) are also necessary. The purpose of this study is to analyze the influence of clinical factors on patient outcome. Analyzed material consists of 12 patients (age 45 to 78, average 68) treated at the Neurosurgery Department in Poznań (from 01.2015 til 03.2017). We are currently still observing 7 patients, while 5 patients died. Analysis was carried out on the influence of age, sex, patient interview, neurological examination and laboratory test results on clinical outcome. During statistic analysis, Mann-Whitney test, t-student test and Fisher's exact test were performed. Statistic relevance was set to p=0,05. The results displayed statistically relevant relation between Nottingham-Barcelona scale score (p=0,033), location of the lesion and patient outcome (p=0,031). Some relation was also found between patient outcome and age, state of consciousness, Karnofsky scale score, multilocation lesions (statistical relevance slightly over p=0,05). Conclusion: Based on the performed study, usefulness of Nottingham-Barcelona scale in predicting patient outcome with PCNSL is proven.

Progression of Thalamic and Third Ventricular Volume in First Episode Psychosis: A Three-year Follow Up Study

Marta Grzywacz[1]**,** Theophilus Akudjedu[1], Giulia Tronchin[1], Shane McInerney[1], Cathy Scanlon[1], Joanne Kenney[1], John McFarland[1], Conor O'Kelly[1], Peter McCarthy[2], Dara M. Cannon[1], Brian Hallahan[1], Colm McDonald[1]

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Neuroanatomical abnormalities have long been associated with first episode psychosis (FEP), however their progression throughout the trajectory of the illness remains yet to be established. Research suggests that changes in the thalamus and third ventricle may be associated with symptomology; therefore a longitudinal analysis was conducted to evaluate progressive structural and symptomatic changes. A three-year follow-up design was employed to investigate the progression of thalamic and third ventricular volumes of 28 FEP patients and 28 controls. T-1 weighted MR images were acquired at both time-points along with sociodemographic and clinical assessment. The volumes were segmented using the longitudinal pipeline analysis in FreeSurfer software. Multiple analysis of covariance revealed a significant difference between the volume change of the thalamus in patients and controls, with the patients having a more pronounced decrease in both thalami. The results support the hypothesis that progressive structural changes are present in FEP patients and that larger abnormalities are associated with more severe negative symptoms. The findings may be attributable to a disturbance in the cortico-thalamo- cortical and cortico-striato- thalamo-cortical loops, which arise in psychotic symptoms and cause damage to the higher order nuclei of the thalamus, reflected by the overall damage of the structural integrity and volume loss.

Endovascular treatment of basilar artery occlusion – case series presentation

Karol Wdowiński[1], Robert Juszkat[2] , Radosław Kaźmierski[3], Katarzyna Stanisławska[2] , Magdalena Sielewicz[1], Roman Jankowski[2]

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Basilar artery (BA) occlusion results in up to 90% death rate and depending on occlusion site manifests with broad

possible symptoms spectrum. Treatment possibilities include intravenous thrombolysis (IVT) and various intra-arterial techniques. We present a series of 4 patients - females aged 52 – 69 years old: one of them presented with critical BA stenosis and 3 with acute BA thrombosis. All patients were disqualified from intravenous therapy due to a time window exceedment. In all cases successful recanalization of the artery was obtained, no complication occured. Intra-arterial thrombolysis, mechanical thrombectomy and balloon angioplasty were performed in 2 cases respectively. Stent was implanted in 3 patients. In 2 cases significant neurologic improvement was achieved, in 1 case neurologic dysfunction was persistent and undergoes rehabilitation. 1 patient died despite the satisfying radiological outcome. Restoration of blood flow in BA plays a crucial role in severe neurological impairment prevention. Endovascular intervention appears as a safe and effective alternative treatment method for patient disqualified from intravenous thrombolysis. Stent implantation following angioplasty constitute an integral part of efficacious BA stenosis treatment.

POSTER SESSION I:
17.30 – 18.30
pages: 59-84

PLENARY LECTURE:
18.30 – 19:30

Neuronal Mechanisms of Performance Monitoring and Adaptive Control

Markus Ullsperger

Otto von Guericke University Magdeburg, Germany

Monitoring for erroneous and unexpected action outcomes is essential to determine when adaptation is needed to optimize goal achievement. First, I will give an overview of EEG and fMRI correlates of performance monitoring. Building on current theories relating performance monitoring to reinforcement learning mechanisms, I will discuss which signals are represented in a key region of performance monitoring, the posterior medial frontal cortex, and how they are weighted to determine the need for adaptation. The second part of the presentation will focus on neuronal mechanisms of post-error adjustments. In particular, I will present neuroimaging and invasive and non-invasive electrophysiological studies in humans addressing the trial-by-trial adjustments post-error slowing and post-error attentional control and their neuronal underpinnings. Showing data from a large EEG study using an online measure of decision formation, lateralized beta power over motor cortices, I will contribute to the current debate as to whether post-error slowing is adaptive or rather disruptive for subsequent performance.

APRIL 21, 2018 (Saturday)

PLENARY LECTURE:
9.00 - 10.00

On the role of alpha and gamma oscillations for routing and prioritizing information in the working brain

Ole Jensen

University of Birmingham, UK

Networks in the brain must rely on powerful mechanism for routing, maintaining and prioritizing information processing. From a larger set of attention and memory studies we now have evidence for the notion that alpha oscillations (9 – 12 Hz) are inhibitory and serve to route information: 'gating by inhibition'. The alpha band activity is under top-down control by areas in the dorsal attention network. As such the alpha oscillations – previously believed to reflect a state of rest – serve an important role for shaping the functional architecture of the working brain. Gamma band activity (50 – 100 Hz) reflects feed-forward processing is coupled to the phase of the alpha oscillations. Importantly, new findings suggest that representations activate in a phase specific manner along the alpha cycle. Our empirical framework has been developed using MEG, DTI/MEG, TMS/MEG, fMRI/EEG and non-human primate data.

BRAIN STATE DEPENDENT OSCILLATIONS

10.00 - 11.30
chaired by: **Mehrnoush Zobeiri** (Westfälische Wilhelms-Universität, Münster, Germany)

Brain state dependent modulation of physiological and pathological thalamic activity

Magor L. Lőrincz

Department of Physiology, Anatomy and Neuroscience, University of Szeged, Hungary

In the absence of sensory input, the mammalian brain exhibits a wide array of structured, state dependent spontaneous activities. Periods of active wakefulness are associated with dilated pupils, depolarized cortical membrane potential, asynchronous firing and fast oscillations, whereas periods of quiet wakefulness are associated with constricted pupils, hyperpolarized cortical membrane potential, synchronous firing and large amplitude low frequency oscillations. In order to characterize the activity of thalamocortical neurons during these rapid brain state transitions we performed juxtacellular or intracellular recordings of identified dorsal lateral geniculate nucleus (dLGN) neurons of awake, head restrained mice while monitoring their pupil size. The firing rate of some dLGN neurons showed clear correlations with the pupil size on a rapid time scale indicating that LGN neurons exhibit brain state dependent activity changes. To reveal the effect of rapid state changes on sensory coding the response to visual stimuli (moving gratings of different orientations) was compared between periods of different pupil diameters. We found that the orientation tuning of some TC neurons is brain state dependent. These results indicate that the activity of TC neurons can change during brain state transitions on a rapid timescale resulting in altered sensory responses. Our preliminary experiments also indicate a state dependency of pathological thalamocortical oscillations in rodent models of absence epilepsy. In conclusion physiological and pathological thalamocortical activity is brain state dependent and its mechanisms and implications will be discussed.

Oscillations and brain connectivity in thalamocortical dysrhythmia

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Oscillatory activity of thalamocortical system is central to a number of neurocognitive and physiological functions, including attention, cognition, arousal and sleep. Due to the abnormal increase in burst activity of the thalamic

neurons, the naturally occurring thalamocortical rhythms can transform into pathological oscillations termed as thalamocortical dysrhythmia (TCD). Several types of neurological and psychiatric disorders including schizophrenia and epilepsy are categorized as TCD. On the cortical EEG, TCD is characterized by an increase in slow frequency (delta/theta) oscillations which can cause a resonant activity-lock between thalamus and cortex. The hyperpolarization of the membrane potential in TC neurons due to excess inhibition or disfacilitation has been proposed as the underlying mechanism for TCD. To identify different features of TCD and changes in brain network connectivity in TCD, we used two different genetically modified mice models. We showed that changes in thalamic and cortical ionic conductances of HCN channels in TRIP8b -/- mice alter the corticothalamic network connectivity during wakefulness and sleep compared to control animals. We also demonstrated that abnormal synaptic plasticity in Neuregulin-1 overexpression model of schizophrenia results in an atypical absence epilepsy phenotype. These examples demonstrate that the phenotype depends on the type of the disturbance within the thalamo-cortical system.

Region-specific adenosinergic modulation of the slow cortical rhythm in urethane-anesthetized and freely moving rats

Máté Pethő, László Détári, Dóra Keserű, Tünde Hajnik, Örs Szalontai, Attila Tóth

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Slow cortical rhythm (SCR) is a rhythmic alternation of active (UP) and silent (DOWN) states during natural sleep and anesthesia. SCR-associated slow waves (delta waves) may be related to the homeostatic function of sleep. Adenosine is an endogenous sleep-inducing factor accumulating during prolonged wakefulness and sleep deprivation (SD). It may play a role in the delta power increment seen during recovery sleep following SD. In our study, adenosine was administered topically to the frontal, somatosensory and visual cortices during urethane-anesthesia. In freely moving rats, adenosine was injected into the visual cortex and adenosine A1 receptor antagonist (DPCPX) was injected i.p. after 4 hours of sleep deprivation. Local field potential and multiunit activity was recorded during the experiments. Topically administered adenosine evoked region-specific effects as delta power increment was either different in its kinetics or was absent in the examined cortical areas. In the visual cortex of freely moving rats, adenosine increased the delta power and the time spent in deep sleep, respectively. DPCPX attenuated the characteristic delta increment of recovery sleep although time spent in deep sleep was increased. Thus, adenosine may directly modulate SCR in a complex manner and its effect may show region-specificity.

Silencing visual cortex does not influence light responsiveness in the rat dorsal lateral geniculate nucleus

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The thalamic dorsal lateral geniculate nucleus (dLGN) is a retinorecipient nucleus en route to the primary visual cortex (V1). Although the modulatory input from the V1 to the dLGN is well characterized, little is known about its influence upon its signal transmission. Urethane is a model to study thalamocortical interactions, because state-dependent alternations of general brain state activity are clearly visible under this anaesthesia in EEG recordings. We aimed to verify whether these changes influence light responsiveness of the dLGN neurons and how light responses are shaped under attenuated V1. We addressed both questions by recording multielectrode electrophysiological activity in the dLGN of Long-Evans rats (n=9) over three cortical conditions: synchronization, desynchronization and attenuation of V1 by topical muscimol application. We found that the amplitude of light responses does not change between cortical phases and after muscimol application. Majority of neurons (70%) did not change their light response pattern between the conditions. Importantly, in a small population of dLGN cells the type of photoresponse was both state and muscimol dependent. Our data confirmed that the transmission of light information within the rat dLGN is a complex process, that seems to have the priority upon cortical modulatory influences.
Supported by: 2013/08/W/N23/00700.

DECISION MAKING

10.00 - 11.30

chaired by: **Adrian Fischer** (Otto von Guericke University Magdeburg, Germany)

Exploring the neural basis of metacognition in decision making

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Computational modelling and single-cell recordings suggest that perceptual decision-making involves integrating noisy sensory evidence towards up to an action triggering threshold. A recent series of studies has also characterized a neural signature of this evidence accumulation process in human brain recordings. This electrophysiological signal, called the Centro-Parietal Positivity (CPP), builds gradually at a rate that reflects the difficulty of the perceptual decision and reaches a stereotyped amplitude immediately prior to response execution. In more recent work, Rys and O'Connell investigates the role of this decision-making signature in the formation of confidence judgements. By adopting a novel random dot motion paradigm, where dot motion was interrupted for simultaneous judgements of motion and confidence, subjects adopted behavioural strategies congruent with dimensional reports of confidence. Further analysis showed that both the rate of accumulation and amplitude of the CPP during coherent motion also predicted the judgements of confidence.

When three is greater than five: EEG and fMRI signatures of erroneous decisions

Ewa Beldzik, Aleksandra Domagalik, Magda Gawłowska, Tadeusz Marek, Justyna Mojsa-Kaja

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Understanding why humans make erroneous decisions is one of the key questions in cognitive neuroscience. In this study, this question was addressed in EEG and fMRI experiments, which were conducted using the numerical and physical Stroop tasks. Group ICA revealed one centro-parietal EEG component and one temporo-parietal fMRI neural network, which exhibited similar pattern to behavioural outcomes. The activity of centro-parietal EEG component was linked to the process of accumulating evidence until reaching a decision. Linear fits to the centro-parietal positivity provided evidence for distinctive characteristics between numerical and physical tasks, thereby explaining the behavioural outcomes: errors are committed due to accumulation of evidence in favour of the other (wrong) task instruction. The architecture of the temporo-parietal network is highly consistent with the recently established core "number network". These findings link perceptual decisions with the generalized magnitude system and impart novel insights into the neural determinants of errors in humans.

Advanced EEG statistics in studies of decision making

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While electrophysiological recordings give rise to a wealth of data, decision making studies usually add another layer of complexity at the level of experiment design and behaviour. Linking these two 'complexities' in the analysis is not always straightforward. I will present two examples of using more advanced analytical approaches to EEG data analysis: one in the context of multi-attribute choice task and another in perceptual decision making. In the first example I showcase how using rich single-trial statistical models can help to disentangle overlapping EEG signatures of various decision making components while controlling for multiple comparisons at the same time. In the second example I demonstrate how to consider neural activity as a bridge between perception and action using mediation analysis. Both approaches are well suited to leverage complexity present in behavioral and neural data in decision making experiments and can help to uncover interesting relationships buried in the data that would be harder to detect with simpler methods.

Beta power reveals the dynamics of human choice formation

Adrian Fischer

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Otto von Guericke University Magdeburg, Germany

The formation of mutually exclusive decisions is assumed to reflect noisy evidence accumulation in favour of one or another response. This process is formally described by sequential sampling models. In order to adapt to varying time horizons, it has been proposed that decision boundaries may dynamically change in the time-scale of hundreds of milliseconds, yet such neural signals have not been shown in humans. Here, we measure lateralization of EEG beta band power desynchronization in a speeded dual choice task. This provides an online index of decision formation. This beta signal complies to various predictions of accumulator class decision models, including pre-lateralization before the evidence accumulation begins determining speed and accuracy of subsequent responses, as well as collapsing decision boundaries that terminate decision making under time pressure. This indicates lateralized beta power as a valid online marker of decision formation that can be employed in various tasks.

PAIN IN MULTISENSORY SPACE

10.00 - 11.30

chaired by: **Valéry Legrain** (Université catholique de Louvain, Belgium)

Impaired sensorimotor interaction and spatial perception in pathological pain

Janet Bultitude

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Problems integrating signals for sensations and movements might underlie some painful conditions such as Complex Regional Pain Syndrome (CRPS). To examine this proposal, we tested upper and lower limb CRPS patients and controls on a task involving spatial motor (M), visual (V), and visuomotor (VM) localization. Patients had higher endpoint variability than controls when locating targets using index-finger pointing movements without vision (M). This cannot be solely attributed to weakness/stiffness, since some lower limb patients had significantly higher variability than controls although they performed the task with their (unaffected) arms. Over half of the patients had higher variability than controls when verbally indicating the location of a target using visual landmarks (V). This suggests that the variability may arise from problems representing or maintaining spatial location information. When performing the task using both movement and vision (VM), controls reduced their variability by combining visual and motor information. This sensorimotor interaction was disrupted in CRPS patients. Across all three tasks, abnormal performance was more frequent when patients performed the task with the hand of their affected body-side, or when targets were presented in the affected side of space. Overall, these results suggest impaired sensorimotor interaction and spatial perception in CRPS.

Altered spatial representations in pathological pain and how they could be targeted for treatment

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There is emerging evidence that patients with Complex Regional Pain Syndrome (CRPS) have a bias of attention away from the affected limb and its surrounding space. Considering high individual variability in the manifestation of this bias, a case series approach was applied to better understand the representations of different regions of personal and external space in pathological pain. Examination of three CRPS patients using visual and tactile Temporal Order Judgement tasks revealed significant hyper-attention to the affected side as compared to healthy controls. Attention bias manifested in patients' personal space, hands working space, and near space on eye-level. Interestingly, one case

showed a dramatic change from inattention to hyper-attention to the affected side between sessions. Overall, lateralized attention bias could not be attributed to sensory impairments in peripheral vision or tactile detection and discrimination. Moreover, it contradicted neurological signs of neglect and extinction of the affected side upon confrontation testing. The findings suggest that spatial attention bias is not necessarily directed away from the affected side, stable across time, or reflective of sensory changes and neurological signs. This individual variability has ramifications for how to implement prism adaptation treatment for CRPS, which aims to reduce pain by normalising spatial attention.

Danger in the dark! Localization of nociceptive stimuli in normally sighted and congenitally blind people

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To defend our body against potential physical threats, it is crucial to identify which body part is being damaged, but also to locate the threatening stimulus in its surroundings. Therefore, the brain coordinates the representation of the body with that of external space. To this aim, somatosensory inputs are remapped from the somatotopic towards a spatiotopic representation. The development of this spatial remapping would mainly rely on early visual experience. To test this hypothesis, we compared the ability of normally sighted and congenitally blind individuals to localize nociceptive stimuli. Participants performed temporal order judgement tasks during which they had to discriminate the temporal order of two nociceptive stimuli, one applied on each hand, with either their hands uncrossed or crossed over the body midline. While congenitally blinds were not affected by the posture, the performance of the sighted decreased in the crossed as compared to the uncrossed condition. This indicates that nociceptive stimuli are automatically remapped into a spatiotopic representation (where are the hands?) that interferes with the somatotopic representation (which hand is stimulated first?), whereas congenitally blinds seemed to only rely on a somatotopic map. This suggests that the way we perceive nociceptive stimuli is shaped by visual experience.

Updating peripersonal space and body representation during acute pain

Axel Vittersø[1,2]**,** Monika Halicka[2], Michael J Proulx[2], Mark Wilson[1], Gavin Buckingham[1], Janet Bultitude[2,3]

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The representations of our body and its surround space are constantly updated as we interact with external space, for instance during active tool-use. People with certain painful conditions, such as Complex Regional Pain Syndrome, can present with distorted representations of their body and peripersonal space when compared to pain-free individuals. It is not known how such distorted representations may arise, and if they reflect a difference in cognitive processing, or are a direct consequence of pain. To test the latter, we induced acute pain in healthy individuals using 1% Capsaicin cream and examined its effect on participants' abilities to update the representation of their body (using tactile distance judgements on their arms) and peripersonal space (using a crossmodal congruency task). Our findings showed that acute pain did not interfere with updating the representations of the body and peripersonal space when compared to two control conditions. Therefore, this suggests that acute pain is not sufficient to account for the distorted representations of the body and its surrounding space commonly observed in people with painful condition.

MEDICAL SESSION II

10.00 – 11.30

chaired by: **Roberto Furlan** (INSpe, Milan, Italy)

Intrathecal cytokine delivery for the treatment of experimental neuroinflammation

Roberto Furlan

INSpe, Milan, Italy

Selective interference with immune processes in the central nervous system (CNS) is a very difficult task because of the limitations associated to the delivery of immunomodulatory molecules across the blood brain barrier. Systemic administration of immune-mediators, either by conventional routes or by intramuscular or intravenous gene therapy, is hampered by severe side effects and alters immune-system functions also in peripheral organs. To overcome these problems, different gene therapy strategies have been developed to deliver immunomodulatory molecules directly within the central nervous system. The use of engineered CNS antigen-specific circulating cells as selective delivery vehicles, the direct injection of gene vectors into the brain parenchyma or through the ependymal route, and the use of engineered extracellular vesicles, have been proposed as possible alternative gene therapy protocols to selectively interfere with immuno-pathological processes in the CNS. I will review here our experience using lentiviral vectors or engineered extracellular vesicles to interfere with established neuroinflammation delivering anti-inflammatory cytokines such as IL-4, IL-27, and IL-35.

Comparative derivation of 3D human midbrain-like organoids from human induced pluripotent stem cell (iPS) lines of single donor origin

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One of the major goals of neurobiology is to understand nervous system development and modelling of cellular interactions within the human brain. Recent achievements in stem cells 3D culture systems enable generation from human induced pluripotent stem cells (iPS) of midbrain like organoids. The aim of this study was to create model of 3D midbrain like-organoids derived from iPS cells generated from different cell types isolated from one cell donor. Peripheral blood mononuclear cells and keratinocytes were reprogrammed using the Sendai-virus reprogramming system. The transgene-free iPS lines were verified by immunofluorescent staining for pluripotency markers. The embryonal markers expression was evaluated in these cells by RT-PCR. Generated iPS lines were able to differentiate into the 3 germ layers in vivo and were also positive for alkaline phosphatase. The differentiation of human induced pluripotent stem cells into a large multicellular organoid-like structure was performed. The 3D organoid-like structures were positive for Tuj1 and Pax6 as shown by immunofluorescent staining. These 3D organoid models showed a universal in vitro system to study the human midbrain. There were no correlation between origin of iPS cells and generated organoids.

The project was supported by the grant from the National Science Centre in Poland: K/PBO/000376.

Time-related morphometric studies of CD34 antigen expression in vessels in brain contusions

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In forensic neurotraumatology age determination of brain contusion is of key importance. In the previous work, we discussed the importance of neurofilaments in this field. The aim of this study is to present the possibility of using angiogenesis in brain contusions to determine their age in the human material by morphometric evaluation of CD34 antigen expression in vessels in the area of contusion. The studied groups consisted of 10 cases of victims who died at the scene, immediately after head injury, and after 12 and 24 hours, as well as 2, 3, 4, 5, 6 and 7 days after the injury. The immunohistochemically stained CD34 antigen was quantitated using the Met-Ilo program. The obtained results were then subjected to statistical analysis. In the light of the Kruskal-Wallis test results, the number of blood vessels can be considered significantly different in the period from 0 to 7 days after the occurrence of the injury, but the Dunn test levels of significance in pairwise comparisons do not show statistical significance. Morphometric analysis of CD34 antigen expression in the vessels in the area of brain contusion showed, therefore, lack of its practical usefulness in determining the age of such injuries in forensic medicine.

Levels of glutamine and glutamate in tinnitus patients assessed with proton magnetic resonance spectroscopy

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Tinnitus is a subjective auditory percept, experienced in absence of an external auditory source. Glutamine and glutamate are neurotransmitters whose dysfunction can be related to tinnitus. The aim of the study is to determine the influence of tinnitus on levels of glutamine and glutamate in patients with tinnitus. Thirty adult patients with chronic unilateral and bilateral tinnitus participated in a hydrogen magnetic resonance spectroscopy (HMRS) study. We used the single-voxel technique in four locations: the right and the left temporal lobe as well as the right and the left frontal lobe. Each participant took part in audiometric and psychological tests (a Tinnitus Questionnaire, THI, TFI, KPD and STAI). Relative ratios of glutamine and glutamate to creatine levels were obtained in four brain sites. We observed correlations between the relative concentration ratios of neurotransmitters and the tinnitus side. In patients with unilateral tinnitus the relative ratio of glutamine and glutamate were lower on the side of tinnitus than on the other side. Determination of the relationship between tinnitus and glutamine/glutamate concentration in the brain can help develop new treatment methods for patients, including pharmacological.

NEUROPEPTIDES

12.00 - 13.30
chaired by: **Christoph Schwarzer** (Medical University of Innsbruck, Austria)

Neuropeptides - Functional Role and Therapeutic Options in Epilepsy

Christoph Schwarzer[1], Alexandra Agostinho[1], Mario Mietzsch[2], Luca Zangrandi[1], Iwona Kmieć[1], Anna Mutti[1], Regine Heilbronn[2]

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Epilepsies are one of the most frequent neurological diseases with an incidence of about 50 new patients / 100 000 per year and a prevalence of about 5-8 patients per 1000 persons. Over the last three decades more than 40 antiepileptic drugs entered the market. Still, the number of patients who become seizure free through pharmacological treatment is still 30 % on average. Surgical removal of the epileptogenic focus is a final solution for some, but only 50 % remain seizure free after one year. Therefore, novel treatment options needed. In the quest of novel, disease-modifying treatment strategies neuropeptides and their receptors represent promising candidates. Neuropeptide receptors belong to the class of G-protein coupled receptors and are seen as neuromodulators, influencing the excitability of neurons and thereby controlling network activity. We and others have demonstrated

the importance of endogenous peptides like dynorphins in seizure control. We provided proof that Kappa opioid receptor (KOPr) agonists act beneficial in models of acute seizures and epilepsy. Most importantly, G-protein biased agonists offer pharmacological separation of beneficial and aversive effects of KOPr stimulation. Since long-term treatment is needed in epilepsy, viral vector derived, locally restricted expression of dynorphins by gene therapy may represent an interesting option. We therefore evaluated the potential of prolonged dynorphin overexpression as treatment of focal epilepsy in a pharmaco-resistant model of temporal lobe epilepsy (TLE). Therefore, we tested rAAV expressing either human preprodynorphin (pDyn-AAV) in a pharmaco-resistant model of TLE induced by injection of kainic acid into the dorsal hippocampus of mice. Dynorphins expressed in the epileptogenic focus suppressed generalized seizures and hippocampal paroxysmal discharges. By contrast control animals displayed 1-3 generalized seizures per day and frequent hpds. Moreover, treatment of mice 1 or 2 weeks after kainic acid injection conserved spatial learning ability (as tested by Barnes maze) up to 6 months, while control animals lost this ability already after 1 or 2 months. Our data provide clear evidence, that activation of KOR may potentially help at least some of the patients suffering from drug-resistant epilepsies.

Functional neuroanatomy of prodynorphin

Iwona Kmieć[1], Mario Mietzsch[2], Luca Zangrandi[1], Lill Andersen[3] , Thomas Rülicke[3] , Regine Heilbronn[2], Christoph Schwarzer[1]

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Dynorphins (Dyn) and kappa opioid receptors (KOR) are abundantly expressed throughout limbic brain areas and were shown to be involved in the regulation of emotion and stress control. In line with this, the Dyn/KOR system is implicated in the pathophysiology of depression and addiction. Understanding the highly complex organization of the Dyn/KOR system is a prerequisite for potential therapeutic intervention. To gain deeper insight into the functional neuroanatomy of the Dyn/KOR system, we implemented independent, yet complementary strategies based on restricted pDyn knock-out or pDyn re-expression within the extended amygdala. Such mice were tested in paradigms related to anxiety and stress-coping behaviour and cocaine-induced conditioned place preference. Stress induced reinstatement of the conditioned place-preference was observed in wild-type animals and several control groups. By contrast, no reinstatement was observed in animals deficient for pDyn in the central amygdala, or neurokinin B-positive neurons. Still these animals re-expressed place preference upon cocaine challenge. Interestingly, no differences in trait anxiety or stress coping behaviour was observed applying standard tests. Our findings suggest critical involvement of specific populations of dynorphinergic neurons in stress-induced relapse of drug abuse.

The role of opioid modulation of D1 dopaminoceptive cells in social contact initiation

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Opioid signaling plays a major role in controlling reward-related and social behavior. However, little is known about the contribution of opioid receptors expressed on specific neuronal cell types to the control of above mentioned behaviors. Here, we tested the role of μ and δ opioid receptors on D1 dopaminoceptive cells in reward-driven and social behavior. We have generated transgenic mice with miRNAs targeting the μ and δ opioid receptors specifically in cells expressing dopamine receptors D1. Knock-down efficiency and specificity was assessed by qPCR and immunostaining for the eGFP protein co-expressed with the transgene. Mutant mice had normal exploration, anxiety, saccharin consumption and morphine conditioned place preference. Interestingly, they showed a delay in approach to a novel mouse in social interaction paradigm. No difference in overall social interaction time, walking initiation or the time to find buried food was observed. Finally, when a novel object was used instead of a mouse no effect of the mutation was apparent. Hence, the observed deficit in social approach timing could not be explained by anhedonia, impaired exploration, anxiety or olfactory acuity. Our data indicate that opioid modulation of D1 dopaminoceptive cells plays a specific role in social contact initiation.

Searching for neuronal mechanism of neuropeptide's orexigenic action - relaxin-3 signalling in paraventricular nucleus of hypothalamus

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Relaxin-3 is a highly conserved neuropeptide expressed mainly by discrete neuronal populations in brain stem of vertebrates. Central injections of RLN3 and activation of its cognate receptor (RXFP3) in hypothalamus stimulate food intake in rats; with important brain homeostatic center - paraventricular nucleus of hypothalamus (PVN), considered the main site of RLN3/RXFP3 orexigenic action. We have shown that a selective RXFP3 agonist - RXFP3-A2, is a potent inhibitor of PVN neurons in vitro. Current studies utilise a combination of patch clamp recordings, immunostaining and tract-tracing techniques to delve deeper into relaxin-3/PVN interaction: from potential sex differences in magnocellular neurons sensitivity to RXFP3 activation, neuroanatomy of relaxin-3 system in hypothalamus, to ionic mechanisms of RXFP3-mediated inhibition. RXFP3-activation strongly inhibited majority of magnocellular PVN neurons (both oxytocin- and vasopressin-synthesising) in male and female rats, which is underlined by potassium conductance activation. Unexpectantly, immunohistochemical staining and tract-tracing studies revealed only sparse RLN3 fibers in the PVN and few RLN3-immunoreactive neurons innervating this area in both sexes. Our data for the first time provide the evidence for direct relaxin-3 action in hypothalamic paraventricular nucleus of rat, a putative neuronal mechanism of relaxin-3 stimulatory effect on food intake.
Funding: NSC, Poland UMO-2017/24/T/NZ4/00225, MSHE, Poland 0020/DIA/2014/43.

CANINE MODELS OF HUMAN NEUROCOGNITION

12.00 - 13.30
chaired by: **Attila Andics** (Eötvös Loránd University, Budapest, Hungary)

Imaging the awake dog brain

Attila Andics

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To better understand the evolution of the neural capacities for processing communicative signals in mammals, our group aims at exploring how the brains of different species analyze vocal and social cues from their conspecifics and other, phylogenetically distant but socially close species. Dogs present an ideal case for such investigations. An in-house developed training method enables us to run fMRI studies in awake, unrestrained, cooperating dogs. At the moment only very few groups can do that worldwide. In the first dog-human comparative brain imaging study we found that voice areas preferring conspecific vocalizations exist not only in primates, but also in dogs, and that basic biological meanings in vocal signals are processed species-independently (Andics et al., 2014). In another study on how dogs process human words (Andics et al., 2016), we showed that dog brains, just like human brains, can separately analyze and also combine lexical and intonational cues: what we say and how we say it. These findings show that awake dog brain imaging may open up new horizons for comparative mammalian social neuroscience. In the talk I present promising future directions in this research, and also some methodological challenges central to dog fMRI, with possible solutions.

Investigation of canine brain activity during sleep using noninvasive polysomnography

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Sleep is of vital importance for human well-being with brain activity during sleep being both related to individual characteristics and influenced by pre-sleep experiences. However, very little is known about other species (with the exception of laboratory rodents), despite the fact that non-humans' sleep is known to show both similarities to and differences from humans'. In an attempt to widen our knowledge about the function and evolution of sleep we developed a non-invasive polysomnography method that allows us to monitor dogs' brain activity during sleep. Here we present two studies using this method. First, we address memory consolidation in dogs and show that their sleep EEG spectrum changes after learning new commands (as opposed to practicing known commands), most notably in the delta range during non-REM sleep. Second, we show that social interaction with a human has markedly different effects on dog's sleep macrostructure (including a drastic change in REM sleep duration) depending on whether it is positively versus negatively valenced. Together our results validate the family dog as a model species for studying the effects of pre-sleep activities on EEG pattern under natural conditions and thus broaden the perspectives of the rapidly growing field of canine cognition research.

The dog as a model animal for studying sleep spindles – emerging evidence for an analogy regarding function and age-related changes between dogs and humans

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The study of dog behavior experienced a focus-shift to the brain and offered so far exciting tokens of comparability with humans, as is the case with verbal processing. However, little is known with regard to classical neural signatures that are long established in the literature on humans and rodents. Sleep spindles are well studied and documented bursts of activity traceable with surface EEG, which predict sleep-dependent memory recall in humans, rats and mice, and are promising biomarkers of aging in humans. They were only morphologically described in dogs, with diverging propositions about their characteristics. We were able to show with the aid of automatic detection that transient bursts in the sigma range, as opposed to other frequency ranges previously proposed for dogs, predict sleep-dependent learning in this species. In addition, we present preliminary findings suggesting that in dogs spindle amplitude declines with age, as in humans, but surprisingly spindle density increases. Next to confirming a functional role of sleep spindles in the dog for the first time, our findings imply that canine spindles are more comparable to the corresponding human oscillation than previously thought and may also prove helpful in evaluating the dog as a model for studying cognitive aging.

Cerebral activity in dogs related to perception of human faces

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Dogs are a unique model in the study of face perception because they not only have the cognitive ability to perceive dog faces but they have also developed a remarkable ability to extract valuable information from human faces. Our aim is to describe the cerebral correlates in the perception of faces in dogs, using fMRI. Functional images were acquired on a 3-T Philips scanner (TR/TE = 1750 / 30 ms with 2x2x3 mm resolution), seven awake, unrestrained and trained pet dogs participated. Each participant underwent 5 runs observing human faces and objects and 5 runs observing dog faces and objects. We found a posterior to anterior pattern of cerebral activity depending of the category of visual stimuli: occipital cortex to all categories, while temporal cortex responds to all facial stimuli -regardless of species-, and frontal cortex and caudate respond preferentially to human faces. Our findings are consistent with the importance of temporal cortex in face processing in primates and sheep. A neural specialization to process faces might represent an adaptation that helps dogs to overcome the challenges of living in an anthropogenic environment.

Decoding human emotional faces in the dog's brain

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Dogs can interpret emotional human faces and use them to modulate their behavior. But the cerebral correlates of this process are unknown. Our goal was to describe the cerebral correlates of the perception of emotional human faces in dogs, using fMRI. In Experiment 1, dogs (n = 8) observed happy and neutral faces, and we found increased brain activity in the temporal cortex and caudate related to happy faces. In Experiment 2, dogs (n = 4) observed human faces expressing happiness, anger, fear, or sadness. Using the resulting cluster from Experiment 1 we trained a linear support vector machine classifier, and found that it could only discriminate between happiness and all other emotions. So, with independent data we demonstrated that the cluster found in Experiment 1 is related to processing of happy faces, and not emotional faces in general. Also we evaluated the representation of anger, fear and sadness. A whole brain analysis of the fMRI time courses through a similar classifier allowed us to predict the emotion being observed by the dogs. Our results highlight the sensitivity of dogs' brains toward human emotions, since they are a social species adapted to live in an anthropogenic environment.

AUDITORY NEUROSCIENCE

12.00 - 13.30

chaired by: **Inga Griskova-Bulanova** (Vilnius University, Lithuania)

Processing of periodic sounds in the brain: importance and practical applications of auditory steady-state responses

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The analysis of brain responses to periodic auditory stimulation with modern neuroimaging methods stands as a valuable tool to explore brain functioning in norm and pathology. One of the most widely used options is the auditory steady-state response (ASSR) approach. During the talk, an overview of important applicational areas of auditory steady-state responses will be presented with particular focus on two major domains. First, the known task-modulatory effects on the ASSRs contrasting resting state, distraction from the sound and direct attention to the sound will be reviewed, as important for neuro adaptive technologies (i.e brain-computer interface) and for practical application in clinical settings. This will be followed by the presentation of known ASSR changes in neuropsychiatric disorders (particularly schizophrenia and bipolar disorder) with an emphasis on the relationship between the responses and cognitive functions. The importance and the advancement of the experimental settings for ASSR generation would be discussed.

How the level of consciousness can affect auditory steady-state responses

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Fluctuations of the level of consciousness from wakefulness to deep sleep or resulting from severe brain injury can profoundly alter brain activity. Auditory steady-state responses (ASSRs) have been proved to be sensitive to those variations, specifically in the loss of consciousness during sleep or general anaesthesia. In this talk we will present the results where we used specific deep NREM sleep phases as an unconscious state and then broaden the test domain to the clinical group of patients with prolonged disorders of consciousness (PDOC). We explored the sensitivity of low and intermediate rates of amplitude modulation tones, in the 4 - 40 Hz range. We observed diminishing of phase

coherency and power parameters of ASSRs during deep NREM sleep as compared to waking state. Moreover, we found correlation between ASSR parameters and scores obtained with Coma Recovery Scale - Revised clinical tool. We suggest the role of low and intermediate frequency ASSRs in discriminating states of altered consciousness. We will also discuss what these responses can tell us about brain responsiveness to external auditory stimulation in conscious and unconscious human brain.

Assessing auditory steady state responses by means of magnetoencephalography

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Auditory steady-state responses (SSR) originate from primary regions within the auditory cortex; they can be evoked by periodic stimuli and mirror important sound features like, for example, intensity, modulation depth, and frequency content. Here, we use magnetoencephalography (MEG) to investigate how SSR are shaped by properties of the stimulus itself, and by the processing characteristics of the auditory periphery. We demonstrate that the SSR magnitude is a cortical correlate of neural synchronization at subcortical processing stages which, in turn, depends on basilar membrane motion; this is also corroborated by physiologically plausible computer simulations of the cochlear mechanics. These findings suggest that the SSR are closely associated both with the stimulus peak factor, and with phase alignment in the cochlea. Furthermore, we demonstrate that consonant and dissonant sounds elicit specific SSR in the auditory cortex, and that the frequency content of these sounds is surprisingly well preserved in the neuromagnetic activity. Together, our results show that cortical SSR provide a highly precise representation of both stimulus attributes and peripheral processing properties; this might be exploited in future research to study the neural signature of hearing deterioration in normal aging or in auditory impairments like, for example, chronic tinnitus.

Auditory steady state responses in cochlear implant users

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Neural processing of the envelope modulations is important for speech understanding. Auditory steady state responses (ASSRs) are electrophysiological responses that can be used to quantify the sensitivity to amplitude modulations. Measuring ASSRs for discrete modulation frequencies specifies the temporal modulation transfer function (TMTF) and provides information at different levels of the auditory pathway. The objective of this research is a longitudinal study to investigate the process of auditory maturation after cochlear implantation in children. ASSRs, in a range of modulation frequencies relevant for speech (phoneme, syllable rate) will be used as an objective measure to assess the progress of rehabilitation and will allow to monitor the auditory maturation in cochlear implant (CI) users. In this first maturation study, Electrically evoked auditory steady state responses (EASSR) were measured in EEG recordings from the TMTF in 5 adult CI user (Gransier et al. 2016). With the application of appropriate artifact reduction techniques, EASSRs can be effectively detected in CI users. At the conference results of this preparatory study in adults and new analysis approaches intended to quantify the auditory maturation will be discussed. Data for a range of modulation frequencies will be presented with focus on the phase-locked component of the response.

Implication of synchronous spiking to the auditory steady-state response interpretation: an EEG study

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Periodic stimuli are widely used to study perceptual and neuronal responses in animals and humans. However, the neuronal processes involved are not well known. This study proposes new elements to determine the neural coding

involved in auditory steady states responses (ASSR) and to give support to either entrainment or superposition theory. EEG (64 electrodes) was recorded in 70 subjects during the presentation of single auditory clicks and click trains at different stimulation rates (12-55Hz). The minimal pre-processing and filtering was applied to preserve the dynamics of the neural response. Power, evoked response waveform, phase and phase coherence analyses were performed for each stimulation rate and for isolated clicks. This systematic analysis revealed the importance of synchronous spiking in the evoked response. The observed spiking is stimulus-locked and can be removed from the EEG signal in order to reveal the entrainment in response to periodic stimulation. The two mechanisms – entrainment and superposition- occur concurrently in the EEG signal during ASSR and the commonly used methods cannot disentangle them. This study gives new direction to separate stimulus-locked contribution from entrainment.

POSTER SESSION II:
14.15 – 15.15
pages: 85-111

PANEL DISCUSSION: **INDUSTRY MEETS ACADEMIA – WHAT ARE CAREER OPTIONS?**
15.15 – 16.00
chaired by: **Dagmar Ehrnhöfer** (BioMed X Innovation Center, Heidelberg, Germany)

panelists: **Phil Skolnick** (CSO Opiant Pharmaceuticals, Santa Monica, USA), **Bastian Hengerer** (Boehringer Ingelheim, Germany)

SYSTEMS NEUROSCIENCE
16.45 – 18.15
chaired by: **Marcin Szczot** (NIH/NCCIH, Bethesda, USA)

Under Your Skin: Molecules and Cells for Touch and Pain

Alexander Chesler

National Center for Complementary and Integrative Health, NIH, Bethesda, USA

The somatosensory system provides us with the ability to detect touch, temperature, and painful stimuli. Dr. Chesler will describe how studying patients with a rare and inherited disease helped reveal a key molecule for detecting touch and proprioception, the so-called “sixth sense” that enables the awareness of one’s body in space. He will also discuss how recent advances in genetics and functional imaging in model systems are being leveraged to uncover mechanisms involved in acute and chronic pain.

Immunohistochemical classification of neurons in layer V of the medial entorhinal cortex with proven convergent input from the subiculum and the retrosplenial cortex

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Neurons in superficial layers of the medial entorhinal cortex (MEC) provide a major input to the hippocampus. The subiculum (Sub) - one of the hippocampal output structures - mainly sends a projection to the layer V of MEC. Layer V also receives a dense input from the retrosplenial cortex (RSC), another brain’s navigational system part. Layer V of MEC can be subdivided into a superficial layer Va, and a deeper layer Vb. Neurons in these sublayers express different

transcription factors Etv1 and Ctip2, respectively. We aimed to analyse the morphology and transcriptional identity of neurons that had convergent input from Sub and RSC, established with in vitro electrophysiology. Layer V MEC neurons were investigated using the following protocols: i/ immunohistochemistry methods to stain them for the respective transcription factors. Therefore, establishing an accurate protocol constituted one goal of the project; ii/ confocal imaging to visualize them; iii/ morphological analysis to establish the type of the neurons. The Ctip2 staining protocol was established successfully and we found that the inspected neuron population consisted mostly of horizontal and pyramidal neurons. Most of horizontal cells were located in layer Va, whereas the majority of pyramidal cells were found in layer Vb.

Prefrontal cortex neuronal activity underlying fear extinction

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Medial prefrontal cortex (mPFC) is known to be engaged during the acquisition as well as extinction of cued conditioned fear. At first it has been shown that dorsal part of the prefrontal cortex, prelimbic cortex (PL), is necessary for the expression of the conditioned fear response, freezing, while more ventral region, infralimbic (IL) cortex, is involved in the consolidation of the extinction memory. In the present study we recorded in dorsal and ventral regions of the mPFC single cell activity during extinction session. Extinction sessions were long enough to induce large reduction of fear expression upon CS (conditioned stimuli) presentation. We were able to observe differential CS-evoked responses depending on the dorso-ventral axis of the mPFC. CS-evoked activity of the mPFC diminished over the extinction session, with ventral mPFC units activity being more stable across the extinction session. CS-evoked patterns of activation were very similar for PL as well as IL. These results suggest different involvement of the mPFC in processing the extinction of conditioned fear. To further investigate to relation and the influence of the PL on the IL we have planned to conduct the optogenetic experiments and we will be showing the preliminary results of those experiments.

Prefrontal cortex catecholaminergic activity regulates cue-induced cocaine craving

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Medial prefrontal cortex (mPFC) hypoactivity correlates with cocaine craving. The prelimbic (PrL) part of the mPFC, engaged in cognitive processing of conditional stimulus (CS), is directly modulated by the afferent fibers arising from the dopaminergic ventral tegmental area (VTA) and noradrenergic locus coeruleus (LC). Thus we examined the effect of catecholaminergic activity in the PrL cortex on CS-induced cocaine craving. We used SD-Th- Cre tm1sage rats transduced with channelorhodopsin (ChR2)-containing adenoviral vector into the VTA and LC. We studied effects of brief photo-stimulation of the ChR2-expressing Th+ axon terminals in the PrL cortex on CS-induced cocaine seeking under extinction conditions. Effectiveness of Th+ neurons transduction was verified using immunostainings and in vivo single unit recordings. In control studies, we performed CS-induced food-seeking, real time place preference, ultrasonic vocalizations (USV) recordings, intracranial optical self-stimulation and open field test. Our results indicate that photo-stimulation of catecholaminergic axon terminals in the PrL cortex during CS presentation modulates CS-induced cocaine seeking. In contrast, photo-stimulation had no effects on real time place preference, USV, self-stimulation, locomotor activity or anxiety-like behaviors. Our data suggest that catecholaminergic activity in the PrL cortex selectively process CS effects on cocaine craving during abstinence.
Acknowledgment: Polish National Science Center grant UMO-2014/13/B/NZ4/00146

NEUROSCIENCE OF LANGUAGE

16.45 - 18.15

chaired by: **Marcin Szwed** (Jagiellonian University in Krakow, Poland)

Neural signatures of reading and spelling deficits in children

Agnieszka Dębska[1], Katarzyna Chyl[1], Gabriela Dzięgiel[1], Agnieszka Kacprzak[1,2] Magdalena Łuniewska[1,2] Joanna Plewko[1], Artur Marchewka[1], Anna Grabowska[1], Katarzyna Jednoróg[1]

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It is reported that children with dyslexia (with both spelling and reading problems) have hypoactivated left hemisphere language regions. However it remains unknown which of the reported alterations could be attributed to reading and which to spelling disorder. This is a first large fMRI study that aimed at identifying the basis of reading and spelling deficits in brain activity. We examined 170 Polish-speaking children (aged 8-13) with different cognitive profiles: typical in reading and spelling (n=65), with isolated reading (n=20) and spelling impairment (n=30) and with deficits in both spelling and reading (n=55). All participants performed a battery of phonological tasks in fMRI. Series of two-ways ANOVAs were used to distinguish the unique contribution of spelling and reading effects in each task. The main effect of reading was found in underactivation of the left temporo-parietal cortex (dorsal stream), connected with the phoneme-to-grapheme mapping whereas main effects of spelling in the left occipito-temporal cortex (ventral stream) associated with the orthographic representations. Additionally, compensatory mechanisms in the right hemisphere were present in ventral regions for poor readers and in dorsal for poor spellers. This is the first direct evidence of differences between spelling and reading deficits in a phonological brain network.

Phonological awareness in children developing dyslexia - a longitudinal fMRI study

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We investigate how learning to read affects the neural correlates of phonological awareness. We focus on typically reading and dyslexic children, who either present or lack familial history of dyslexia. Beginning readers (N = 92) repeated reading-related tasks three times with a year-long interval, and their brain activity during auditory rhyme judgement was measured at first and last time-point. We contrast children who developed dyslexia (n = 20) with typical readers (n = 72). Independently, we compare children who had familial history of dyslexia (FHD+, n = 56) with children who did not present such risk factor (FHD-, n = 36). We found that dyslexics show decreased reading and phonological skills even at the very beginning of education. Literacy acquisition reduced brain activation to phonological awareness in typical readers in left dorsal structures, whereas in dyslexia it increased activation of right dorsal areas. FHD+ and FHD- children present similar level of reading and phonological skills. Learning to read reduced brain activation to phonological awareness in FHD- children in left perisylvian areas, whereas in FHD+ it increased activation in left motor and somatosensory cortex. As beginning readers, FHD+ children despite typical phonological skills show extensive hypoactivation in the speech processing cortex.

Voxel and surface based morphometry in elementary school late talking children with and without developmental dyslexia

Agnieszka Kacprzak[1,2], Katarzyna Chyl[1], Agnieszka Dębska[1], Gabriela Dzięgiel[1], Magdalena Łuniewska[1], Joanna Plewko[1], Anna Grabowska[1], Ewa Haman[2], Katarzyna Jednoróg[1]

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Late time of speech emergence constitutes a risk factor for later reading deficits (Scarborough & Dobrich, 1990) and brain structure alterations (Raschle et al., 2015). In order to check common and distinct neuronal correlates of late speech emergence and dyslexia we investigated gray matter volume (GMV) and brain surface (two methods can give complementary information) in 119 elementary school children aged 7.23-10.7 (M=9.14, SD=0.61). Four groups were selected: dyslexic late talkers (N=17), typically reading late talkers (N=26), dyslexic on-time talkers (N=38) and typically reading on-time talkers (N=38). The preliminary analyses using voxel based morphometry (VBM) showed increased GMV in late talkers' right inferior frontal gyrus (IFG), consistent with the role of IFG in speech processing (Giraud & Poeppel, 2012). Late talkers showed also increased GMV in left planum temporale, a crucial region for both speech comprehension and production. The main effect of dyslexia was found in increased GMV in right gyrus rectus, a structure less activated by dyslexics in a phoneme deletion task (Pernet, et al. 2009). There was no interaction found between the age of speech emergence and dyslexia on GMV. The results mentioned above are going to be discussed along with the results of ongoing surface based analyses.

Functional changes during the acquisition of spoken and written Greek

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Learning a second language (L2) involves visual and auditory processing of initially meaningless stimuli. Integration of sensory information into the ventral and dorsal streams of the language processing network allows access to conceptual-semantic information, and to a sensory-motor interface (Hickok, 2012). Proficiency mediates changes in the L2 processing network (Wartenburger et al., 2003). In the present study, we investigated changes in functional plasticity in response to lexical and semantic decisions in participants, enrolled in a 8-months Greek course. Participants were invited to 5 fMRI sessions before, during and after the course. Tasks in the scanner were presented in L1 (Polish), and L2 (Greek), auditory and visually. We analyzed the longitudinal data set focusing on the development of L2 network relative to L1 network over time. Unique effects of time in the L2 network in the visual modality are driven by the first months of instruction. In the auditory modality, these effects are weakened or absent. For visual processing we observe time-related changes within the conceptual-semantic interface (inferior temporal gyrus), the sensory-motor interface (supplementary motor area, precentral gyrus) and fusiform gyrus. These networks are comparable to those observed in beginning readers for L1 (Chyl et al., 2017).

EMOTIONAL MODULATION OF ATTENTION AND PERCEPTION

16.45 - 18.15

chaired by: **Hadas Okon-Singer** (University of Haifa, Israel)

Neural Modulation of Emotional Reactions: Focus on Attention and Personality

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Models of emotional processing highlight the interactions between emotional and attentional systems. These views are based on evidence that emotional information is prioritized and impact attentional functions, as well as evidence that attention and control mechanisms mediate reactions to aversive stimuli. In this talk, I will present evidence that attention mechanisms and anxiety-related personality traits and tendencies modulate behavioral, neural and autonomic (basic motor-related blood pressure) reactions to highly-negative material. I will further discuss the possible role of the thalamic pulvinar nucleus in this process. Finally, I will present evidence for abnormal reactions to aversive information among individuals with high subclinical levels of anxiety and depression, as well as those diagnosed with attention deficit hyperactivity disorder (ADHD). Taken together, these findings suggest that individual characteristics shape the connectivity within a neural network that is involved in the reactions to emotional stimuli, and that activation in this neural network is further modulated by attention.

Truth from within: physiological responses to emotionally charged photos of real-life events predicts judgments of photo authenticity

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Research has consistently demonstrated that affect influences the perception and appraisal of visual information but often neglects the ecological validity of the stimuli used. In a period of intensive exposure to digital media and "post-truth" debates it is crucial to understand how people form judgments of picture authenticity. In a series of studies, we explored the hypothesis that emotional engagement and physiological responses to photos of real-life events informs cognition and biases the tendency to consider the pictures as real or fake. Using a participant-by-participant and trial-by-trial analysis method, we show that participants' subjective experience of arousal and cardiac reactivity to emotionally charged photojournalistic stimuli predicts their individual judgments of photo authenticity in a later "real vs fake" surprise task. These studies provide first evidence to the suggestion that what we consider to be real may be partially grounded in bodily and affective responses to the perceived stimuli.

Freezing modulates early visuocortical activity in humans

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An adaptive response to threat requires optimal detection of relevant sensory cues.This optimization is thought to be aided by freezing – an evolutionarily preserved defensive state of immobility that is accompanied by parasympathetically mediated fear bradycardia. Behavioral observations in humans and animals have shown increased visual sensitivity during freezing, particularly for coarse visual information, but underlying neural mechanisms remain unclear. We induced freezing in healthy volunteers using threat of shock and measured threat-related changes in stimulus-independent (baseline) and stimulus-evoked visuocortical activity to low- and high-spatial frequency gratings using fMRI. We found a threat-induced increase in baseline visuocortical activity that was retinotopically nonspecific, and accompanied by increased connectivity with the amygdala. This increase was positively correlated with fear bradycardia, and accompanied by increased functional connectivity between the amygdala and PAG - core regions in generating freezing. Retinotopically-specific visuocortical responses to gratings did not differ between threat and safe conditions across participants. However, individuals with better discrimination performance for low-spatial frequency showed reduced stimulus-evoked V1 responses under threat. These findings identify pathways for neural integration of visual and defensive processes during freezing, and imply that anticipatory fear states such as freezing may contribute to increased visual sensitivity by enhancing background visuocortical activity.

The role of the right posterior parietal cortex (PPC) in emotional attention

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The right posterior parietal cortex (PPC) is implicated in spatial attention, but its specific role in emotional spatial attention remains unclear. In the present talk, I will discuss studies in which we used transcranial magnetic stimulation with a fear conditioning paradigm to test the role of the right PPC in attentional control of threatening stimuli. Results from these studies suggest that the right PPC is specifically involved in disengagement of attention from threat and less in attentional capture by threat. The findings are interpreted in terms of a neurobiological model of emotional attention.

Independent vs. interactive effects of emotion and basic visual features during word reading

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Previous electrophysiological studies have reported increased brain activity in response to emotional relative to neutral visual stimuli, suggesting preferential attention allocation as a function of biological relevance. However, it is unclear whether this enhanced activity reflects independent processing of emotional content or, instead, emotion amplifies the analysis of basic low-level visual properties. This pre-registered event-related potential (ERP) study explored the impact of emotional valence on physical size and contrast during word reading. Results showed strong and reliable effects of low-level features at the level of word detection and discrimination (P1 and N1 components), attention allocation (EPN), and memory formation (LPP). Emotion only had a small additive role in modulating amplitude values of the EPN component when font size was manipulated. These results suggest that the social relevance of learned symbolic items might not communicate the same urgency of biologically salient stimuli and, consequently, its interaction with low-level properties may be contingent upon other factors (e.g., task demands).

PLENARY LECTURE:
18.15 - 19.15

Gating pain; from normal to pathological transmission

Yves De Koninck

Laval University, Québec, Canada
CERVO Brain Research Centre, Québec, Canada

A key to the future of chronic pain management is to understand the neurobiological mechanisms that govern how our brain adapts and maladapts to an imbalance in our sensory system because of an injury to our body or a disease condition. This is critical to be able to target the root cause of abnormal, pathological pain for therapeutic development. The drama is that most drugs used for treating chronic pain to date have emerged from off-label use and are therefore not designed to directly address the source the problem. My lab has pursued to identify key mechanisms explaining aberrant pain processing by the nervous system as well as co-morbidities that develop from sustained pain hypersensitivity. This includes the discovery of impaired inhibition resulting from chloride dysregulation in neuropathic pain conditions, leading to cross-talk between sensory channels and ectopic activity possibly underlying spontaneous pain. I will illustrate how such discoveries open new perspectives to understand abnormal pain and how it affects our thinking for therapeutic design. I will also describe how this work has led us to unravel some basic mechanisms underlying the adaptive and maladaptive response to opioid treatment, revealing that opiate tolerance, hyperalgesia and withdrawal result from distinct mechanisms. Each can be targeted independently, without affecting the analgesic effect of opioids, introducing avenues for adjuvant therapies to improve prolonged opioid use. I will conclude with some outlooks on prospects for pain research, exploiting light to probe and manipulate pain circuits, linking cellular and molecular studies with behavior, an essential step towards improving translation of basic research findings into clinical applications.

APRIL 22, 2018 (Sunday)

PLENARY LECTURE:
9.30 - 10.30

Imaging cell biology at work in the awake mouse brain

Thomas Kuner

University of Heidelberg, Germany

Cell biological mechanisms are typically studied in cell culture models while current techniques allow for direct observation of "cell biology at work" in the intact organism. To what extent can results obtained in the cell culture dish be extrapolated to the in vivo state, here referring to brain function in anaesthetised and awake mice? This question will be explored in two different scenarios. (1) In vivo imaging of large dense core vesicle trafficking revealed that most transport features were similar to measurements done in cell cultures, yet they showed additional features such as a slowing of transport at presynaptic en-passant boutons. Transport directionality could be identified by simultaneous imaging of microtubule plus-end extension and differed between anaesthetised and awake states. (2) The distribution of intracellular chloride and pH was imaged in vivo in layer 2/3 pyramidal neurons of motor cortex. This is important, because intracellular chloride regulation is tightly linked to pH, cation homeostasis and metabolism, factors only reliably implemented in the intact tissue. We found an average resting chloride concentration of 6 mM that increased to approximately 22 mM when deleting KCC2 in a sparse subset of neurons. In contrast to previous reports, chloride was homogeneously distributed along the somato-dendritic domain. In summary, these examples illustrate that imaging cell biological mechanisms in the intact animal is required to extrapolate results obtained in the culture dish to in vivo brain function in a systematic and rigorous manner.

SYNAPTIC PLASTICITY

11.00 - 12.30
chaired by: **Anna Błasiak** (Jagiellonian University in Krakow, Poland)

Mechanisms and consequences of kainate receptor regulation for synaptic plasticity, health and disease

Jeremy Henley

University of Bristol, UK

Kainate receptors are present at both pre and postsynapse and are key regulators of synaptic transmission and neuronal excitability. Importantly, KAR malfunction implicated in many neurological diseases including epilepsy and autism. In this presentation I will discuss some recent work from our lab on novel actions of kainate receptors that highlight previously unexpected roles of kainate receptors in neuromodulation and synaptic plasticity.

Activity-dependent trafficking of PSD-95 after LTP and LTD

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The ability of the nervous system to learn and form new memories, hence adapt, is believed to be based on activity-dependent modifications of synaptic connections. These are accompanied by their morphological alterations. It is not yet known what exact molecular mechanisms underlie these morphological changes. PSD-95, a major scaffolding protein of the postsynaptic density (PSD) is involved in the regulation of LTP (long-term potentiation) and LTD (long-term depression), two major forms of synaptic plasticity. Trafficking of PSD-95 out of dendritic spines is regulated by phosphorylation of serine 73 (S73) via αCaMKII. Here we investigated PSD-95 trafficking after chemically-induced

LTP and LTD in vitro in the stratum radiatum of CA1 hippocampal neurons with immunofluorescence. The level of total PSD-95 decreased 30 min after both LTP and LTD. Furthermore, using AAV transfection approach we have found that unphosphorylable PSD-95 S73A overexpression prevented elimination of PSD-95 after LTP but not after LTD. These results indicate that activity-dependent trafficking of PSD-95 out of dendritic spines is a common mechanism for both LTP and LTD. However only in LTP this process is regulated by phosphorylation of PSD-95 serine 73 via αCaMKII. Overall this study contributes novel finding towards better understanding of molecular mechanisms of memory.

Synaptic plasticity of natural and addictive rewards

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Since few years, it is claimed that drug addiction is a type of Hebbian learning, similar to natural reward learning. In this process, paired activation of neurons contribute to synaptic plasticity and it is believed that occurring changes are encoded information - engrams. However, drugs of abuse hijack these engrams and create new durable memories. Thus, in this study we were testing whether the initial exposure to addictive substances shares similarities with natural form of learning. As a model of "addictive" learning we chose cocaine intraperitoneal injections (IP), while sucrose self-administration mimicked the natural one. We were performing series of experiments on a specific brain pathway, known from processing positive memories: connection between posterior Basolateral Amygdala (pBLA) and Central Medial Amygdala (CeM). To ensure pathway specificity, we were injecting viruses into pBLA allowing for the channelrodopsin-2 expression in neurons. Synaptic changes were tested by whole-cell patch clamp electrophysiology recordings with use of an optogenetic stimulation. Our results indicate that indeed both cocaine and sugar change the pBLA-to- CeM pathway in a similar way. We observed generation of silent synapses (with stronger effect after cocaine exposure), which are immature synaptic contacts functioning as substrates for increased learning.

A multi-fractal approach for studying neuronal activity

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In this study, we provide the results of the extracellular field potential time series analysis using the multifractal detrended fluctuation analysis (MF-DFA). Single spiking neurons and local field potentials (LFPs) were collected from the primary visual cortex of awake macaque monkeys. Using the MF-DFA on the raw data of LFP signals, we first estimated generalized Hurst exponent h(q) and the singularity spectrum, f (α). We then introduce the integral of singularity spectrum, as a new measure for inferring the activity of spiking neurons. The obtained tuning curves measured with this method were consistent with the tuning of the single spiking neurons recorded simultaneously from the same electrode tip. Moreover, we found that a low pass filtration of the data under 1000 Hz will almost flatten the h(q) vs. q curve which indicates that nonlinear features of the signal (i.e. spikes) are strongly suppressed when it is highly filtered. This finding can be interpreted as the spikes do not leak in the LFP. Finally, by comparing the generalized Hurst exponent of the original time-series with the shuffled, surrogated, and ranked-wise Gaussian signal, we have elaborated that multifractality is mainly due to the linear/nonlinear correlations that exist in the analyzed time-series.

MOTOR ACTIVITY

11.00 - 12.30

chaired by: **Rob van der Lubbe** (University of Twente, The Netherlands)

How to demonstrate a normal contralateral organization of hand-motor areas at an individual level for children affected by Cerebral Palsy?

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Unilateral cerebral palsy (CP) is a disorder that often affects the ability to move one of the upper limbs in a proper way. CP may be caused by brain damage at an early stage of a child's life when there is still high neuroplasticity. As a consequence, the affected limb may get controlled by the ipsilateral rather than the contralateral hemisphere. Rehabilitation techniques may benefit from knowing which hemisphere controls the affected limb. Awsingle-participant EEG (electroencephalographic) approach was followed to enable such an assessment. EEG was measured while a participant performed a cued motor task. The required response hand was kept constant per block. Five blocks for each hand were administered in a randomized order. We focused on differences in μ power between the left and right hemisphere preceding response execution. The method of Bulté and Onghena (2008) was employed to perform single-case randomization tests. Analyses on the data of three participants consistently revealed a statistically significant reduction in contralateral μ power. This reduction may reflect a release of cortical inhibition that is required for executing the response. Our results demonstrate that individual EEG data can be used to demonstrate a normal cortical organization of hand-motor areas.

Examining the motor observation and motor imagery capacity of typically developing children and children with unilateral cerebral palsy – an EEG study

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Studies with adult stroke patients have shown that explicit motor imagery (MI) can be effectively used within rehabilitation programs. However, studies addressing the effect of MI-based interventions in children hint at a compromised MI ability in children with motor disabilities. To determine whether children with unilateral cerebral palsy (uCP) would benefit from MI training, two studies were conducted. In study one, the effect of age on the MI ability in children (aged 6-12 years) was examined. In study two, the MI ability in children with uCP was examined. In both studies, the EEG signal was recorded during an EO (eyes open), an AO (action observation), a ME (motor execution) and a MI condition. We examined the mu rhythm, which is normally suppressed during AO, ME and MI compared to EO. In control children, mu-suppression was observed in both the AO and MI conditions at all ages. In children with uCP, mu-suppression was also observed during AO and MI. However, this mu-suppression was only observed over the non-affected hemisphere. Interestingly, the affected hemisphere only showed mu-suppression during AO. Our findings suggest that MI ability in children with uCP is compromised. However, AO might be a useful approach in future rehabilitation programs.

Decoding functional grasps of tools from brain activity: An fMRI Multi-Voxel Pattern Analysis study

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Utilizing multivoxel pattern analysis (MVPA) we investigated neural networks underlying preparation of complex manual movements involving tools. We used data from 20 participants who planned functional grasps of tools with either their dominant (right) or non-dominant (left) hands. The analyses –region of interest (ROI), and searchlight– showed patterns of activity resembling those obtained with traditional subtraction contrasts. The key areas involved subdivisions of the intraparietal sulcus (IPS), supramarginal gyrus (SMG), lateral occipital (LO) cortex, dorsal premotor cortex (PMd) and mid-to-caudal superior parietal lobule (SPL). Nevertheless, MVPA also revealed a more critical contribution from anterior SMG, which is known for integration of signals from IPS and posterior SMG for grip formation, the retrieval of physical object properties and knowledge of their mechanics, as well as the involved manipulation. Outcomes within LO indicate that MVPA is particularly sensitive to representations of visual object properties. Finally, the revealed contribution from superior parieto-frontal cortices is consistent with their role in processing variable affordances, i.e., transient representations of tool features for generating proper hand postures. All in all, by putting emphasis on different aspects of information processing, MVPA turns out to be a great tool providing profound insights into the mechanisms underlying functional grasp formation

Neural underpinnings of actions involving complex tools: an fMRI study

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Tools extend our capabilities to efficiently interact with an environment and tool-use skills are mediated by our brains' abilities to transform bodily movements into mechanical actions of tool parts. Whereas simple tools were extensively studied, little is known about neural underpinnings of complex tool use, which requires compound, often multi-phase motor-to-mechanical transformations. We utilized functional magnetic resonance imaging (fMRI) in 20 right-handed participants to investigate neuronal activity underlying planning and execution of functional grasping and subsequent usage of complex tools vs. actions involving simple tools and control, non-tool objects. In two scanning sessions, wherein the right and left hands were tested separately (counterbalanced), we studied higher-order, hand-independent mechanisms underlying interactions with such complex objects. Within the left-lateralized parieto-frontal network involved in the control of actions with tools regardless of their complexity, the anterior supramarginal gyrus and anterior-to-mid intraparietal sulcus were involved significantly more in performance of functional grasps of complex tools. These outcomes are in line with the current literature positing that the left inferior parietal lobule is a key region not only devoted to the control of tool use but also for computations underlying prospective conversion of motor-to-mechanical coding for later execution of compound actions with complex objects.

FACTORS AFFECTING EMOTIONAL PROCESSING

11.00 - 12.30

chaired by: **Mirek Wyczesany** (Jagiellonian University in Krakow, Poland)

A social brain: How attributed social context modulates verbal emotional feedback processing

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Recent findings reveal that attributions of social context amplify early (P2/EPN) and late (P3/LPP) event-related potential (ERP) correlates of emotional language processing. In the absence of any physical stimulus change, ERPs are considerably amplified, when single word messages are perceived as directly addressing experimental participants. Effects are larger when the senders are made out to be human rather than machines and larger again for humans

with greater attributed expertise. Particularly at late processing stages, relevance induced by variations of communicative context acts upon emotional stimuli in a multiplicative fashion. Convergent fmri data reveal activation of subcortical structures such as the amygdalae and the ventral striatum by contexts that are perceived as more relevant as well as by emotional contents. Finally, contents embedded in even minimal social context are incidentally remembered better than the same contents presented for explicit learning. Together, these findings reveal how evolutionarily old mechanisms of biological motivational systems are conserved in the processing of symbolic representations of emotion and further extended to social motivational relevance that plays a prominent role in humans as a group-living species.

Noninvasive stimulation of the ventromedial prefrontal cortex enhances pleasant scene and face processing

Constantin Winker[1], Maimu A. Rehbein[1], Dean Sabatinelli[2], Mira Dohn[1], Julius Maitzen[1], Carsten H. Wolters[1], Volker Arolt[1], Markus Junghöfer[1]

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Affective visual processing is strongly influenced by top-down processing of cortical areas like the ventromedial prefrontal cortex (vmPFC). In previous fMRI and MEG studies in our lab, excitatory transcranial direct current stimulation (tDCS) of the vmPFC led to enhanced processing of appetitive compared to aversive scenes while an opposite activation pattern was found after inhibitory stimulation. Towards affect-generalization, we here tested modulatory effects of excitatory and inhibitory vmPFC stimulation on processing of emotional faces. Magnetoencephalographic and behavioral results support the idea that the affect-modulating impact of this region can be tuned in excitatory and inhibitory fashion by means of non-invasive tDCS.

On the impact of ventromedial PFC stimulation on emotional picture processing in major depression: Magnetoencephalographic correlates

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Major depressive disorder (MDD) patients often show biases towards negative emotional material as well as abnormalities in distributed neural network activation that may be ameliorated with successful treatment. Recent magnetoencephalography (MEG) studies presenting positive and negative emotional scenes revealed an overall reduced activation of parietal and temporal cortices in MDD patients vs. controls at baseline, which normalized under effective antidepressant treatment. Here, we further investigated the neural correlates of emotional picture processing in MDD and its course across successful treatment. In addition, we evaluated the contribution of transcranial Direct Current Stimulation (tDCS) of the ventromedial prefrontal cortex to a normalization of neural network activation. Two groups of MDD patients undergoing current inpatient treatment and additionally two weeks of daily verum or sham tDCS stimulation respectively viewed emotional scenes before and after treatment in the MEG. Results replicated the temporo-parietal hypoactivation that normalized with effective treatment and suggested awsignificant contribution of prefrontal tDCS. They also showed valence-specific changes in activation of prefrontal cortex regions. The findings point towards dysfunctional affective visual processing in MDD and reveal specific activation patterns that may potentially help to predict treatment success.
This work was supported by the Interdisciplinary Center for Clinical Research (IZKF; Ju3/024/15).

How much reappraisal is in reappraisal? The role of unspecific factors in attenuating emotional response

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Reappraisal is an emotion regulation strategy which involves changing the interpretation of emotional stimuli. It decreases measures of negative affect together with markers of emotional processing. However, emotional

processing can also be attenuated by various tasks requiring cognitive effort. As such, the effects of cognitive load in understanding of reappraisal results has been neglected. We would show that changing the interpretation of the emotional stimuli is the one but not the only factor that has a power to attenuate emotional processing in the reappraisal procedures. Another factor attenuating emotional processing during reappraisal is an unspecific cognitive load. Our conclusions are supported by two studies where cognitive change of unpleasant pictures and noxious stimuli was investigated. Using classic ERP and source localization methodologies we show importance of non-specific factors in attenuating emotional responses in both visual and pain domain.

Uninstructed emotional regulation: implicit reappraisal attenuates emotional processing

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Nonconscious strategies for regulating emotions, despite their predominance in everyday life, received little scientific attention so far. In the study we explore neural substrates of two implicit modulatory strategies: pre-appraisal and implicit induction of reappraisal goals. Using classic ERP analyses as well as source localization methods we show that they are able to modify emotional responses, even though the subjective ratings of emotional stimuli remain unchanged. The possible designs of control conditions are also discussed, as factors which may implicitly affect neural responses to emotional content.

POSTER SESSION III:
13.15 – 14.30
pages: 113-139

NEUROPATHOLOGY

14.30 - 16.00
chaired by: **Dagmar Ehrnhöfer** (BioMed X Innovation Center, Heidelberg, Germany)

Modelling Alzheimer's disease-related tau pathology - from human brain dysfunction to in vitro models and back again

Dagmar Ehrnhöfer

BioMed X Innovation Center, Heidelberg, Germany

Many forms of neurodegenerative disease are chronic, late-onset conditions that take decades to develop in human patients. Yet, in the lab, both in vitro and in vivo systems that recapitulate the most important features of the disease in a shorter timespan are needed to study disease pathways and develop urgently needed therapeutics. In Alzheimer's disease (AD), researchers additionally face the challenge of modelling a predominantly sporadic disease with complex genetic risk factors that is characterized by two main neuropathological hallmarks, the accumulation of beta-amyloid plaques and neurofibrillary tangles composed of tau protein. Tau is heavily modified with a large variety of post-translational modifications (PTMs), and dysregulation of PTM pathways has been associated with AD. My laboratory is focussing on post-mortem human brain samples to define disease-associated changes in tau, with a focus on early disease stages. We then use neurons differentiated from patient-derived iPS cells, where we are able to recapitulate these changes in vitro. Quantitative and sensitive ELISA methods ultimately allow for high-throughput screening to uncover modulators of tau PTM pathways, without the need for the expression of tau mutants that are often used to evoke phenotypes in animal model systems. Hits uncovered in such in vitro approaches can then be validated by targeted studies in human brain samples, confirming their disease relevance. Our work demonstrates that iPS-derived human neuron cultures are a powerful tool for the discovery of disease-relevant pathways and patient cells can recapitulate disease phenotypes even in the absence of known pathogenic mutations.

Asparagine endopeptidase cleaves tau at a novel cleavage site in vivo

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Truncations of the microtubule-binding protein tau are associated with enhanced aggregation propensity and thus with several neurodegenerative diseases displaying abnormal tau aggregation, including Alzheimer's disease (AD). The lysosomal enzyme asparagine endopeptidase (AEP) can cleave tau in the brains of AD patients at N368. Furthermore, AEP activity is upregulated in the brain with aging and in AD patients. Using a mass spectrometry approach, we detected a novel AEP cleavage site for tau at N167 in AD patient brain samples, in addition to the reported cleavage at N368. Cleavage of tau by AEP in a cell model system generates the tau168-368 fragment. This process can be blocked by site-directed mutagenesis of N167 and N368. Tau fragmentation is furthermore blocked with the lysosomal acidification inhibitor ammonium chloride, suggesting that proteolysis by AEP occurs mainly within lysosomes. While we confirm tau168-368 in human brain, fragment levels do not differ significantly in the soluble fraction between control and AD patient samples. However, as tau168-368 is prone to aggregation in vitro, it may accumulate in the insoluble fraction in AD brain. While tau proteolysis by AEP is a physiologically relevant process, its relevance for the pathogenesis of AD and other tauopathies thus remains to be established.

Ultrastructural rescue effects of matrix metalloproteinase 9 inhibition in Fragile X Syndrome mouse model

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Lack of expression of Fragile X Mental Retardation Protein (FMRP) is the most common monogenetic cause of autism. It results in Fragile X Syndrome (FXS), characterized by a wide array of social and intellectual impairments. Clinical studies on FXS patients and experiments in Fmr1 knockout mice (Fmr1 KO) showed abnormalities in morphology and number of dendritic spines in hippocampus and cortex. However, there is hardly any data on structural abnormalities of dendritic spines in amygdala, a brain structure essential for emotional processing. The mechanisms underlying the structural changes of synapses in FXS are largely unknown, although, it has been shown that, in both humans and mice, lack of FMRP leads to elevated translation of matrix metalloproteinase-9 (MMP-9), an enzyme involved in activity-dependent reorganization of dendritic spines architecture. Using face-block scanning electron microscopy we described changes in dendritic spines morphology, including increased level of presynaptic bulbs, multi-innervated spines and shaft connections in Fmr1 KO. Further, we observed rescue effects of inhibition of MMP-9. Injection of nanoparticles gradually releasing MMP-9 inhibitor changed synaptic morphology back towards the one observed in wild-type mice. The results suggest that increased MMP-9 level is responsible for ultrastructural changes observed in FXS.

Genetic architecture of hippocampal subfield volumes: shared and specific influences

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Background: The hippocampus is a heterogeneous structure, comprising histologically distinguishable subfields. These subfields are known to be differentially involved in memory consolidation, spatial navigation and pattern separation, complex functions often found to be impaired in individuals with brain disorders associated with reduced hippocampal volume, including Alzheimer's disease (AD) and schizophrenia. Given these structural and functional differences, we sought to characterize the subfields' shared and specific genetic architecture. Methods: T1-images (n= 17418, 16 cohorts) were processed with the hippocampal subfields algorithm in FreeSurfer v6.0. We calculated the SNP-based heritability of 12 subfields, as well as their genetic correlation with each other, with other structural brain

features, and with AD and schizophrenia. We further ran a genome-wide association analysis on each subfield, correcting for total hippocampal volume. Results: Volumes of all subfields showed significant heritability. The parasubiculum showed a genetic correlation with AD. We found ten independent whole-genome significant loci across five subfields. Top SNPs were mapped to genes associated with neuronal differentiation and locomotor behaviour Conclusions: Hippocampal subfields have partly distinct genetic determinants, associated with specific biological processes and traits. Taking into account this specificity may aid in furthering our understanding of hippocampal neurobiology and associated disorders.

MOTIVATIONAL NEUROSCIENCE

14.30 - 16.00

chaired by: **Marek Wypych** (Nencki Institute of Experimental Biology, Warsaw, Poland)

Attenuated brain activity during error processing and punishment anticipation in procrastination – monetary Go/No-go fMRI study

Marek Wypych[1], Jarosław M. Michałowski[2], Dawid Droździel[1], Magda Borczykowska[3], Michał Szczepanik[1], Artur Marchewka[1]

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Procrastination is a self-regulatory failure in which people voluntarily but irrationally delay some tasks (i.e. learning to exams), despite knowing that such a behavior will lead to discomfort. Trait procrastination is estimated to affect 15-20% of a total population and leads to significant decrease in performance and quality of life. Procrastination is related i.a. to impulsivity and impaired inhibitory control and emotion regulation. The aim of this study was to investigate the neuronal mechanisms behavioral control in procrastinators exposed to negative emotions. Non-student subjects recruited to low (LP, N=18) and high procrastination (HP, N=18) groups were asked to perform monetary Go/No-go task in punishment, reward and neutral conditions, during fMRI scanning. No between-group differences were found in task performance nor in brain activity during correct inhibition. After errors however, HP showed significantly lower activity in ACC and left insula. Moreover, during punishment condition HP showed lower activity of right DLPFC. Obtained results suggest that impaired error processing mechanisms in procrastinators may add to persistence of procrastination through difficulty in correction of faulty behaviors. Procrastination seems also to be related to impaired coping in contexts of negative emotions. Future interventions could address impulse control and emotion regulation difficulties in procrastinators.

Out-of-the-loop pilots: Study of an applied phenomenon through performance-monitoring EEG measures

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The out-of-the-loop phenomenon is an aeronautics operational problem, characterized by a difficulty to monitor highly automated system and to detect system errors. To characterize this phenomenon, we used recent insights into the neuro-functional substrates of action monitoring in humans, as well as state-of-the-art signal processing techniques. To this purpose, two experiments were designed to explore the performance monitoring mechanism in a supervisory context. In the first experiment, participants had to supervise either a human being or a computer, performing a modified flanker task with varying levels of difficulty. Using both classical analysis and a non-parametric signal processing technique (i.e., the cluster-based permutation test), we identified the ERP signature of other agent's error detection and showed the impact of task difficulty and type of agent (human vs. system) on these ERPs. The second experiment explored performance monitoring when participants supervised an air traffic collision

avoidance system. Using time-frequency analysis, we identified error detection signature in a more applied context. In the next step (study under way), we propose to explore the degradation of this mechanism during the out-of-the-loop phenomenon. In an applied perspective, a degradation of performance monitoring correlates could serve as a physiological marker of the out-of-the-loop phenomenon.

The Role of Autistic Traits in Reward Anticipation

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Autism Spectrum Conditions may be associated with abnormal reward responsiveness (Kohls et al., 2012). However, prior work is inconclusive about the scope of this effect. The current study aims at identifying the influence of autistic traits in neurotypical participants (Autism Spectrum Quotient (AQ); Baron-Cohen et al., 2001) on reward processing. 25 volunteers performed a cued incentive task. Event-related potentials and pupillary responses were recorded. The data revealed decreased pupil sizes during reward anticipation in participants with higher AQ scores ($p<.01$, $d=1.47$). In a sample subset with extreme scores (low-AQ: n=7, m=9.86, sd=3.02; high-AQ: n=7, m=28, sd=5.03), the descriptive effects pointed at group effects in the contingent negative variation (CNV) amplitudes ($d=.36$). High-AQ was associated with descriptively smaller amplitudes of CNV (high-AQ: m=-.92, sd=1.86; low-AQ: m=-2.27, sd=2.4). According to power analyses, sample size will be increased to n=50 (power at .85). The results from the full data set will be presented at the conference. Given the main effect of group in pupillary data, and the descriptive trends in CNV amplitudes, we conclude that the results point to atypical reward processing in individuals with higher AQ scores. By using a population-based approach, this study contributes to understanding reward sensitivity in autism spectrum.

Observational fear learning in humans – toward greater ecological validity

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Learning how to avoid threats often happens indirectly, through observation of others. The involved processes can be studied in humans using the observational fear learning paradigm and pre-recorded videos (Haaker et al., Nature Protocols, 2017). In order to improve its ecological validity we recruited pairs of friends, one of whom (demonstrator) was asked to perform an aversive conditioning task while being observed by the other (observer) through a video stream. After the observation phase, the observer was asked to perform an identical task (direct expression phase), but no aversive stimuli were administered to him. We assumed that the observer should develop a conditioned response to stimuli used without directly experiencing aversive stimulation and that the acquisition of fear would be reflected in galvanic skin response, fear-potentiated startle and cortisol level. According to preliminary results, observation of a friend receiving electric shocks evoked strong electrodermal responses in observers. They also showed increased reactions related to the presentation of the reinforced stimuli in the direct expression phase. Elevated cortisol and skin conductance levels were observable throughout the whole experiment. Described study suggests that the modified version of the observational fear learning paradigm is effective and constitutes a valid framework for further studies.

Learned-predictiveness but not valence modulates unconscious neural activity in early visual cortex

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It is currently unknown whether early visual cortex is sensitive to the unconscious impact of valence (reward and penalty) or motivational salience (high and low probability of outcome). To examine this, we asked participants to learn to associate specific faces with modest monetary rewards or punishers that occurred with either a high or low probability outside the scanner. First, face stimuli portraying a neutral expression were imbued with different

expected values (gain, loss, or no-outcome) in a choice task (phase 1), which was followed by a series of experiments using face-position discrimination under a continuous flash suppression paradigm (Phase 2). Phase 2 of Experiment 1 was conducted inside the fMRI scanner. Phase 2 of Experiment 1 was conducted outside the scanner. In Experiment 1, we found that neural activity in early visual cortex as well as in medial orbitofrontal cortex was higher for invisible faces with high predictive of outcomes (relative to low), irrespective of their associated valence (gain/loss). In Experiment 2, we found that face with high predictive of outcomes (relative to low) break through suppression faster. Incorporating both the valence (gain and loss) and motivational saliency (high and low) in the same study, we challenge previous findings by showing that motivational saliency, rather than reward, drives the saliency of visual stimuli, thereby modulating neural activity in visual processing in brain areas.

CORTICAL PLASTICITY AND REORGANISATION

14.30 - 16.00

chaired by: **Katarzyna Cieśla** (World Hearing Center, Warsaw/Kajetany, Poland)

Tonotopic organisation of auditory cortex in sensorineural hearing loss

Katarzyna Cieśla, Tomasz Wolak, Artur Lorens, Krzysztof Kochanek, Monika Lewandowska, Mateusz Rusiniak, Agnieszka Pluta, Joanna Wójcik, Henryk Skarżyński

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The auditory system has tonotopic organization. For every point along the basilar membrane in the cochlea there is a frequency range that causes its largest deviation. Tonotopic organization is preserved in the human primary auditory cortex (PAC), as shown in several fMRI studies. Is it also preserved in sensorineural hearing loss (SNHL)? Twenty six patients with symmetrical sloping SNHL (38.1±9.1;12 men) and 32 controls participated in a sparse fMRI study. Participants passively listened to 8s-complex tones with 5 central frequencies: 400 HzCF, 800 HzCF, 1600 HzCF, 3200 HzCF and 6400 HzCF, delivered binaurally via headphones at 80 dB(C). The winnermap approach (showing relative locations) revealed a typical V-shape arrangement of high-frequency gradients surrounding those responding to low frequency sounds in AC. In patients only responses to 400 HzCF - 1600 HzCF were visible, due to the severe/profound HL for higher frequency ranges ($p<0.05$; FWE). At a more lenient statistical threshold ($p<0.001$, FDRc), the regions responsive to 400 HzCF were found statistically larger in patients with a prelingual HL onset (before language acquisition), as opposed to a postlingual onset in PAC as well as in secondary AC when all patients' outcomes were contrasted with controls. The outcomes show that large-scale tonotopic organisation is preserved in SNHL and can be further refined following auditory experience.

Auditory cortex recruitment for visual rhythms in musicians

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The perception of temporal patterns depends on the modality in which they are perceived (auditory, tactile, etc). Recently we showed that congenitally deaf subjects recruit task-specific auditory regions for visual rhythm perception (Bola et al., PNAS, 2017). Here we ask if a similar effect can be arise in non-deprived through lifelong training. Awgroup of 17 professional pianists took part in the fMRI study. Participants were asked to compare between sequences (rhythms) presented visually (series of flashes) or auditorily (series of sounds). The control condition consisted of simply observing regular auditory or visual sequences. An additional condition in which participants were asked to imagine pairs of same or different rhythmical patterns controlled for imagination. The results show consistent activation of auditory regions (right Middle Temporal Gyrus) for visual rhythmical task comparing to the control condition. A larger but overlapping region was recruited in musicians for auditory rhythms when compared to the auditory control condition. Importantly auditory activation was not present for rhythmical imagination conditions suggesting that sensory input is necessary to induce cross-modal recruitment. We conclude that auditory cortices activation may support visual processing due to extensive training in the domain of musical rhythms perception.

Functional hierarchy for tactile processing in the visual cortex of sighted Braille readers

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Growing number of studies suggest that the visual cortex in sighted people is behaviorally relevant for certain tactile tasks, such as discrimination of grating orientations or Braille reading. However, it is still unclear how tactile input reaches the visual cortex and is incorporated into a functioning visual network. Here we addressed these questions in a chronometric transcranial magnetic stimulation (TMS) experiment, in which we investigated the spatio-temporal dynamics of Braille processing in the visual cortex. Seventeen sighted subjects participated in a Braille course and then were tested on a Braille letter reading task. During the task, TMS was applied to the early visual cortex, the visual word form area (VWFA) or the early somatosensory cortex, at five different time windows. Decreases in subjects' accuracy indicated that the early visual cortex, but not VWFA, was critical for Braille letter reading at 120-220 ms after Braille letter presentation, whereas VWFA, but not the early visual cortex, was critical at the 320-420 ms time window. This temporal double dissociation shows that tactile processing might be incorporated into a typical visual processing hierarchy, with relatively low-level processing occurring in the early visual cortex, and more complex, abstract computations being performed in higher-order visual areas.

Visual evoked potential plasticity and gamma power in the EEG of healthy participants

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Modulations of visual evoked potentials (VEPs) using high intensity visual stimulation appear to be mediated by long term potentiation-like synaptic processes in the visual cortices (1), and are possibly affected in psychiatric disorders (2-4), while gamma power in time-frequency decomposed electrophysiological measurements seem to index feedforward visual processing (5). 64-channel EEG was sampled from 144 healthy controls during exposure to a VEP paradigm similar to (4). VEP modulation was measured as the differences in peak amplitudes of C1, P1, and N1 components at the Oz electrode before and after long duration visual stimulation. Power at 50-70 Hz was preliminarily calculated in a subset of 18 pseudo-randomly selected participants. VEP plasticity was apparent after long duration visual stimulation for both the C1 ($d = 0.71$, $p = 2.54e\text{-}14$), P1 ($d = 0.76$, $p = 8.75e\text{-}16$), and N1 ($d = -0.21$, $p = 0.01$) components. Event-related perturbations in gamma power were apparent during visual stimulation, but were not associated with VEP plasticity ($r = -0.17$, $p = 0.53$). Conclusion. VEP plasticity was replicated in a large sample of healthy participants, but very preliminary analyses did not provide evidence for any association with spectral perturbations at gamma frequencies.

CLOSING LECTURE:
18.30 – 19:30

How experience shapes brain specializations

Amir Amedi

Hebrew University of Jerusalem, Israel

"The best technologies make the invisible visible" - Beau Lotto

My lab study the principles driving specializations in the human brain and their dependence on specific experiences during development (critical periods) versus learning in the adult brain. In the main part of my keynote I will cover the work done under our ERC www.BrainVisionRehab project which focuses on studying Nature vs. Nurture factors in shaping category selectivity in the human brain. A key part of the project involves the use of sensory substitution devices (SSD). I will focus on work with the EyeMusic algorithm developed in my lab which convert invisible visual input to blind using music and sound. From basic science perspective the most intriguing results came from studying blind without any visual experience using SSDs to understand online visual feed arriving from a video camera. I will also discuss initial results from our new ERC ExperieSense project which focuses on studying Nature vs. Nurture factors in shaping topographical maps in the brain. In this project we focus on transmitting invisible topographical information to individual with normal senses by using similar training and SSD protocols to couple it with input from 'invisible' sensors like infrared or ultrasound images and testing whether novel topographical representations can emerge in the brain to input that was never experienced during development or evolution. Specifically, I will discuss work aiming at unraveling the properties driving the sensory brain organization and at uncovering the extent to which specific unisensory experiences during critical periods are essential (or not essential) for the development of the natural sensory specializations. Our work focused on two fundamental discoveries: 1- Using the congenitally blind adult brain as a working model of a brain developing without any visual experience, we documented that essentially most if not all higher-order 'visual' cortices can maintain their anatomically consistent category-selectivity (e.g., for body shapes, letters, numbers or faces) even if the input is provided by an atypical sensory modality learned in adulthood, and that such task-specific sensory-independent specializations emerge after few hours of specific training (e.g. Abboud et al., 2015 Nat Comm; Amedi et al Trends Cog Sci 2017). Our work strongly encourages a paradigm shift in the conceptualization of our sensory brain by suggesting that visual experience during critical periods is not necessary to develop anatomically consistent specializations in higher-order 'visual' regions. I will integrate this theory with a prominent theory in cognitive neuroscience, "neural recycling", by the Dehaene lab, and will propose an integrated framework supporting the notion of the brain as a task-machine rather than as a sensory machine as classically conceived. Under this framework we also suggested the potential mechanisms underlying the emergence of sensory brain specializations: a) pre-programmed sensory-independent task-specific computations that each specialized area/network processes (e.g., 3D reconstruction of geometry in object related area independently of the sensory modality input); and (b) partly innate network connectivity biases linking each specific cortical area to `the rest of the brain (Heimler et al., 2015 Curr Opin Neurobiol; Hannagan et al., 2015 TICS). Our emphasis on the task-selective and sensory independent brain organization also led to a paradigm shift in rehabilitation by suggesting that multisensory rather than unisensory training might be more effective (e.g. Reich et al Curr Opion in Neuorl 2012; Heimler et al., 2015 Curr Opin Neurobiol). (See also Amedi et al. Task Selectivity as a Comprehensive Principle for Brain Organization. Trends in Cognitive Sciences 2017).

POSTER SESSION I

NEUROPATHOLOGY

1. *Overexpression of MUL1 and parkin as a genomic therapy against Parkinson's Disease symptoms induced by rotenone in Drosophila melanogaster*

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One of the sporadic forms of Parkinson's Disease (PD) is that caused by rotenone. Rotenone is a lipophilic neurotoxin which affects mitochondrial I complex leading to development of PD symptoms. Damaged mitochondria can be eliminated by mitophagy, which depends on mitochondrial ligases. In our study, we found that overexpression of two major mitochondrial ligases MUL1 and PARKIN restores synaptic proteins and behavior of flies fed with rotenone. Because rotenone reduces the level of synaptic proteins: DISC LARGE, SYNAPSIN, and SYNAPTOTAGMIN, this probably results in abnormal behavior. Rotenone also causes degeneration of dopaminergic neurons, inhibition of autophagy as well as accumulation of free radicals. After feeding flies with rotenone in which MUL1 and parkin were overexpressed the reduction of synaptic proteins, neurodegeneration of dopaminergic neurons and locomotor defects were not observed. It suggests that high level of proteins involved in the degradation of damaged mitochondria, such as MUL1 and PARKIN, could be a novel genomic therapy against PD.

2. *Neuroprotective effects of germanium-containing compound on the streptozotocin (STZ) - induced retinopathy*

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Aim of the investigation was to investigate electroretinogram (ERG) in rats with experimental diabetes, induced with STZ (50,0 mg/kg, i.p.) after treatment with derivatives of oxietilyden-diphosphonate — germanate (NicH)2 [Ge(OH)2 (Oedph)]. H20 (MIGU-4). Those rats with glucose level 300 mg/dl were included into observation. In 0,5 months from the moment of STZ injection and during next two months treatment with MIGU-4 (25,0 mg/kg, i.p.) was performed with the next ERG registration. Gained results revealed that in rats with STZ-induced diabetes latency of b-wave in ERG by 8,7% along with the reduction of its amplitude by 2,1 times pertained to intact rats was seen in diabetic animals ($P<0,05$). At the same time the latency of a-wave was greater by 23,2% ($P<0,05$), while the dynamics (velocity of increment) of a-wave amplitude was slower by 2,3 times ($P<0,05$). In MIGU-4 treated rats with STZ-diabetes the elevation of b-wave amplitude, which exceeded that one in control group (saline treated rats with STZ-diabetes) by 19,5% ($P<0,05$) was registered. The velocity of a-wave amplitude dynamics also exceeded such one in the control group (by 40,1%, $P<0,05$). Hence, gained data revealed the protection of retinal neurons from diabetes – induced functional deterioration with germanium – containing compound.

3. *The protective effects of cystamine in the murine model of Parkinson's disease*

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Parkinson's disease (PD) is a common neurodegenerative movement disorder characterized by a progressive loss of dopaminergic neurons and an accumulation of intraneuronal Lewy bodies containing misfolded a-synuclein. Current treatment of PD are only symptomatic and do not block neuronal loss. Recently enormous amount of work has been conducted to identify molecules that could be used as neuroprotective drugs. One of them is cystamine – the inhibitor of transglutaminases activity. Male C57Bl/10 Tar mice 1 year-old were used in this study. Cystamine (40 mg/kg) was injected intraperitoneally for 14 days, beginning 13 days prior to 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP, 40 mg/kg) intoxication. The changes in the mRNA level of tyrosine hydroxylase, tissue transglutaminase 2 and inflammatory factors in striata were examined using Real-Time PCR. Neurotransmitters levels were evaluated by high-performance liquid chromatography. Our study demonstrated that chronic administration of cystamine before MPTP intoxication improved striatal levels of dopamine and its metabolites, as compared to MPTP-treated groups. We observed also an inhibition of inflammatory reaction induced by MPTP. Cystamine preserves nigrostriatal function after MPTP intoxication and may have the treatment efficacy in PD. However, further research must be conducted to provide more evidence of protective role of cystamine in PD.

4. *Protective effects of curcumin against rotenone-induced rat model of Parkinson's disease: in vivo electrophysiological and behavioral study*

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Curcumin is a naturally occurring phenolic yellow chemical isolated from the rhizomes of the plant Curcuma longa (turmeric), and is a major component of the spice turmeric. Curcumin has protective effects against rotenone-induced neural damage in Parkinson's disease (PD). The present study aims at providing new evidence for the validity of the rotenone rat model of PD by examining whether neuronal activity in the hippocampus is altered. Male albino rats were treated with rotenone injections (2.5 mg/ml intraperitoneally) for 21 days. We examined the effects of curcumin (200 mg/kg) on behavior and electrophysiology in a rat model of PD induced by rotenone. Motor activity was assessed by cylinder test. The electrical activity of neurons was measured in hippocampus. Rotenone causes significant reduction of neuronal activity. The results show that curcumin can improve the motor impairments and electrophysiological parameters and may be beneficial in the treatment of PD.

5. *Interaction of agonist with allosteric site of PITRM1 play role in enhancing the cleavage of amyloid beta*

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PITRM1 is a metalloprotease involved in clearance of peptides inside mitochondria, which includes the amyloid beta and transit peptides. PITRM1 binds directly to amyloid beta, agonists like antioxidants are identified to enhance the activity of the protease. The molecular mechanism by which the agonist (glutathione, ascorbic acid, lipoic acid, uric acid, retinol and Ubiquinol) enhances the activity is been investigated using in silico docking and interaction studies. Allosteric sites of PITRM1 were predicted and followed by docking with agonists using Autodock. Retinol showed best interaction in the predicted allosteric site with a docking score of -7.9 binding to the linker region. This interaction could activate the change of closed conformation of PITRM1 to an open state which is similar to insulin degrading enzyme. We here with conclude that the retinol might bind to the linker region and activates PITRM1 to act as agonist thereby which could help induce the degradation process of amyloid beta during Alzheimer pathology.

6. *Comparison of cortical models of photothrombotic ischemic stroke in rats – evaluation of cerebral blood flow with Laser Doppler Flowmetry and Magnetic Resonance Imaging*

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Cerebrovascular diseases are causes of mortality and disability worldwide. 80% of all strokes are ischemic. Magnetic Resonance Imaging is used to image stroke patients for diagnostic and therapeutic purposes. Laser-Doppler flowmetry has been used to trace hemodynamic changes in experimental stroke research. The aim of our study was to compare size of cortical ischemia and regional cerebral blood flow in photothrombotic cortical models of stroke with imaging techniques on 9,4T-MRI and Laser-Doppler. We carried out prospective study, experimental group was 35 male Long-Evans rats. 20 rats underwent small stereotactic cortical ischemia, 10 typical cortical ischemia, 5 were sham. All underwent pre- and postsurgery Laser-Doppler flowmetry and 5 with stereotactic cortical ischemia underwent MRI-imaging (T2-weighted, DWI, PWI, ADC-map) with animal dedicated 9,4T-scanner. We measured size of: an ischemia, „PWI-DWI-mismatch" and cerebral blood flow. We observed statistically significant reduction of rCBF in ischemic area measured with Laser-Doppler. Mean ischemic area size on T2-weighted imaging were 2,1mm ±0,1 mm, and was similar on DWI-imaging. rCBF of ischemic core was <20 ml/100g/min in all cases, rCBF of penumbra was 15-50 ml/100g/min and rCBF of contralateral similar location >80 ml/100g/min. Based on the „PWI-DWI-mismatch" we precisely located penumbra area. MRI have potential for studying animal-models of brain ischemia.

7. Differentiation properties of human dental pulp cells of neural crest origin

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Dental tissue of the craniofacial region serves as a source of dental pulp stem cells (DPSCs) which are developed from the ectodermal neural crest. Their origin from this transient embryonic structure results in the expression of neural markers even in undifferentiated state and upon in vitro culture. We aimed to study their properties, so we isolated cells from dental pulp of adult human donors and established primary cell cultures. Cells were examined for their proliferative potential and metabolic activity with MTS assay; thereafter they were checked for osteogenic differentiation potential using alkaline phosphatase (ALP) activity assay. After a lag phase, cells showed high proliferative potential and, as expected, they differentiated into osteoblasts upon ascorbate and dexamethasone treatment. Neurogenic differentiation of DPSC was evaluated preliminarily using a protocol of Pisciotta (Pisciotta et al. BMC Dev Biol, 2015) with 2-mercaptoethanol (BME), butylated hydroxyanisole (BHA) and dimethyl sulfoxide (DMSO) as differentiation factors. BME, BHA and DMSO have drastically changed cell morphology from fibroblastic to neuronal-like. Further studies are scheduled to determine neural properties of human DPSC isolated from couple different donors.

8. Impact of elastin-derived peptides (EDPs) on tissue inhibitors of metalloproteinases -1, -2, -3, -4 (TIMP-1, -2, -3, -4) mRNA expression in mouse astrocytes in vitro

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Degradation products of elastin, elastin-derived peptides (EDPs) are involved in various physiological and pathological processes. EDPs are detectable in cerebrospinal fluid of healthy subjects and patients with ischemic and hemorrhage stroke. Tissue inhibitors of metalloproteinases (TIMPs) play important roles during the repair phases of cerebral ischemia, particularly during angiogenesis and cerebral blood flow recovery. Furthermore, TIMPs are involved in healing process after stroke. Therefore, the aim of this research was to investigate the impact of elastin-derived peptide (VGVAPG) on mRNA expression of tissue inhibitors of metalloproteinases -1, -2, -3, -4 (TIMP-1, -2, -3, -4) in mouse astrocytes in vitro. The primary mouse astrocytes were cultured in phenol red-free DMEM/F12 medium supplemented with 10 % FBS and were exposed to 50 nM, 1 μM or 50 μM of VGVAPG peptide for 3 and 6 h. Afterwards, mRNA was collected and gene expression was measured by qPCR method. The results showed that after 3 and 6 h of exposure to studied peptide gene expression was changed in a dose- and time-dependent manner. To conclude, VGVAPG affects mRNA expression of all studied TIMPs in mouse cortical astrocytes in vitro, which suggests initiation of healing process.

9. *Prenatal exposure to Poly I:C causes changes in the hippocampal level of CX3CR1 of young offspring rats*

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The neuron – microglia interactions are mainly controlled by specialized protein systems, mostly CX3CL1-CX3CR1 and CD200-CD200R. It seems that prenatal insults, both of bacterial and viral origin, may lead to malfunctions of these systems, thus consequently contribute to the basis for schizophrenia development in adulthood. The aim of this study was to determine CX3CL1, CX3CR1, CD200 and CD200R levels in the hippocampus (Hp) of young offspring rats in the animal model of schizophrenia, based on the administration of the viral component – polyinosinic:polycytidylic acid (Poly I:C). Pregnant rats were injected intravenously with Poly I:C (4 mg/kg) at GD15. 7-day-old offspring male rats were sacrificed and the protein levels in Hp were measured using ELISA assays. The obtained data demonstrated that the young offspring after prenatal exposure to Poly I:C exhibit reduced concentration of CX3CR1 in Hp. The levels of CX3CL1, CD200 and CD200R in Poly I:C-exposed offspring were not affected. In conclusion, the present study revealed that the exposure to Poly I:C leads to disturbances in a homeostasis of the brain of young offspring rats. Perhaps, the observed changes, if long-lasting, may be a harmful factor leading to disorders in adulthood.
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10. *NP-POL, a nonapeptide component of Colostrinin, protects PC12 cells against oxidative stress induced by 6-hydroxydopamine*

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6-hydroxydopamine (6-OHDA) exerts detrimental effect on neural cells in Parkinson's disease. 6-OHDA toxicity is connected with overproduction of free radicals (ROS) and induction of oxidative stress. NP-POL was isolated using Bio-Gel P2 molecular sieve chromatography and its amino-acid sequence (RPKHPIKHQ) was determined. It was recently identified that NP-POL has potential neuroprotective abilities. In present study, we examined the ability of NP-POL to prevent 6-OHDA neurotoxicity in neuron-like PC12 cells. The effect of NP-POL on ROS production triggered by 6-OHDA was estimated by DCFH method. The intracellular total glutathione levels and GSSG/GSH ratio were measured in 6-OHDA-treated cells incubated with NP-POL. The activity of glutathione reductase (GR) and intracellular superoxide dismutase (SOD) was measured in treated and untreated cells. The intracellular ROS level in 6-OHDA-treated cells was significantly decreased after incubation with NP-POL. Moreover, NP-POL increased total glutathione levels and GSSG/GSH ratio. These may be connected with activity of enzymes involved in cellular oxidation/reduction mechanisms. The results show that NP-POL is able to reduce the 6-OHDA toxicity and show potential neuroprotection against oxidative stress. It is supposed that NP-POL could be useful in Parkinson's disease therapy.

11. *Effects of selected antioxidants on reactive oxygen species (ROS) generation and metabolic activity of neuronal cells after exposure to airborne particulate matter (PM)*

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There is a connection between neurodegenerative disorders morbidity and air pollution with particulate matter (PM) due to its ability to oxidative stress induction and proinflammatory activation within immune system. Antioxidative agents may be regarded as beneficial attempt to counteract them. The superoxide dismutase and catalase mimetics, TEMPOL (4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl) and MnTMPyP (manganese(III)tetrakis(1-methyl-4- -pyridyl)porphyrin) were investigated for their ability to reduce ROS generation (assessed with fluorescent probe, 2',7'-dichlorodihydrofluorescein diacetate) and to improve metabolic activity (assessed with resazurin reduction test) in neuronal SH-SY5Y cells exposed to two forms of PM: NIST1648A (standard material) and LAp120 (NIST1648A with diminished organic content). PM caused an increase in ROS generation shortly after exposure, which results in a decrease in metabolic activity clearly visible 48 hours later. MnTMPyP and TEMPOL did not reduce ROS generation in exposed SH-SY5Y cells nor improved their metabolic activity. The negative influence of PM, related to increased ROS generation, were not improved by none of antioxidant under study.
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12. The effect of butylated hydroxytoluene on mouse hippocampal neurons in primary cultures

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Butylated hydroxytoluene (BHT) is a phenol derivative, which is used in a wide variety of every-day products i.e. pharmaceuticals and cosmetics. It is also used as a food preservative because of its antioxidant activity. There is some evidence of a protective effect of BHT in the central nervous system, but neurological symptoms after ingestion of BHT were observed as well, indicating its potential neurotoxicity. The aim of this study was to investigate the effect of BHT on neurons isolated from 19 day embryonic mouse hippocampal tissue. The cells were plated in serum-free Neurobasal medium, supplemented with B27. Afterwards BHT (1-100μM) was added for 24 and 48 hours. To analyze the influence of examined substance on neurons the level of the extracellular lactate dehydrogenase (LDH) and the potential of the mitochondrial membrane were estimated using appropriate assays. Immunofluorescence microscopy was used to visualize changes in neuron cultures. Results indicated increased level of released lactate dehydrogenase and decrease of the mitochondrial membrane polarization in the presence of higher concentration of BHT. To conclude, this study shows dose-dependent cytotoxic (apoptotic or necrotic) effect of BHT on mouse hippocampal neurons health. This research was supported by the National Science Centre grant (DEC-2014/15/B/NZ7/00892).

13. Evaluation of the effect of benzophenone-3 on the viability of neurons in primary hippocampal cultures

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Benzophenone-3 (BP-3) is a compound most commonly used as a UV filter in a variety of sunscreen and personal care products. BP-3 due to its low molecular weight and lipophilic character is well absorbed through the skin. The aim of the study was to evaluate the effect of BP-3 on the viability of neurons in primary hippocampal culture. The primary neuronal culture was obtained by isolation of hippocampal tissue from the mice P19. Neuronal cells were cultured in a serum free neurobasal medium supplemented with B27. The experiments were carried out 7 days after plating. BP-3 at concentrations 10-4, 10-5 and 10-6 M was added to wells for 24-48h. To determine the necrotic damage, cell viability and apoptosis activation we performed the LDH assay, JC-1 assay, Hoechst 33342 staining as well as the activity of caspase-3/-7. In the preliminary studies, BP-3 at concentration dependent manner reduced cell viability, increased release of LDH to the culture medium and caused the formation of apoptotic cells. Benzophenone-3 reduces the viability of neurons in primary hippocampal cultures, so BP-3 may be responsible for initiation of neuronal cell damage in the pathway of apoptosis or necrosis.
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14. The influence of tianeptine on the activity of primary microglial cultures

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Microglia cells are the main immunocompetent cells in the central nervous system. As they are the main source of inflammatory factors, it is plausible that the regulation of their activation may be a potential therapeutic target. The aim of this study was to assess the effect of tianeptine on the chosen parameters of microglial activity in basal conditions and after lipopolysaccharide (LPS) stimulation. Pregnant rats were subjected to restraint stress. Primary microglia cultures were prepared from cortices of 1-2 day old offspring. Tianeptine were added at a dose of 0,1-50 μM for 24 hours. Microglia were exposed to immune system activator - LPS in the concentration of 100 ng/ml. Cell viability was determined by MTT test, cell death by LDH test and nitric oxide (NO) synthesis by Griess reaction. Administration of tianeptine at a dose of 10 μM resulted in an increase of cell viability and decrease mortality of the LPS-stimulated microglia cells. We noticed also an increase in NO synthesis in cells stimulated with LPS, which was normalized by administration of tianeptine at a dose of 10 μM. Our study showed beneficial property of tianeptine on microglia cells activation.
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15. The tibia nerve regeneration after neuroplasty

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Plastic repair of the injured nerve trunks promotes faster growth of regenerating nerve fibers, but the degree of their myelination remains approximately similar to that of the control. To influence myelination we used a Lipin that had been administered subcutaneously daily for 10 days two weeks after surgery. The data on impregnation with silver nitrate show that in the Lipin groups many more newly formed axons have penetrated the peripheral segment of the nerve in a more ordered fashion, with more mature nerve fibers observed. Electron microscopy shows more fibers with a thick myelin sheath in animals with alloneuroplasty in the presence of Lipin therapy. These nerve fibers were surrounded by active Schwann cells and macrophages, which included lipid drops. In some cases fat drops surrounded the Schwann cells from the basement membrane side which can be interpreted as the usage of the drug from the depot followed by the formation of myelin lamellae. Morphometric analysis revealed a larger volume and number of myelin nerve fibers in the groups using the drug. These findings show that Lipin use allows to achieve better outcomes of the peripheral nerve regeneration due to the targeted influence on the process of nerve fibers myelination.

16. Regulation of NLRP3 inflammasome gene expression in the hippocampus by maternal diabetes

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Inflammasome NLRP3, the multiprotein cytosolic molecular platform, can control the secretion of proinflammatory cytokines interleukin IL-1β and IL-18 in metabolic stress. Activation of the NLRP3 inflammasome is a key mechanism that induces metabolic inflammation and insulin resistance. We investigated the influence of maternal diabetes on the relative gene expression of NLRP3 components (NLRP3, ASC, caspase-1) and proinflammatory cytokines in basal and LPS-stimulated conditions in the hippocampal organotypic cultures. Cultures were prepared from hippocampi of 7-day-old rats-offspring of control and diabetic dams. Hippocampi were sectioned into slices and transferred onto membrane inserts. On the 7th day in vitro hippocampal slices were stimulated for 24h with LPS (lipopolysaccharide). We showed increase in nlrp3 and caspase-1 gene expression in hippocampal slices obtained from offspring of diabetic and control dams after LPS stimulation. Moreover, after LPS we observed the elevated levels of

proinflammatory cytokines expression, which are connected with NLRP3 inflammasome activation. Summing up, maternal diabetes can be a risk factor of excessive inflammatory activation in offspring brain.
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17. Gene expression in various brain disorders and brains

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Genome wide association studies (GWAS) have associated single nucleotide polymorphisms with several brain disorders and traits. However, underlying brain expression mechanisms are poorly understood. Thus, we generated gene expression maps in the brain for multiple disorders (Schizophrenia, Alzheimer's disease (AD) and attention deficit hyperactivity disorder (ADHD)) and examined associations between them. Based on publicly available GWAS summary statistics we calculated whole brain mRNA average expression maps, so that each disorder was represented by one expression map. Brain expression maps were calculated based on 6 donors data from the Allen Human Brain Atlas. Analysis of gene expression maps revealed that SCZ was negatively correlated with ADHD (r=-0.60), and positively with AD (r=0.38). The spatial distribution of gene expression provides a valuable insight for underlying mechanisms of different brain disorders. For example, our results indicate that the genetic contribution of SCZ and ADHD are spatially non-overlapping.

PAIN

18. Blockade of CXCR3 by (±)-NBI-74330 inhibits neuropathic pain in rats by modulating release of CXCR3 ligands

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Recently, chemokine receptors have been suggested as emerging targets for pain control, however, the role of CXCR3 is not clear yet. Therefore, our experiments were conducted to evaluate the function and involvement of CXCR3 and its ligands (CXCL4,CXCL9,CXCL10,CXCL11,CCL21) in neuropathic pain development. We studied the time course changes in the mRNA/protein level of CXCR3 and its ligands in the spinal cord/DRG in rats following chronic constriction injury (CCI) of the sciatic nerve. Moreover, we examined the influence of intrathecal administration of (±)-NBI-74330, CXCR3 antagonist, on pain-related behavior and the associated biochemical changes of nociceptive factors. Our data give evidence that CXCR3 ligands exhibit pronociceptive properties and play an important role in the initiation, development and maintenance of neuropathic pain. (±)-NBI-74330 reduced the neuropathic pain-related behaviour, as measured in von Frey/cold plate tests. Western blot analysis showed that (±)-NBI-74330 diminished spinal IBA-1 and expression of CXCL4, CXCL9, CXCL10, CCL21 after CCI. Our studies indicate that CXCR3 represents a novel pharmacological target for the treatment of neuropathy.
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19. The (±)-NBI-74330 (CXCR3 antagonist) reduces neuropathic pain and influences the level of nociceptive factors - evidence from in vivo and in vitro studies

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Chemokines system plays an important role in the pathophysiology of neuropathic pain. CXCR3 modulation can have some beneficial properties. Therefore, the aim of study was to investigate the influence of chronic intrathecal administration of (±)-NBI-74330 (CXCR3 antagonist; preemptively 16h and 1h before CCI and then once daily for 7 days) in the modulation of nociceptive interleukins after chronic constriction injury (CCI) of the sciatic nerve, a rat

model of neuropathic pain and in primary glial cultures. Experiments were performed according to IASP rules. Rats were implanted with intrathecal catheters and then we performed CCI. Behavioral tests were conducted seven days after CCI as measured in von Frey/cold plate tests. Our results showed that (±)-NBI-74330 diminished neuropathic pain symptoms. Using Western blot analysis, we demonstrated that (±)-NBI-74330 diminished the pronociceptive IL-1β and IL-18 levels in the spinal cord and/or the DRG. Additionally, in primary glial cells, (±)-NBI-74330 reduced IL-1β and IL-18 factors after LPS stimulation. Our data provide new evidence that CXCR3 may indeed play a significant role in neuropathy by modulating neuroimmune interactions, suggesting that its blockade may have potential therapeutic utility.
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20. Zaprinast reduced pain and enhanced opioid analgesia in a rat neuropathic pain model

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G protein-coupled receptor 35 (GPR35) is an orphan receptor, that has garnered interest as a potential therapeutic target through its association with a range of diseases, including neuropathy. Therefore, the aims of our research were to elucidate how zaprinast that acts as both an agonist of GPR35 and an inhibitor of cyclic GMP (cGMP)-specific phosphodiesterase (PDE) can influence neuropathic pain. Chronic constriction injury (CCI) of the sciatic nerve was performed in rats under sodium pentobarbital anaesthesia. The mechanical and thermal hypersensitivity was measured using von Frey and cold plate tests, respectively. The single zaprinast administration attenuated the mechanical and thermal hypersensitivity observed 3h after the injection 7 and 14 days after CCI, the effect lasted up to 24h. Results also demonstrated that zaprinast potentiated the analgesic properties of morphine and buprenorphine. In summary, our data suggest that in a neuropathic pain model, zaprinast significantly reduces pain symptoms and enhances the effectiveness of opioids. Moreover, our study gave evidence that GPR35 is a promising pharmacological target for neuropathy in clinic, which require further studies.
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21. Changes in cytokines level in cortex and hippocampus induced by traumatic brain injury in mice

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Traumatic brain injury (TBI) is a common cause of death, and in western world is hard and expensive to manage. Inflammatory reaction initiated and regulated by cytokines seems to play a crucial role in TBI progression. Here we have analyzed the pattern of expression of proinflammatory cytokines (IL-1β, IL-18, IL-6, CCL 2, CCL9, Xcl-1) in mouse model of TBI at day 4th and 7th after injury. mRNA levels were measured in two brain structures (cortex and hippocampus) using qRT-PCR. We observed strong up-regulation of IL-1β, IL-6, CCL 2, CCL9, Xcl-1, but not IL-18, in cortex. Within the hippocampus level of IL-1β, IL-6, IL-18, CCL 2, CCL9 was also elevated. However, we did not observe expression of Xcl-1 in this structure. Moreover, the expression of tested factors have different pattern of activation, which was time- and structure-dependent. Our data showed a visible chance to control inflammation by inhibition of proinflammatory factors or blocking their receptors. Summing up, amount of proinflammatory compounds rise significantly after TBI what makes them very attractive therapeutic targets.
Acknowledgments: Supported by the NCBiR grant.

22. *Antinociceptive effects of novel histamine H3R receptor antagonist, E-162, and its influence on morphine analgesia of neuropathic pain in the mouse*

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Effective pain therapy is one of society's needs. The expression of histamine H3R receptor in regions related to nociceptive transmission has been shown, which makes this receptor a promising target for the development of new analgesics. The aim of our study was to determine the analgesic effects of H3R antagonist in mouse model of neuropathy (CCI, chronic constriction injury). We investigated the effects of newly synthesized H3R (E-162; 1-(5-(naphthalen-1-yloxy)pentyl)piperidine) antagonist on mechanical (von Frey) and thermal (cold plate) stimuli in CCI-exposed males and/or females 7 days post-injury. We evaluated the effects of antagonist on morphine analgesia and participation of H1R in E-162 effects. Using primary microglial and astroglial cell cultures, we revealed the presence of H3R. E-162 reduced nociception and potentiated morphine analgesia. E-162-induced effect was reversed after pyrilamine (H1R antagonist) pretreatment. We provide the evidence for the analgesic potency of E-162 and its beneficial properties for morphine effectiveness, which is consistent with multimodal pain therapy. We have also evaluated sex-dependent differences in effects of H3R antagonist.
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23. *The role of selected endogenous ligands of CCR2 in neuropathic pain-related behaviors in mice*

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Neuropathic pain results from somatosensory neurons injury. Preclinical studies revealed that not only amplified neuronal response, but also activated glia producing cytokines is crucial for neuropathic pain development. It was suggested that CC-chemokines play pivotal role in neurological disorders, including neuropathic pain. To better understand the role of chemokines acting through CCR2, we examine the time-dependent changes in spinal level of CCL2,CCL7,CCL12 in mice after sciatic nerve chronic constriction injury (CCI). Then, we investigate effects of examined chemokines and their neutralization on pain-related behaviors. Naive/CCI-exposed mice received examined chemicals using the lumbar puncture technique. To assess pain-related behaviors the von Frey and cold plate tests were used. The RT-qPCR analysis indicated that mRNA level of examined chemokines was increased in the early phase of neuropathic pain, however only CCL2 and CCL7 remained upregulated till day 28 after CCI. We provided evidence that single injection of CCL2 and CCL7, but not CCL12, dose-dependently induce pain in naive mice. Furthermore, neutralization of CCL2 and CCL7 effectively reversed neuropathic pain. Our results suggest the critical role of CCL2 and CCL7 in pathogenesis of neuropathic pain.
Acknowledgments: National Science Centre Poland OPUS-11-2016/21/B/NZ4/00128, statutory funds of Institute of Pharmacology, Polish Academy of Sciences.

24. *Targeting endocannabinoid system with dual target FAAH inhibitor and TRPV1 antagonist in osteoarthritis treatment: novel insight into molecular mechanism of TRPV1 upregulation and sensitization*

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Osteoarthritis (OA) is a chronic joint disease in which cartilage degeneration leads to chronic pain. Current treatment does not provide satisfactory relief and often cause adverse side effects. Our results discuss the benefits of dual-target

over single-acting compounds interacting with endocannabinoid system. Experiment was performed on monoiodoacetate (MIA) model of OA. Single target compounds (URB597 – FAAH inhibitor; SB366,791 – TRPV1 antagonist) and dual-acting OMDM198 (FAAH inhibitor/TRPV1 antagonist) were used in the present studies. Changes in mRNA expression after treatment were evaluated at day 21 post MIA injection in lumbar spinal cord by RT-qPCR. Following MIA administration, we observed strong mRNA upregulation of endocannabinoid receptors (Cnr1, Cnr2, Trpv1) and their metabolic enzymes (Faah, Ptgs2, Alox12) together with TRPV1 sensitizing kinases (Mapk3, Mapk14, Prkcg, Prkaca) in lumbar spinal cord. Both FAAH inhibitors, OMDM198 and URB597 abolished the expression of Mapk14, Prkcg and Alox12 in the ipsilateral part of spinal cord. Our results shed a light on the inflammatory component of OA that is related to TRPV1 sensitization. Apparent interplay between articular, immunological and nervous system in pathophysiology of OA is a strong justification for novel multi-target drug strategies.
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25. Novel pyrazolyl-pyridine based scaffolds targeting CB2 receptors in treatment osteoarthritis-related pain

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Osteoarthritis (OA) is a common, slowly progressive disease, leading to degradation of joint structure and articular cartilage, causing movement limitation and chronic pain. Current therapeutic possibilities are limited and concentrate only on reducing pain. Endocannabinoid system is involved in pain perception via cannabinoid receptor 2 (CB2). However, further studies are required to clarify the molecular mechanism by which CB2 exerts anti-inflammatory and analgesic actions. Here, we focused on the role of novel CB2 receptor modulators in treatment of pain, resulting from cartilage degradation in an animal OA model. We tested new pyrazolyl-pyridyne derivatives – COR1114 (full agonist of CB2) and COR1073 (inverse agonist of CB2) and its potential role in osteoarthritis treatment. Although both compounds reduced allodynia in dose-dependent way, they differently regulated cnr2 and MIF (macrophage migration inhibitory factor) mRNA level in human osteoarthritic chondrocytes. Our data indicate that analgesic mechanism of action of COR1114 might be related with its direct interaction with CB2 whereas the action of COR1073 can contribute to the inhibition of pro-inflammatory cytokines produced at the periphery by activated monocytes and macrophages. Future studies will verify the above hypothesis.
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26. Synergistic effect of sub-analgesic-dose ambroxol and pregabalin in oxaliplatin-induced cold allodynia

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Neuropathic pain is one of the most frequent adverse effects in patients receiving antineoplastic agents such as oxaliplatin or paclitaxel. In this research we investigated a potential utility of combination drug therapy: ambroxol and pregabalin to attenuate cold allodynia. To induce neuropathy a single dose of intraperitoneal oxaliplatin was used. Cold allodynia in response to a thermal stimulus of 2.5C was measured in the cold plate test 3h and 7 days after oxaliplatin administration. Pregabalin and ambroxol were used as single drugs, or in combinations administered in a time-shifted manner to attenuate cold hypersensitivity. Hot plate test was used to assess antinociceptive properties of ambroxol. Locomotor activity and motor coordination were also evaluated. A hyperadditive, statistically significant antiallodynic effect of sub-analgesic dose of ambroxol combined with pregabalin was demonstrated. This effect was particularly strong when these drugs were given 4h apart. Both drugs used in combination reduced animals' locomotor activity but they did not impair motor coordination. Ambroxol did not show activity in hot plate test. Time-shifted co-administration of sub-analgesic ambroxol and pregabalin seems to be an interesting option to attenuate oxaliplatin-induced cold allodynia resistant to available drugs.
This study was financially supported by the National Science Centre grant UMO-2015/17/B/NZ7/02937

27. GPR35 agonist (Zaprinast) inhibits neuropathic pain-related behaviour and upregulation of pronociceptive factors in a rat model

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Unsatisfactory management of neuropathic pain results in poor clinical outcomes and impairs daily activities, quality of life, and social functions for patients all over the world and forces people to change their lifestyle due to their condition. Therefore, the aims of our research were to elucidate how a substance that acts as both an agonist of G protein-coupled receptor 35 (GPR35) and an inhibitor of cyclic GMP (cGMP)-specific phosphodiesterase (PDE) can influence neuropathic pain. Here, we demonstrated that preemptive and repeated intrathecal (i.t.) administration (16h and 1h before injury and then after nerve ligation daily for 7 days) of zaprinast (1 μg/5 μl) significantly attenuated the mechanical (von Frey test) and thermal (cold plate test) hypersensitivity measured on day 7 after chronic constriction injury (CCI) in rats. Our data provide that zaprinast diminished the activation of spinal microglia/macrophages and, as a consequence, the levels of IL-1beta, IL-6, IL-18, and NOS2 in the spinal cord and/or in the DRG. Our findings indicate that modulation of GPR35 could be an important strategy for innovative pharmacological treatments designed to decrease neuropathic pain.
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SYSTEMS NEUROSCIENCE

28. Shutting down dopaminergic system by optogenetic activation of the rostromedial tegmental nucleus and lateral habenula

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Rostromedial tegmental nucleus (RMTg) is the main source of inhibitory input to the midbrain dopaminergic neurons located in the ventral tegmental area (VTA) and substantia nigra pars compacta (SNc), which form the brain reward and motivation system. Lateral habenula (LHb), which is predominantly involved in responses to aversive stimuli, profoundly inhibits VTA/SNc neurons via activation of RMTg. Our aim was to verify the optogenetic methodology within the LHb -> RMTg -> VTA/SNc circuit. For this purpose rats were stereotaxically injected into the RMTg or LHb with adenoviral vectors containing Channelrhodopsin-2 (ChR2) and yellow fluorescent protein (eYFP) genes. After ChR2 (blue light-sensitive cation channel) expression, in vivo electrophysiological recordings were conducted. Dopaminergic neurons' activity in VTA/SNc was recorded, while RMTg/LHb was optogenetically stimulated using laser blue light. After each experiment ChR2-eYFP expression within RMTg/LHb borders and localisation of recorded neurons within VTA/SNc were histologically verified. Obtained results revealed that all dopaminergic neurons were strongly inhibited by optogenetic activation of the RMTg and LHb. Additionally, profound rebound excitation was observed following the inhibition. In conclusion, results showing that both RMTg and LHb are strong inhibitory sources for the midbrain dopaminergic system, sufficiently prove the effectiveness of the method.
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29. Neurons of the nucleus incertus give rise to highly collateralized innervation of different brain regions

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Nucleus incertus (NI) is a bilateral structure formed of GABAergic projection neurons located in the dorsal tegmental pons. NI innervates many nuclei in the forebrain, midbrain and hindbrain. However, it is not known if there are subpopulations of NI neurons innervating specific brain sites or NI neurons' axons highly collateralize to form nonspecific system of innervation. To address this question selected brain nuclei innervated by NI (ventral tegmental area, VTA; interpeduncular nucleus, IPN; medial septum, MS) were injected with CAV-Cre virus, which expresses Cre recombinase in cells that retrogradely internalize the virus. In each animal used in the study (Sprague Dawley rats) only one structure (VTA, IPN or MS) was injected. At the same time, all animals received NI injection of AAV virus carrying Cre-dependent reporter gene of fluorescent protein (mCherry). After two weeks brains were extracted, fixed and sliced to allow microscopic observation of axons of NI neurons retrogradely transfected from a specific brain nucleus. We observed that retrograde transfection of NI neurons from a single brain site results in labelling of fibres in numerous, functionally different brain regions (e.g. VTA, MS, IPN, hippocampus). This shows that NI is an origin of nonspecific brain system. Funding: NSC, Poland UMO-2014/15/B/NZ4/04896.

30. Cholinergic stimulation of the ventral tegmental area and electrical hippocampal activity in rats

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Theta rhythm is highly synchronized electrical activity of the hippocampus, which plays a key role in processes important to the right functioning of human beings such as learning and memory, spatial navigation, cognitive processes and REM sleep. Theta registrations in deep narcotic rats are used in studies of selected structures of the rhythm control system. Recent experience has shown that the ventral tegmental area (VTA) stimulation is also accompanied by the theta rhythm in the hippocampus, that is why we are talking about a parallel to the classic, "complementary" impulse pathway led by VTA. While the effect of VTA glutamatergic activation on theta has already been described, there is currently no data showing the effect of cholinergic VTA stimulation on induction of this rhythm. The aim of the experiments was to investigate the effect of pharmacological cholinergic activation (carbachol) and inactivation (atropine) of VTA on the formation and regulation of hippocampal theta rhythm. The results allowed us to verify the hypothesis of significant effect of cholinergic activation (analogous to PPN) in VTA for induction of theta rhythm and to better understand the functioning of neuronal circles involved in the induction of this rhythm from the brainstem level.

31. Rostromedial tegmental nucleus efferents in the ventral tegmental area regulate CS-induced cocaine seeking during extinction

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Exposure to conditional stimuli (CS) associated with cocaine use evoke phasic activity of the ventral tegmental area (VTA) dopamine (DA) neurons and initiate cocaine seeking behaviors. GABAergic neurons from the rostromedial tegmental nucleus (RMTg) project to the VTA where their stimulation results in rapid but transient inhibition of the VTA DAergic neurons. Such activity has been proposed to underlie extinction learning, thus, we aimed to investigate whether activity of the RMTg efferents in the VTA regulates CS-induced cocaine seeking during extinction. We used male Sprague-Dawley rats transduced with ChR2-containing adenoviral vector into the RMTg and cocaine self-administration paradigm. To study the effects of RMTg activity in the VTA, we applied photo-stimulation to the axon terminals of ChR2-expressing RMTg neurons in the VTA during CS-induced cocaine-seeking under extinction conditions. In control studies we performed real time place preference and locomotor activity in the open field tests. Photo-stimulation of the RMTg terminals in the VTA selectively attenuated CS-induced cocaine seeking but did not modulate hedonic state or locomotor activity. Our results indicate that activation of the RMTg GABAergic terminals in the VTA decreases CS-induced cocaine-seeking providing a new physiological mechanism to reduce cocaine craving.
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32. Adrenergic receptor signaling in the ventral tegmental area regulates phasic dopamine release in the nucleus accumbens core

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Noradrenaline modulates neuronal activity in the ventral tegmental area (VTA) via α1, α2 and β adrenergic receptors (ARs). Interestingly, administration of selective AR antagonists into the VTA modulates conditioned behavior dependent on phasic dopamine (DA) release in the nucleus accumbens (NAc) core, such as conditional stimuli-induced cocaine seeking. Thus, we used fast-scan cyclic voltammetry (FSCV) to measure the effects of selective AR-antagonists: terazosin (α1-AR), RX-821002 (α2-AR) and propranolol (β-AR) on electrically evoked phasic DA release in the NAc core in anesthetized rats. Stimulation electrodes fused with a guide cannula were inserted into the VTA and FSCV recordings of DA were obtained after intra-VTA saline micro-infusion (500 nl), followed by intra-VTA drug administration. Relative change in DA peaks evoked by electrical VTA stimulation after each drug vs saline were recorded. We demonstrated that intra-VTA AR signaling modulates phasic DA release. In particular, α1-AR blockade with terazosin reduced DA release in the NAc core in a dose-dependent manner (23% after 0.5 μg , 33% after 1 μg, versus 7% in saline control). Our results suggest that noradrenergic signaling in the VTA modulates phasic DA release in the forebrain.
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33. Locus coeruleus noradrenergic innervation of the mesocortical dopamine system

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Mesocortical dopamine (DA) system, constituting of ventral tegmental area (VTA) DA neurons and their axon terminals in the prefrontal cortex (PFC), encodes learning and memory. Recently, we demonstrated crucial role of noradrenergic signaling in memory formation. We aimed to demonstrate noradrenergic projections from the locus coeruleus (LC) – main source of the noradrenaline (NA) in the forebrain - to the VTA and the PFC. We used SD-Th-Cretm1sage rats micro-infused with Cre dependent adenovirus into the LC to restrict expression of reporter protein (YFP) to tyrosine hydroxylase (TH)+ neurons. We evaluated efficiency/specificity of the viral transduction. We mapped NA innervations of the mesocortical DA system by analysing YFP signal in the VTA and the PFC. Our results revealed presence of the YFP-expressing fibers in the interfascicular nucleus and parabrachial pigmented nucleus - parts of the VTA with distinct number of the DA neurons. In contrast, LC innervates molecular layer of the mPFC, whereas VTA DA afferents were present in the internal pyramidal layer. These results suggest that LC NA system innervates the VTA DA-ergic and non-DAergic areas. In contrast, LC NA-ergic afferents are not well positioned to modulate VTA DA-ergic innervations in the mPFC.
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34. Habenula's role in integrating brain-wide signals

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The habenula is an evolutionarily conserved mid-brain nuclei connecting forebrain structures with the monoaminergic brainstem regions releasing acetylcholine, dopamine and serotonin. Its functions include processing of experience-dependent information and a role in addiction, depression and sleep disorders. We are studying habenula's ongoing activity and its potential sources. By using a combination of brain-wide two-photon calcium imaging and electrophysiology we measured the ongoing and sensory evoked activity in the zebrafish habenula and the telencephalon. Our results showed that the ongoing activity of the habenular neurons is temporally and spatially organized. The patterned ongoing activity of distinct neuronal clusters is correlated with the activity in other brain regions, such as the olfactory bulb or telencephalon regions. Next, we examined the functional connectivity between telencephalon regions and the habenula by combining targeted electrical microsimulation with imaging of the habenula neurons. Further, we tested how these sensory and limbic inputs are integrated in the habenula. Our data demonstrates non-linear integration and sensory representation modulated by limbic inputs. These results suggest that the habenula is a hub that integrates and processes information from external world and internal brain states and further transmits it to its to monoaminergic brainstem targets that control animal's behavior.

35. The colocalization between Fos and serotonin positive cells after electrical stimulation of the raphe magnus nucleus in rats

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The main serotonin synthesis area in the brain are raphe nuclei. They are collections of neurons, with poorly defined cytoarchitectonic borders. The dorsal and median nuclei mainly constitute the rostral group of raphe nuclei. In turn, the raphe magnus nucleus (RMg), is the largest one from the caudal group. In our research we focused on the RMg. We analysed if electrical stimulation of the structure affected the number of serotonin positive cells (5-HT+) and if it was connected with the Fos proteins response in rats. The experiment was conducted on 26 rats. Each animal had an electrode implanted into the RMg. 15 animals were stimulated during 13-day procedure with current range between 60-140 μA determined individually. Brain slices were analysed after immunostaining procedure. We observed increased number of 5-HT+ after stimulation in arcuate and periventricular nuclei (both in the hypothalamus), the dental gyrus and motor cortex. In turn, the number of 5-HT+ was decreased in the reticular thalamic nucleus. Furthermore, the number of Fos proteins were almost 30% higher after stimulation in all these structures.
This project has been financed by Polish National Science Centre grant (2014/15/N/NZ4/04844).

36. Characterization of a novel population of Chrna2-expressing striatal interneurons

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The striatum is composed almost entirely of GABAergic neurons, most of which are the medium spiny neurons, strongly modulated by small yet heterogeneous population of local GABAergic interneurons such as fast-spiking (FSI), low-threshold spiking (LTS) or 5Ht3a-, NPY-, and TH–expressing interneurons. The aim of the project was to describe and characterize newly observed GABAergic population expressing cholinergic receptor subunit in striatum. In this study, we used a newly generated transgenic mouse line that labels interneurons expressing the gene coding for the cholinergic receptor subunit α2 (Chrna2). Using ex vivo whole-cell recordings combined with optogenetics, we obtained a detailed characterization of the electrophysiological, morphological and synaptic properties of Chrna2 cells. Chrna2 interneurons were sparsely expressed in the dorsal striatum, with possible developmental age-related change in expression.While majority of Chrna2 cells showed strong similarity to FSI in terms of electrophysiological

properties and expression of parvalbumin (PV), a small Chrna2+ subpopulation expressed LTS-like behavior. Surprisingly, striatal Chrna2 interneurons do not resemble Chrna2 neurons recorded form hippocampus or neocortex in terms of intrinsic properties or molecular markers. Optogenetic activation of Chrna2 interneurons induced strong inhibitory responses in MSNs, resembling stimulation of PV+ interneurons.

VISUAL PROCESSES

37. The influence of behavioral relevance of visual stimuli on the patterns of anterior-posterior connectivity and prefrontal activity

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It is a matter of ongoing debate whether involvement of prefrontal cortex (PFC) is needed for conscious perception. Some theoretical accounts, like the Global Neuronal Workspace theory postulate that areas in the PFC are critical part of the neuronal correlates of consciousness (NCC), whereas other theories, like the Local Recurrency theory posit that actual NCC are localized only in the posterior areas of the brain. One possibility is that PFC activity may reflect task- or report-related cognitive processes that are hard to disentangle from 'proper' NCC. Here we used fMRI (N=31) to measure PFC activity and functional connectivity of anterior-posterior connections during presentation of visual stimuli that were either relevant or irrelevant to the experimental task requirements. Functional connectivity was calculated by applying beta-series correlation method. Then we used Network-based statistics and graph theoretical measures to identify correlation strength and topology differences between conditions. We anticipated that activity of PFC and anterior-posterior connectivity should be increased only with task-relevant stimuli. The results revealed widespread increase of activity and connectivity in task-relevant stimuli condition with significant between condition differences in modularity and clustering coefficient metrics. The obtained results strongly support notion that PFC may not play causal role in visual awareness.

38. Is P3b a correlate of consciousness? Event-related potentials to consciously and unconsciously presented self-related stimuli

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The P3b event-related potential (ERP) — a late brain response observed over parietal electrodes — is hypothesized to constitute a neuronal correlate of consciousness (NCC). However, recent studies refute this hypothesis by showing that P3b can be evoked also by unconscious stimuli provided that these stimuli are salient. The present study was conducted to test a hypothesis that stimuli related to "self", which are known to be processed preferentially, will generate P3b potential even when presented unconsciously. In the conducted experiment 3 types of stimuli were presented for 16 ms: subject's own name, other name, or a blank (empty screen); and followed either by: a blank screen (supraliminal condition), or a backward mask (subliminal condition). Participants (n=23) performed a detection task on each trial. EEG (64 channels) was recorded during task performance. Analysis of a d' measure indicates that perception of subliminal stimuli was degraded, but not fully unconscious. The amplitude of P3b ERP was greater in response to the self name than to other name in the supraliminal condition ($t=3,79$, $p\leq0,00001$), but not in the subliminal condition ($t=1,54$, $p=0,14$). Therefore, the present study did not confirm previous findings of P3b in response to salient subliminal stimuli.

39. The role of short-term visual deprivation on the body representation

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Short-term visual deprivation by blindfolding influences tactile acuity and orientation in space and, on a neural level, leads to enhanced excitability of visual and motor cortices. However, to the best of our knowledge, the possible effects of short-term visual deprivation on body representation have not been examined. In the present study, we tested two groups of 30 healthy participants with the somatic rubber hand illusion, a well-established paradigm to probe the dynamic plasticity of body representation. Before the start of the procedure, the experimental group was blindfolded for 120 minutes, while the control group wore transparent goggles for the same amount of time. We found that although there was no difference in the subjective feeling of ownership of the rubber hand during the illusion, the blindfolded group showed a significantly larger recalibration of hand position sense towards the location of the rubber hand than the control group. This finding suggests that short-term visual deprivation boosts plasticity of body representation in terms of multisensory spatial recalibration of hand position sense.

40. Role of stimulus features in disentangling the proper neural correlates of subjective visibility ratings

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The goal of presented study is to disentangle electrophysiological correlates of visual awareness from other task-related processes through manipulating the level of processing of visual stimuli. Brain activity reflecting conscious perception should only be correlated with subjective visibility ratings, independently of perceptual task. Thirty-six students participated in the experiment (15 male, M=23.41). Every subject performed a visual backward masking task in two conditions (discriminating the color or magnitude of the masked digit) with EEG recording. Participants assessed their subjective visibility of stimuli on the PAS scale. Mean amplitude of components of interest was analysed (VAN - 140-240 ms; LP - 380-480 ms) with weighted regression mixed model. In VAN component time window, the mean amplitude correlated with PAS rating in both tasks. The mean amplitude in LP window correlated with PAS rating in high task, but not in a low task. Both VAN and Late Positivity components were present in all experimental conditions. VAN amplitude was sensitive to PAS Ratings, but there was no significant difference between conditions. Whereas the pattern of LP component was different for low-level and high-level task. Our results contest the interpretation of LP as neural correlate of consciousness.

AFFECTIVE PROCESSES

41. A comparative canine/human conspecific and non-conspecific face and non-face processing fMRI study

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Much is known about the neural bases of face processing in humans; however, less is known about the degree to which face perception is distinct from head perception and whether these results generalize to species with less of a novelty effect, such as family dogs. The aim of this study was to begin addressing these gaps in knowledge. Pertinent comparative work has focused on primates comparisons and has revealed comparable neural substrates to face processing across the species. This study also explores whether an evolutionarily more distant species, the domestic dog also exhibits selective cortical responses to faces. We examined differences in BOLD response to human and dog

faces and occiputs in humans and family dogs in a two-site, awake and non-invasive fMRI study. Findings obtained with humans indicate that face-sensitive regions in STS but not in FFA are particularly responsive to human faces while face-sensitive regions in OG responded more strongly to dog faces. Data collection on dogs is ongoing and thus corresponding comparative results will be included in the conference presentation. Our study demonstrates that in humans conspecific and non-conspecific faces elicit different patterns of activity in face-sensitive regions.

42. Is he hostile or excited? Reading the mind in the eyes of children - introduction to the Nencki Children Eyes Test (NCET)

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The Theory of Mind (ToM) is an ability to accurately read mental states of other people. The Reading the Mind in the Eyes-Test (RMET) was proved to be a valid measure of ToM. In this test, adjectives describing mental states need to be attributed to photographs of eyes region of adults. In recent years, comparable version of the test with the eyes region of children – The Mind in a Child's Eyes task (MCET), was developed. However, behavioral studies utilizing these two tests have led to inconclusive results that could reflect different neuronal processes underlying MCET and RMET. To address this issue, we have developed the Nencki Children Eyes Test (NCET), which is suitable also for fMRI. Here we present preliminary findings, based on data from 8 adult participants (5 males). Participants did not differ in the number of correct responses between NCET and RMET. Both tasks activated the left inferior frontal and superior temporal gyri. However, when compared directly NCET>RMET induced activation in the left amygdala, putamen and right inferior frontal gyrus. Current preliminary results could be interpreted in line with findings suggesting that recognizing emotions of people of their own age is more automatized than distinguishing emotions of children.

43. Feeling other people's pain: an ERP study on facial attractiveness and empathy

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Empathy is the ability to indirectly share emotional states of other people and it consists of two components: neural resonance and cognitive empathy. Both components of empathy can be studied by measuring the reaction of the participants exposed to the pictures of models who feel the physical pain indicated by e.g. a sting with a needle. Research revealed that neural resonance is related with modulation in amplitude of early event-related potentials (ERP) components like N1, P2, N2 and cognitive empathy is linked to P3 amplitude. In our study, we investigated the influence of facial attractiveness on the empathy-related ERP components. Participants (N= 24) were watching photos of physically attractive and unattractive men and women who feel pain. N1 and P2 components were sensitive to facial attractiveness. Amplitude of frontal N2 component was more positive for the stimuli associated with feeling of pain than for neutral stimuli, but only for unattractive faces. The results of our study are consistent with the results of the research concerning cross-racial empathy and feeling other-race pain. Results also support a neural and temporal distinction between two sequential processing stages underlying empathy.

44. Psychophysiological reaction to hand images

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Recognition and discrimination of human faces is an important and engaging task for brain. Many psychophysiological research shows reaction to it at physiological level (heart rate, GSR, eye tracking, EEG, EMG). Reaction of arousal systems is a key indicator of importance of stimuli. Hands seems to be second important body

part for interpersonal communication, so nervous system should also be sensitive for them. Main hypothesis of this pilot research was that hands release stronger physiological reaction than other objects. There are a few publications in this field and they are mainly focused on EEG measurement. This hypothesis was tested with use of AdInstruments PowerLab T26. Galvanic skin reaction (GSR) and heart rate were measured. Subjects reactions were recorded during series of photos presentation - which depicted hands in different arrangements or daily use objects. GSR data was prepared for further analysis using deconvolution method. Results show an influential reaction to the group of images which contained hands ($p < 0.05$) for GSR peak amplitude. This suggest higher sensitivity of human nervous system to hands shape and activity, independently from context. Further tests can bring more interesting information about meaning of hands stimuli.

45. *The Effects of Slow Paced Breathing on Affective State, the Cardiovascular System, and Adequacy of Ventilation*

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The present study aimed to investigate the influence of slow paced breathing on adequacy of ventilation, cardiovascular activity, and affective state. Furthermore, we investigated the effects of the use of a cover story which hides the goal of the experiment. Eighty-three participants were randomly assigned to one of three groups: 0.1 Hz, with and without cover story, and, as a control, paced breathing at 0.28 Hz. We measured the effects of slow paced breathing on affective state (unpleasant and pleasant arousals), adequacy of ventilation as measured by partial pressure of end-tidal CO2 (PetCO2), respiratory sinus arrhythmia (RSA), and sympathetic control of the heart (pre-ejection period; PEP). The use of a cover story did not influence the effects of paced breathing. Slow paced breathing led to increased RSA. Changes in RSA were not related to changes in affective state. In the slow breathing groups, unpleasant arousal decreased only among men. Respiratory frequency did not influence PEP. PetCO2 decreased in all conditions and a larger drop in PetCO2 predicted a greater decrease in unpleasant arousal. We speculate that this relation reflects the influence of pulmonary stretch receptors on suffocation-related increase in unpleasant arousal.

46. *Tracing the melanopsin system: hedonic tone, melatonin and cortisol in prolonged blue-light blockade*

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Melanopsin system transfers the information on environmental light from retinal ganglion cells to suprachiasmatic nucleus and further to pineal gland. It has also numerous projections to various brain structures, including limbic system. Thus, it is thought to directly influence affective functioning. The stimulus is 'blue light' (BL), part of light spectrum ca. 480 nm. In this study 19 young and healthy volunteers were using amber contact lenses, eliminating 90% of that wavelength. During four weeks of constant BL blockade, neural, biochemical and psychological variables were registered. Here, we traced the effects of blocking the BL on affective state (hedonic tone, positive and negative affectivity, anxiety) and daytime sleepiness, as well as on melatonin and cortisol levels. No significant differences in psychological variables and biochemical parameters were observed, except of slight tendency ($p=0.1$) to higher daytime sleepiness and higher mean evening melatonin levels. However, in 6 subjects the positive change (increased hedonic tone) was observed, while in 9 subjects the change was negative. Both ANOVA and correlation analyses showed that negative change was associated with higher baseline sleepiness, anxiety and negative affect, and lower positive affect ($p<0.05$). There were no differences in melatonin and cortisol parameters between the two groups.

47. Arousal and Subjective Significance of words shapes ERP correlates of emotional categorisation task

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The role of activation in form of arousal and subjective significance associated with word meaning (combined in 3x3 orthogonal manipulation scheme) was investigated for an explicit emotional judgment task performed on activation charged words. Valence, concreteness, frequency of appearance, and length of stimuli were controlled in a way that only words with neutral or moderate values on those dimensions were chosen. We expected to find dissociative effects of both factors. The behavioral results showed that the fraction of words perceived as emotional increases with an increase of arousal or subjective significance. The electrophysiological results showed that both factors influence amplitudes of ERP. General effects of subjective significance were found for early (60-120 ms and 120-250 ms) and late (350-490 ms) time ranges. Localized arousal effects were found in 250-350 ms and 350-490 ms time ranges at posterior and left frontal ROIs. Localized Subjective significance effects were found in 250-350 ms time range at right frontal ROI and in 350-490 ms at posterior ROIs. The result of this study suggests that the effects of arousal reported in earlier studies might account for a more complex form of activation that was recently postulated, namely the subjective significance.

48. A session of physical exercise intensifies communication between dorsolateral prefrontal cortex and affective cortical regions: an EEG effective connectivity study

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Growing number of evidence suggest that even a single session of acute physical exercise benefits mood. However, the brain mechanisms underlying such a response remain unclear. Especially, little is known about the influence of acute exercise on patterns of cortical brain connectivity. The aim of this study was to examine whether a single session of acute physical exercise affects interactions between dorsolateral prefrontal cortex (associated with affective control) and affective cortical areas (tempo-parietal regions). The interactions were estimated using Directed Transfer Function (DTF, an EEG effective connectivity method). 18 male adults took part in three testing sessions in a counterbalanced and randomized order: moderate-intensity continuous exercise, high-intensity interval exercise and seated rest condition. During each session, participants cycled or remain seated on a stationary ergometer for 24 minutes. Before and after each protocol, the 3 minutes of resting state EEG was recorded to estimate the information flow rate and direction between predefined regions. The results show a significant increase in communication flow from prefrontal lobe to affective cortical areas, after both sessions of exercise in comparison to seated rest condition. The study suggests that changes in functional connectivity might play a key role in mood improvement after a physical exercise.

49. Regular exercise is associated with greater ability to control negative emotions: an ERP evidence

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Being physically active is known to improve both emotional and cognitive functioning. However, little is known if regular exercise could benefit a specific ability to regulate emotions. The aim of the present study was to verify if being physically active is associated with a greater skill to control negative emotions. A group of highly active (n=26) and low active (n=26) participants were recruited based on physical activity questionnaires. Depending on

experimental condition, their task was either to passively view negative pictures or to control unpleasant feelings evoked by these images. To control emotions, participants were asked to use the reappraisal - a cognitive strategy of reinterpreting meaning of emotional stimuli. During the task, behavioral measures (ratings of perceived unpleasantness) were accompanied by neural assessment (evoked response potentials, ERPs) in response to pictures. Although, both groups equally assessed the negativity of pictures, neural data showed that the highly-active group was characterized by a greater reduction of the late positivity potential (LPP) in response to pictures for which emotion control was applied. As the LPP serves as a neural marker of emotional experience, the acquired data indicates that being physically active might be associated with a greater ability to control negative emotions.

50. Neural bases of positivity bias in ageing

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Studies on emotional processing in ageing have shown age-related changes in the preference of positive information often referred to as 'the positivity bias'. This effect has been found in studies on attention and memory, but its neural bases are still undiscovered. Our study aims at investigating the positivity bias on a level of neuronal activity, self-report, and behaviour. For this purpose, we collected functional magnetic resonance, behavioural, and questionnaire data from older patients and young healthy volunteers. During the scanning session participants completed a modified (affective) version of a lexical decision task. Data analysis focused on the comparison between the two age groups. The preliminary results show a support for the age-related positivity bias in the evaluation of affective stimuli but not in the self-reported affect and the ability to experience pleasure. Moreover, neuroimaging results revealed that comparing to the older group, younger adults showed enhanced activity in the salience network while engaging in the cognitive aspect of the emotion elicitation task used. We suggest that this difference might have contributed to the attenuated emotion processing in the older group observed in the task.

51. Cognitive control over memory – individual differences in memory performance for emotional and neutral material

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It is widely accepted that people differ in memory performance. The ability to control one's memory depends on multiple factors, including the emotional properties of the memorized material. While it was widely demonstrated that emotion can facilitate memory, it is unclear how emotion modifies our ability to suppress memory. One of the reasons for the lack of consensus among researchers is that individual differences in memory performance were largely neglected in previous studies. We used the directed forgetting paradigm in an fMRI study, in which subjects viewed neutral and emotional words, which they were instructed to remember or to forget. Subsequently, subjects' memory of these words was tested. Finally, they assessed the words on scales of valence, arousal, sadness and fear. We found that memory performance depended on instruction as reflected in the engagement of the lateral prefrontal cortex (lateral PFC), irrespective of emotional properties of words. While the lateral PFC engagement did not differ between neutral and emotional conditions, it correlated with behavioural performance when emotional – as opposed to neutral – words were presented. A deeper understanding of the underlying brain mechanisms is likely to require a study of individual differences in cognitive abilities to suppress memory.

52. Brain reactivity to visual emotional stimuli differs between naturally cycling women and oral contraceptive users: an event related potential study

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Introduced more than 50 years ago, oral contraceptives are used by more than 100 million women in the world. Sex hormones are closely linked to women's emotional well-being. There is scarce information available about the impact of synthetic components of oral contraceptives on women's cognitive abilities, brain structure and functions. The late positive potential (LPP) is a reliable electrophysiological index of emotional perception in humans. Higher LPP amplitude reflects stronger allocation of attentional resources to emotional than neutral stimuli. The amplitude is the largest for the stimuli most directly related to biological imperatives. Oral contraceptives users (OC, n = 39) and naturally cycling women (NC, n=39) were presented with visual emotional stimuli from the IAPS. The response was examined using event-related potentials (ERPs) method. NC women compared to OC users demonstrated significantly higher general brain activity 565 – 1000 ms post-stimulus. Significantly higher right shifted positivity in central/ centro-parietal areas was found in NC women as compared to OC users (324 - 1000 ms post-stimulus). NC women demonstrated higher LPP amplitudes than OC users (324 ms post – stimulus). The present study provides electrophysiological evidence that NC women are more reactive to visual emotional stimuli than OC users.

CLINICAL NEUROSCIENCE

53. Mindful acceptance or cognitive reappraisal? Neural correlates of emotion regulation in major depressive disorder

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Cognitive behavioral therapy (CBT) and mindfulness based cognitive therapy (MBCT) were proven to be effective in major depressive disorder (MDD). Both interventions differently address impaired emotion regulation (ER) in MDD. CBT focuses on reinterpretation of the meaning of stimuli, which can alter affective response. Mindfulness focuses on awareness of inner states, and fully accepting them without judging. The goal of this study was to compare brain activity related to both ER strategies. 20 MDD patients took part in an fMRI experiment. Before the scan qualified psychologist gave subjects detailed and exemplified instructions of the task, during which subjects were shown sad or emotionally neutral pictures, with one of three instructions: to change the interpretation to more positive (REAP), to be mindfully aware and accepting (MIND), or just to observe the photos (PASSIV). fMRI results showed extensive activations including ACC and IFG during the REAP, supposedly representing the cognitive effort to reinterpret the viewed scenes. No significant clusters in MIND>PASSIV contrast were found, although insula was expected as was shown to be more active after MBCT. This can suggest that the subject naïve to mindfulness techniques have difficulties in engaging in this kind of ER strategies.

54. Can frontal alpha asymmetry be still treated as a biomarker of depression and mood disorders?

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Previous studies using EEG (electroencephalography) showed that depression was associated with disturbed normal brain lateralization. It has been observed that depressed patients display asymmetry of alpha power in the frontal cortex (difference between the left and right brain hemispheres) (Davidson, 1994, 2004; Bench, Friston, Brown, Scott, 1993). This effect is often treated by researchers as a biomarker of depression (Iosifescu et al., 2009. Baskarana, Milevc, McIntyre, 2012). Recent studies and meta-analyzes (Olbrich, Arns, 2013, Thibodeau et al., 2006, van der Vinne et al., 2017) question the relationship between asymmetry and depression. So far, few studies have attempted to determine how much the asymmetry index coincides with the mood level (but see: Jiang et al., 2016). We will present results of several analyses in two independent studies (Study 1: N=87, Study 2: N= 62) with resting state EEG. Prior to registration, each participant completed questionnaires determine the current level of mood. Our work tries to set a

higher standard for EEG alpha asymmetry studies by using multiple comparisons with relevant correction, always presenting topographical results and testing not only group contrasts but linear relationships. In both studies we did not find significant relationship between alpha asymmetry and mood level. This may indicate that although alpha asymmetry may be a marker of depression vulnerability, it cannot be interpreted as a marker of mood level.

55. *Decreased left temporal cortex connectivity as a correlate of depressive rumination in clinically depressed patients*

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Depressive ruminations are repetitive thoughts associated with symptoms, causes, and consequences of one's negative feelings. This maladaptive coping strategy has been shown to prolong and deepen depressive episodes and to increase their recurrence. The aim of this study was to explore cortical effective connectivity related to rumination in depressed patients. 15 clinically depressed patients and 15 healthy controls took part in an EEG study. Electrophysiological data was collected during induced state of depressive ruminations and compared with positive and neutral conditions. Effective connectivity was investigated using the Directed Transfer Function method which is based on a Granger causality. We hypothesized that depressed patients would differ from healthy control in effective connectivity among the emotional regulation brain circuit. Mixed effects models were used to calculate interactive effects between group and valence. It was revealed that left temporal cortex outflow to parietal and left dorsolateral prefrontal cortices was decreased in depressed patients during rumination. Moreover, effective connectivity of depressed patients was less differentiated between conditions. This connectivity pattern might be related to less effective emotional regulation in depressed patients when ruminating. Connectivity of the left temporal cortex might be an important correlate of depressive rumination in depressed individuals.

56. *Neural correlates of ruminations in an extreme ruminators sample*

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Cognitive-attentional syndrome (CAS) is a common feature of various emotional disorders, according to meta-cognitive approach. Its main symptom is a pattern of persistent negative thinking (rumination). There are no published studies of neural correlates of CAS. 45 participants, aged 18-45, with no current psychiatric treatment, with high results in CAS measures (high-ruminators) underwent Rumination Induction during fMRI procedure. Ruminative (RUM) and abstract (ABS) sentences were used to provoke thoughts. Each condition consisted of 10 sentences each (30s), separated by a fixation cross (10s). Neuroimaging data were analyzed using SPM software and are reported at $p<0.05$ FWEc. During RUM condition we observed activations in medial LH-prefrontal cortex, LH-precuneus, LH-angular gyrus, LH-temporal cortex and occipital poles. Direct contrast of RUM>ABS revealed activation in precuneus, middle part of LH-cingulate cortex and LH-occipital part of fusiform gyrus. Neural activation in high-CAS participants during Rumination Induction task is similar to Default Mode Network pattern, which is often interpret as equivalent of rumination in depressive patients. Results specific for RUM condition concerns activation of regions engaged in self-referential processing, and retrieval of memories of social and emotional situations. These neuroimaging results could be interpreted as manifestation of what constitutes a phenomenological description of rumination experience.

57. *Alterations in resting-state functional connectivity of the Theory-of-Mind network in adult women with a history of childhood maltreatment compared to comparisons*

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Background. Childhood maltreatment is a risk factor for the development of psychopathology in adulthood and is associated with impairments in social and emotional functions, such as mentalizing or Theory-of-Mind (ToM). However, no study to date has examined the resting-state functional connectivity of the ToM network in maltreated individuals. Methods. Images were acquired using a 3T Magnetom Siemens TrioTim MRI scanner. The seed regions were defined based on the peak coordinates of areas activated by a ToM localiser task (bilateral temporoparietal junction, dorsomedial prefrontal cortex, bilateral temporal poles and precuneus), plus the bilateral amygdala, known to be involved in mentalizing. Resting-state functional connectivity (RSFC) was run to compare the connectivity of these areas to the rest of the brain in 35 adult women with a history of child abuse versus 31 unaffected comparisons. Results. Child abuse was associated with increased RSFC relative to unaffected comparisons between the left amygdala and the precuneus, various ToM regions and the brainstem, and the dorsomedial prefrontal cortex and the cerebellum. Conclusions. Childhood maltreatment influences various nodes of the ToM network at rest, confirming its role in the social difficulties manifested by maltreated individuals.

58. Latent profiles of antisocial behaviour in a male offender sample

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Antisocial behaviour is a heterogeneous construct and is generally associated with antisocial personality disorder and psychopathy. The purpose of the present study was to identify distinct antisocial profiles in male offenders based on a self-report measure of psychopathic traits and investigate how these profiles differentiate based on associated personality traits, externalizing behavior and criminogenic factors. Latent profile analysis using the Self-Report Psychopathy Short-Form identified four antisocial profiles: generic offenders, impulsive-antisocial traits offenders, non-antisocial psychopathic traits offenders, and psychopathic traits offenders. The validity of the profiles was supported by their links with external variables concerning psychopathic personality correlates, externalizing behavior and criminogenic factors. These results were consistent with findings of previous subtyping studies that were based on the Psychopathy Checklist-Revised, which is the golden standard clinician-rated measure of psychopathy. The present study provides relatively extensive and multifaceted characterizations of the different antisocial profiles. In the future, profiles that are not only well-characterized in terms of personality correlates, but also incorporate biocognitive dimensions, could provide a more complete view of the individual (Brazil et al., 2016). This will aid diagnosis and foster the development of personalized treatment programs for individuals showing severe antisocial behaviour (Baskin-Sommers et al., 2015).

59. Effect of psychopathic personality traits on approach avoidance behavior

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Psychopathy is a disorder characterized by emotional dysfunction and antisocial behaviour with psychopathic traits being distributed normally in the general population. Behavioral and ERP studies have indicated that Psychopathic individuals showed disturbed performance on a basic level of automatic tendencies in response to emotional stimuli and that prefrontal motivational networks are involved in the processing of these tendencies (von Borries et al.2012, Ernst et al. 2013). The present study aims to investigate the effects of psychopathic personality traits on behavioral and electrophysiological correlates of approach and avoidance behavior. Participants performed an affective approach-avoidance task while EEG was recorded. Their level of psychopathic traits was assessed using the Self-Report Psychopathy Short-Form (SRP-SF), which discriminates four factors of psychopathy (interpersonal, affective, lifestyle and antisocial). Preliminary behavioral findings suggest that impulsive-irresponsible traits are positively related to avoidance to angry faces. Furthermore, preliminary ERP findings suggest an effect of psychopathic traits on early processing of angry faces. Identifying the neural correlates behind disturbed automatic tendencies may elucidate the mechanisms underlying aggressive or antisocial behavior.

60. Early life adversity and social cognition in schizophrenia

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In the last two decades, there has been a substantial number of studies indicating a link between schizophrenia (SZ) and early life adversities, such as childhood trauma (CT). However, less is known about the associations between CT and social cognition, defined as a set of mental operations underlying social interactions. Social cognitive deficits are a hallmark feature of SZ, which may result in impaired social and occupational functioning. Thirty patients with SZ (mean age=43.93; SD=11.8) and thirty healthy controls (mean age=33.07; SD=9.88) completed the Childhood Trauma Questionnaire (CTQ), which assesses the frequency and severity of five types of CT. Furthermore, all participants underwent three social cognitive tasks: the Emotion Recognition Task (ERT), the Reading the Mind in the Eyes task (RME) and the Hinting Task that evaluate the ability to infer emotions and mental states of others. We found that a history of CT, specifically physical neglect, was significantly negatively associated with poorer theory of mind abilities (measured with the RME task) and deficits in recognising disgust (measured with the ERT task) in patients, but not in healthy controls. These results suggest that the experience of CT has an impact on emotion recognition and theory of mind abilities in patients with SZ.

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MOTIVATIONAL PROCESSES

61. Enhanced Motivational Significance of Feedback-Based Performance Monitoring When Goal Impact is Transiently Increased

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Performance monitoring (PM) is crucial in goal pursuit. Its evaluative component has been investigated through two event-related potential (ERP) markers: the Feedback-Related Negativity (FRN) and P3. We recently showed that motivational demands can influence and shape the course of PM at the level of these components. Specifically, we demonstrated that the feedback's goal impact (i.e., relevance or importance to one's goal) generally modulated the FRN. In that, regardless of its valence, the feedback of higher goal impact revealed an overall less negative FRN relative to that of lower goal impact, suggesting a reduced monitoring for the former than the latter. Following this up, we ran a between-subjects design experiment whereby 60 participants completed a Go/No Go Task while 64-channel electroencephalography was recorded concurrently. Crucially, they were randomly assigned to high or low goal impact conditions, manipulated through the supposed task's diagnosticity, while keeping reward probabilities constant. While result hinted a similar FRN pattern as previously observed, it highlighted more the generally enhanced P3 in the high impact than the low impact group, with the former presumably assigning the feedback a higher motivational significance than the latter. This stamps further the idea that PM brain processes are influenced by motivational effects.

62. *Reactive control, rather than proactive control, is the predominant source contributing to congruency sequence effect*

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Congruency sequence effect (CSE) that is reflected by the modulation of the previous congruency on the current congruency translates an improved cognitive control. Yet, it remains unclear about which control mode (reactive versus proactive control) is the leading contributor. In this study, we manipulated the proportion of incongruent trials in a block-wise fashion to induce proactive (70% incongruent trials) or reactive (50% incongruent trials) control. Crucially, given the presentation of evaluative feedback is usually used as a means to foster reactive control, we performed a factorial design by presenting evaluative or neutral feedback at the single trial level while participants performed a Stroop task to explore how control mode could interact with another one. Results showed that the modulation of evaluative feedback on CSE was evident under reactive control only, suggesting that CSE is mostly driven by reactive control. More interestingly, we found the negative correlation between cognitive reappraisal (which is regarded as an emotion regulation strategy taken in advance) and CSE under reactive control with evaluative feedback presented, which provided us some exploratory evidences regarding the ties between defensive motivation and conflict-driven control mode.

63. *Modified MultiSource Interference Task (MSIT+) reveals flanker interference effect to reaction time and ERP temporal dynamics*

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Multi-Sensory Interference Task (MSIT) is applied in conflict processing studies and is known to activate anterior cingulate cortex (ACC). The standard MSIT has two conditions: no interference (easy congruent – EC) and multi-source interference (hard incongruent – HI). However, contribution of uni- and multi-source interference to temporal dynamics of brain activation in conflict processing are not well studied yet. We introduced the modified MSIT (MSIT+) with two additional conditions: only spatial (easy incongruent – EI) and only flanker interference (hard congruent – HC), and evaluated effects to RT and temporal dynamics of brain activity. Healthy participants performed MSIT+, while EEG was recorded from 128 active electrodes. Behavioural results showed increasing average RT: EC < EI < HC < HI, ($F(2,18)=12.9$, $p<0.001$, $n=6$). ERP topographic (ERP microstate) analysis revealed significantly ($p<0.05$) prolonged duration of N2/P3-corresponding microstate (characterized by fronto-central negativity and parietal positivity) in flanker conditions (HC, HI) compared to non-flanker conditions (EC, EI), while the sole spatial interference had no effect on ERP dynamics. Fronto-central negativity might reflect ACC activation. Preliminary findings highlighted effect of different conflict types to RT and flanker interference effect to ERP temporal dynamics regardless of spatial congruence.
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64. *An ERP study of the effects of attentional alerting on conflict resolution*

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Attentional alerting may be separated into two phases: a quick, exogenous, phasic alerting, followed by a slower, endogenous, tonic alerting. Recent behavioral studies with a flanker task showed that phasic alerting increased the cost of flanker conflict resolution in both accuracy and speed of responses, whereas tonic alerting decreased the cost of conflict resolution in accuracy, but at a cost of the conflict resolution speed. In the present study, we recorded EEG event related potentials (ERP) to examine the brain processes underlying the relationship between alerting and conflict resolution. Thirty-two participants completed the flanker task with targets preceded by auditory cues. Effects

of phasic alerting were measured with 100 ms cue-target interval (SOA), and of tonic alerting with longer, 800 ms SOA. We analyzed N2pc component as an index of stimulus selection, P3b components as an index of stimulus-response integration, and LRP components as an index of response conflict. The results suggest that the two alerting modes may operate at different stages of the conflict processing: phasic alerting at the early perceptual/attentional stages, and tonic alerting at the later response-selection and conflict resolution stages.

POSTER SESSION II

NEUROPSYCHIATRY

1. *Antidepressant drugs inhibit production of proinflammatory cytokines in mouse dendritic precursor JAWSII cells*

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Antidepressant treatment have proved effective in suppressing contact sensitization in a murine model of contact hypersensitivity (cell-mediated immune response). The aim of present study was to elucidate if the fluoxetine and desipramine are involved in the inhibitory effect on proinflammatory cytokines production by dendritic cells. The JAWSII cell line (immature murine dendritic cells) was stimulated by lipopolysaccharide (50 ng/ml), mixture of cytokines interferon(IFN)-γ/tumor necrosis factor(TNF)-α (10 ng/ml) and 2,4-dinitrofluorobenzene (DNFB; 1 μM/ml), cultured 24 hours. Antidepressant drugs – fluoxetine and desipramine (both: 1 and 5 μM) was added to the culture. Supernatants were collected. The level of proinflammatory cytokines – interleukin(IL)-1β and IL-6 was measured by ELISA assay. The stimulants significantly increased the secretion of cytokines and used antidepressants regulated this inflammatory response. It can be concluded that antidepressant drugs are effective in inhibition of proinflammatory releasing by murine dendritic cells, which may contribute to mechanism of suppression contact hypersensitivity. This study was supported by grant: NCN, PRELUDIUM 7; UMO-2014/13/N/NZ6/00639.

2. *Regulation of alternative Dclk1 kinase gene isoforms by psychotropic drugs*

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Multiple transcript variants of Dclk1 generated by two alternative promoters and alternative splicing are differentially expressed and have different kinase activities. Recent studies showed that Dclk1 along with microtubule polymerizing activity has a role in synaptic plasticity and neurogenesis. However, the process of transcriptional regulation and biological function of alternative variants of Dclk1 remains elusive. We applied next-generation sequencing to analyse changes in the expression of Dclk1 gene isoforms in the brain in response to several psychoactive drugs with diverse pharmacological mechanisms of action. We validated our results with quantitative PCR using isoform-specific designed probes. Drugs that act on serotonin receptors (5-HT2A/C) regulate a subset of Dclk1 isoforms in a brain-region specific manner. The strongest influence was observed for mianserin-induced expression of an isoform with intron retention, called Dclk1-m. We found that the upregulation of Dclk1-m expression is transient, likely lasting only hours, and was not detected after repeated treatment with mianserin. In summary, we identified novel isoforms of the neuroplasticity-related gene Dclk1 that are expressed in the brain in response to psychotropic drug treatments.

3. *Effect of maternal "western diet" in the novel object recognition test in female and male offspring rats*

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Multiple studies performed on humans and animals support the hypothesis linking maternal nutrition to fetal development. It has been shown that the maternal diet effects primarily the conditions such as obesity, diabetes, anxiety and depression in offspring. The aim of this study was to investigate the effect of maternal high carbohydrate diet (HCD) and high mixed diet (HMD) on the working memory concerning novel object recognition task (NOR) in

offspring. Wistar rat dams were maintained ad libitum either on HCD and HMD or standard rodent chow (SD) during gestation and lactation. At postnatal day 67, NOR was performed. The test consists of the habituation phase, the familiarization phase (two identical objects), and the test phase (two objects, one identical to the sample and the other one being novel). The results indicate that neither diet does not affect discrimination index 1h after familiarization phase in offspring. However, after 24h, a significantly increased discrimination index in HCD male was observed, while both diets increased this index in female. Our data suggest that the maternal diet consumption may affect cognition and memory retention, however, the molecular mechanism underlying such changes requires further investigation.
Supported by research grant UMO-2016/21/B/N24/00203 from the National Science Centre.

4. The effect of maternal modified diet on anxiety-like behavior in adolescent male and female rats

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The fetal programming theory describes how external factors such as maternal lifestyle, disease, addictions and diet may influence the fetal development. The aim of this study was to investigate the effect of maternal high carbohydrate (HCD) or rich in carbohydrate and fat diet (HMD) on the anxiety-like behavior assessed in the elevated zero maze test (EZM) in offspring rats. Wistar rat dams were maintained ad libitum either on HCD, HMD or standard rodent chow during gestation and lactation. At 30 postnatal day the EZM was performed. Behavioral measures included time spent in the light open areas and number of entries into the open areas. We have observed that the female offspring rats, which mothers were fed on HMD, there was the tendency to spend more time in open areas, as well as a significant increase number of entries into the open areas, head dips and stretched attend postures. At the same time, in HCD offspring and HMD male no differences were observed. In conclusion, our results may suggest that the HMD can effect the female phenotype, and decrease anxiety-like behavior. The molecular mechanism will be determined in ongoing research.
Supported by research grant UMO-2016/21/B/N24/00203 from the National Science Centre.

5. Investigation of a novel G protein-biased opioid, PZM21, in nociceptive and addiction-like behavioral assays

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Opioid analgesics are among the most popular painkillers, however a wide range of side effects and strong addictive potential make their clinical efficacy limited. The concept of ligands biased towards G-protein pathway with the exclusion of β-arrestin-2-mediated side effects has become a very promising target for the development of efficient and potentially non-addictive opioid therapeutics. Recently discovered functional mu opioid receptor agonist, PZM21, was reported not to cause addiction-like behavior but attenuated only affective component of pain in mice (Manglik et al., 2016). Here, we aimed to further investigate analgesic and addictive aspects of PZM21. In addition to the previous report, we showed that treatment with PZM21 evokes long-lasting, dose-dependent and mu opioid receptor-mediated spinal analgesia measured in tail flick test. Importantly, administration of PZM21 did not result in formation of conditioned place preference, indicating that it does not have rewarding properties. Moreover, PZM21 did not induce other opioid-like behavioral effects such as hyperlocomotion and locomotor sensitization. Taken together, out results reveal that PZM21 has antinociceptive profile in thermal analgesia assays, but does not induce reward-related behavior in mice. Thus, treatment with PZM21 allows to provide pain relief while avoiding undesirable rewarding effects.
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6. 2-Aminoimidazoles: emerging drug-like serotonergic chemotype

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2-Aminoimidazole remains an unexplored highly basic scaffold that has been found to be a common molecular framework of numerous marine alkaloids and synthetic antibacterial agents. In our study, variously modified 2-aminoimidazole have been used as bioisosteres of the classical basic moieties in the design of a 57 member series of 5-HT6 receptor antagonists. The core scaffolds based on 1-benzenesulfonyl-1H-indole served as a prototypical platform to compare the properties of six different basic groups containing aminoimidazole or aminothiazole motif. 5-HT6R is a Gs coupled serotonin receptor involved in the regulation of cholinergic transmission. It has been a long lasting hope for Alzheimer's disease patients since in animal models the receptor's antagonists were shown to significantly relieve the symptoms, possibly by restoring the physiological acetylcholine levels in the brain. Lead compound: AHN-208 (1 mg/kg) reversed the cognitive impairment in rats caused by the administration of scopolamine (1.25 mg/kg) in Novel Object Recognition Test. AHN-208 was shown to be non-toxic (LD50 > 2000 mg/kg p.o.). We suppose, that the 2-aminoimidazole and other amidine based heterocyclic fragments will fill the existing niche in the aminergic scaffold chemical space used for CNS drug design.
This study was supported by the National Centre for Research and Development Grant No PBS3/B7/20/2015 “New non-amyloid therapy of cognitive disorders” and by the Statutory Funds of the Institute of Pharmacology, Polish Academy of Sciences.

7. Effects of central serotonin depletion on attentional processes in the five choice serial reaction time task in rats

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Serotonin (5-hydroxytryptamine, 5-HT) is a monoamine, which is generated early in the developing brain. A rate-limiting step of serotonin synthesis in the central nervous system is tryptophan hydroxylase 2 (TPH2). A wide body of evidence suggests the involvement of 5-HT in modulation of attentional processes and impulsivity. The goal of our research is to investigate the consequences of central serotonin depletion. For this purpose, a zinc-finger nuclease technology was applied to create the TPH2-deficient (Tph2-/-) rats. In the present study, we used the 5-choice serial reaction time task (5-CSRTT) to measure visual attention (i.e., response accuracy and latencies) and impulsivity (premature responses) in Tph2-/- and Tph2+/+ rats. Animals were trained in the 5-CSRTT until they had achieved stable performance. In the training sessions, there were no major differences between Tph2-/- and Tph2+/+ rats in the investigated parameters. It may be suggested that modifications of the basic task (like varying stimulus or inter-trial intervals durations, brightness of the visual signal, or introducing distractors) may be necessary for the behavioural manifestation of this serotonergic manipulation.

8. Modelling communication deficits in rodents

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Communication deficits are hallmark symptoms of Autism Spectrum Disorders (ASD). The evaluation of communication in animal models is also possible, since rodents communicate by means of ultrasonic vocalizations (USVs). For example, newborn rats emit USVs with frequencies between 30 and 90 kHz when separated from their mother and nest. As these calls play an important role in social communication between mother and infant, isolation-induced vocalization has been widely used to model early communicative deficits in ASD. Several studies conducted in rodent models of autism have showed changes in pup isolation-induced USVs emission that include either increases or decreases in call rate or unusual patterns of vocalizations. The aim of the present study was to characterise neonatal USVs emissions in the valproic acid (VPA) model of autism. To this aim, pregnant Sprague-Dawley rats were exposed to VPA on day 12.5 of gestation. On the postnatal day 6, USVs were recorder in isolated

pups. The results demonstrated abnormalities in vocalizations in VPA-exposed animals that may be consistent with communication deficits seen in ASD.
This study was supported by the Polish National Science Centre grant NCN 2016/23/B/NZ7/01131

9. *The ligands of alpha7 nicotinic acetylcholine receptors improve memory processes and social behaviours in the neurodevelopmental model of schizophrenia*

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The alpha 7 acetylcholine nicotinic receptors (α7 nAChRs) are promising drug target for cognitive impairments and negative symptoms (e.g., social withdrawal) of schizophrenia. The activity of α7 AChRs can be enhanced by the agonists and positive allosteric modulators (PAMs). Previous data from this laboratory have shown no differences in the procognitive efficacy of two types of PAMs and of α7 AChRs agonists following acute administration in the rat. Here we evaluated the effects of repeated dosing of two functionally different α7 PAMs and agonist on recognition memory and social impairments in the neurodevelopmental schizophrenia-like model in rats. The novel object recognition and social interaction tests were used to evaluate the effects of subchronic treatment with CCMI, PNU120596 and A582941 in rats at the age of 8 weeks. Memory and social behaviour impairments were induced by prenatal exposition (E17) on methylazoksymethanol acetate (MAM; 22 mg/kg). Sub-chronic treatment with the tested compounds similarly enhanced the recognition memory and time spent in social interactions. The present study demonstrates that both α7 nAChRs PAMs and agonist demonstrate similar procognitive and prosocial activity in neurodevelopmental model of schizophrenia.
Acknowledgements: This study was supported by the Polish National Science Centre NCN grant Preludium 2014/15/N/NZ7/02978.

10. *Dopaminergic drugs in a mouse model of post-traumatic stress disorder: revealing a novel potential therapeutic path*

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Nowadays, the probability of experiencing a strong traumatic event may be up to 50%. Unfortunately, even more than 1/3 of those exposed subjects would develop symptoms of post-traumatic stress disorder (PTSD). Literally, this disorder is defined as a persistent re-experiencing of intrusive recollections of the traumatic event, hyper-arousal, avoidance of cues linked to trauma and numbing in response to stressors that last for at least 1 month. Actually, only 30% of patients achieve a satisfactory therapeutic effect. In this study, the activity of chronic administration of dopaminergic drugs, i.e. rotigotine (10 mg/kg, i.p.) and pramipexole (1 mg/kg, s.c.) in PTSD model-exposed mice was assessed. A single prolonged stress protocol (SPS) was used to induce mouse model of PTSD. The following tests were performed: a forced swim test, an elevated plus maze test, an auditory fear conditioning test and a spontaneous locomotor activity test. The analysis of ultrasound vocalizations was also performed. Our study revealed a strong potential antidepressant-like activity, potential anxiolytic-like activity, greatly reduced fear retrieval following administration of tested drugs in SPS-exposed mice. Simultaneously, no influence on spontaneous locomotor activity test. Our study confirms a far-reaching involvement of dopaminergic structures in PTSD pathologies and finds it worth further evaluation.

11. *Selective adenosine A2A receptor antagonist but not selective adenosine A1 receptor antagonist potentiates antidepressant-like effect of biometals (Mg2+, Zn2+)*

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Adenosine – an endogenous nucleoside, modulates release of serotonin, norepinephrine, and dopamine in the central nervous system. Both nonselective and selective activation of adenosine receptors in the brain produce depressive-like symptoms in some models of depression. Moreover, literature data give evidence that adenosine neurotransmission may modulate the glutamatergic conductance. Magnesium and zinc ions are well known as NMDA receptor ligands and there are a number of studies which have demonstrated their antidepressant-like effect. Accordingly, the aim of our study was to investigate an antidepressant activity of a joint administration of a selective A1 receptor antagonist – DPCPX or a selective A2A receptor antagonist – istradefylline with biometals (Mg2+, Zn2+). The antidepressant-like effect was assessed by the mice forced swim test. The locomotor activity was measured in order to avoid false positive/negative outcomes. The obtained results demonstrated that istradefylline (0.5 mg/kg) but not DPCPX (1 mg/kg) enhanced the antidepressant-like effect of Mg2+ (10 mg/kg) or Zn2+ (2.5 mg/kg). None of the used combinations changed the overall animal locomotor activity. Our outcomes indicated a synergistic action of selective A2A receptor antagonist in combination with the tested biometals, and the lack of such interaction in the case of selective A1 receptor antagonist.

12. Effect of sodium selenite on the antidepressant potential of adenosine receptor antagonists

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Literature data have demonstrated that deficiency of several trace elements is linked to the development of depression, while magnesium, zinc, or selenium supplementation improves mood. It has also been confirmed that magnesium and zinc ions enhance the antidepressant activity of other agents, but little is known about the possible interactions of selenium compounds. Therefore, the main goal of our experiments was to evaluate a potential influence of sodium selenite on the effectiveness of adenosine receptor antagonists with known antidepressant-like activity, i.e. istradefylline (an inhibitor of the A2A receptor) and DPCPX (an inhibitor of the A1 receptor). In order to assess the antidepressant-like potential the mice forced swim test (FST) was applied. When given in sub-active doses, an acute co-administration of selenite ions (0.25 mg/kg, per os) with istradefylline (0.5 mg/kg, intraperitoneally) increased mobility time of animals in the FST. However, the same effect was not recorded after concurrent injection of selenite ions (0.25 mg/kg, per os) and DPCPX (1 mg/kg, intraperitoneally). The obtained results were not influenced by hyperlocomotion of mice. It can be assumed that supplementation of selenium may augment the antidepressant potential of A2A receptor antagonists, whereas it does not affect the effectiveness of A1 receptor antagonists.

13. CB2 cannabinoid receptor ligands augment the antidepressant-like potential of magnesium ions

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Both pre-clinical and clinical studies have demonstrated that altered endocannabinoid signalling is associated with the development of depression, and that CB1 and CB2 cannabinoid receptor ligands exert an antidepressant-like activity. However, still little is known whether modulation of the cannabinoid system could affect the effectiveness of other antidepressant agents when given together. Therefore, the main objective of our study was to investigate the influence of the CB2 cannabinoid receptor agonist (JWH133) and antagonist (AM630) on the antidepressant activity of magnesium chloride. All experiments were carried out on male Albino Swiss mice. The forced swim test (FST) was used to evaluate the antidepressant-like potential, while the spontaneous locomotor activity was measured in order to filter out false positive/negative results. Concomitant acute intraperitoneal injection of sub-effective doses of JWH133 (0.25 mg/kg) or AM630 (0.25 mg/kg) and magnesium ions (10 mg/kg) resulted in prolonged mobility of the tested animals in the FST. The observed effects were not affected by the hyperlocomotion of mice. Our findings suggest that the concurrent modulation of the cannabinoid system via CB2 cannabinoid receptor and supplementation of magnesium ions produce at least an additive antidepressant-like effect.

14. Prenatal exposure to methylazoxymetanol acetate alters pups' ultrasonic vocalisation

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Rodent models of schizophrenia are commonly focused on changes in adult males' behaviour. Although subtle deficits in communication and/or cognition are seen already in childhood, early behavioural changes have not been well characterized in preclinical conditions. In addition, female rodents are rarely included in these studies. Using neurodevelopmental model of schizophrenia, based on the prenatal injection of methylazoxymethanol acetate (MAM; 22 mg/kg; PD 17), we investigated rat pups' behaviour important in the mother-pup interaction and sensitive for changes in early phases of neurobehavioural development. We studied social communication by recording ultrasonic vocalisations (USVs) elicited by removal of 8-day old rat pups from their nests. The results show that on the novel bedding, the pups emitted USVs with reduced center frequency. As compared with controls, MAM-treated pups displayed: i) lower power of the calls, ii) reduced bandwidth and iii) increase in the number of flat sounds. These data demonstrate that male and female MAM-exposed pups show atypical reaction to the maternal separation, which can be interpreted as the dysfunctional behaviour. This communicative behaviour might be considered a marker for early assessment of schizophrenia-like behaviour in rodents. This study was supported by the Polish National Science Centre grant 2014/15/N/NZ7/02978.

15. Analysis of volume of the lateral amygdaloid nucleus in the prepubertal and pubertal Spontaneously Hypertensive Rat as a model of Attention Deficit Hyperactivity Disorder (ADHD)

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Attention-deficit/hyperactivity disorder (ADHD) affects children. It is characterized by hyperactivity, aggression and problems with attention associated with volumetric abnormalities of various regions of the brain e.g. amygdala. Thus, the purpose of this study was to analyze volumetric changes in the lateral amygdaloid nucleus (LNA) during postnatal development in the spontaneously hypertensive rats (SHRs) - an animal model for ADHD and Wistar Kyoto rats (WKYs) used as control animals. The volumes of the LNA were compared using Cavalieri method in adolescent and mature SHRs and WKYs at two age stages: 4 and 10 weeks. Morphometric analysis was manually performed on the frozen sections of the brain stained by immunohistochemistry. The results show that volume of the LNA in both strains was significantly higher in 10 week old animals when compared to 4 week old rats, however, no statistically significant differences in the volume of the LNA were found between both strains at any of the stages studied. In conclusion, present results indicate that volumetric development of the LNA is not affected in rats with ADHD. However, abnormalities in the neurotransmission in this region may also account for ADHD symptoms.
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16. Ketamine protects from development of depressive-like behavior and accelerates the process of returning to the non-depressed state

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Ketamine an NMDA antagonist have gained wide attention due to its rapid antidepressive effects. Despite short biological half-life of ketamine (approx. 2.5h) even its single subanesthetic dose cause long-lasting changes in structural plasticity including alterations in spine density and morphology what seems to correlate with sustained behavioral effects. Recently ketamine has also been recognized as prophylactic against depression in various animal models. In our study, we aimed at determining if prophylactic ketamine injection has a long-lasting impact on structural plasticity in brains of resilient and susceptible mice that had undergone chronic unpredictable stress

procedure and went through the recovery period. We found that administration of ketamine before stress procedure not only cause the increase in the average sucrose preference and a number of resilient animals immediately after the cessation of stress but also seems to positively influence recovery of susceptible animals. Moreover, DiI staining of brain slices of stressed mice revealed that ketamine injected animals show significant differences in dendritic spine densities but not dendritic spine morphology compared to saline-injected ones. These results confirm and expand previous observations concerning the prophylactic action of ketamine in animal models.

17. Comorbid depression and cocaine use disorder: the effects of repeated treatment with 5-HT2C receptor agonist during extinction training on cocaine seeking in bulbectomized rats

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Several clinical reports indicate a high comorbidity between depression and substance use disorder. Depressed patients use addictive substances to feel better and to provide a temporary escape from anhedonia which leads to addiction. The present study investigated the effects of 5-HT2C receptor agonists in rats underwent either olfactory bulbectomy (an animal model of depression) or sham-operated surgery with cocaine self-administration and reinstatement procedures. We verified the hypothesis that chronic treatment with the 5-HT2C receptor agonists during extinction training might alter cocaine seeking behaviours. Male Wistar rats that underwent intravenous catheter implantation and the olfactory bulbs removal (OBX) and SHAM controls were trained to self-administer cocaine. Extinction procedures were instituted and lasted for 10 days, during this phase the animals were given 5-HT2C receptor agonists RO 60-0175 (1 mg/kg, ip) or WAY 161503 (1 mg/kg, ip) before each daily session. Reinstatement was induced by either injection of cocaine or the drug associated cue. Repeated treatment with 5-HT2C receptor agonists during extinction, significantly reduced reinstatement of drug seeking behavior in SHAM-operated and OBX rats. These results suggest that 5-HT2C receptors can be involved in mechanism of co-occurrent depression and cocaine addiction and may be the target for cocaine use disorder effective pharmacotherapy.

18. Effects of acute administration of selected synthetic cathinones on dopamine and serotonin levels in the mouse striatum and DNA damage in the mouse cortex

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Synthetic cathinones are a new group of synthetic psychostimulants that are analogues of cathinone derived from katha edulis plant. They interact with monoamine transporters elevating the extracellular level of monoamines. The aim of our study was to examine the effects of acute administration of methcathinone (MTHC), 3-fluoromethcathinone (3-FMC), α-pyrrolidinopentiophenone (α-PVP), α-pyrrolidinoheptanophenone (PV8), α-pyrrolidinooctanophenone (PV9) and 2,3-methylenedioxypyrovalerone (2,3-MDPV) on the extracellular dopamine (DA) and serotonin (5-HT) level in the mouse striatum and damage of DNA in the mouse cortex. Mice were administered with a single doses of MTHC, 3-FMC, α-PVP, PV8, PV9 or 2,3-MDPV (3 or 10 mg/kg). The striatal release of DA and 5-HT was measured using microdialysis in freely moving animals. The oxidative DNA damage was determined with the comet assay. All drugs produced a robust increase in both DA and 5-HT level in the rat striatum. The strongest DA release occurred after administration of 3-FMC, while 5-HT level was enhanced the most by α-PVP. Significant oxidative damage of DNA observed as single and double-strand breaks was found in the mouse cortex. Synthetic cathinones produced high elevation of DA and 5-HT levels. Toxic metabolites of those monoamines may contribute to oxidative DNA damage assessed in the mouse cortex.

19. Long-lasting amphetamine self-administration procedure: process optimisation leading to obtain addiction-like behavior in rats

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Amphetamine (AMPH) is a popular, cheap and easy accessible psychostymulant drug which causes lots of physiological and emotional alterations while intake. In rodent studies on substance of abuse, increasing attention is given to the so-called appetitive (or 50-kHz) ultrasonic vocalization (USV) being used to monitor changes in emotional states of animals exposed to the drug's action. As long-lasting drug administration is an essential requirement to obtain addiction-like behavior, the aim of our study was to evaluate two different schedules of AMPH self-administration (SA) in terms of maximalizing intensity of voluntary drug infusions. We examined two varied schemes: 6 SA days – 1 day off and 2 SA days - 1 day off in which each session was preluded by short period of drug inaccessibility. In each model, we monitored emotional states changes using 50-kHz USV. Our previous findings suggested that 6 SA days – 1 day off protocol made animals overloaded with AMPH action which resulted in decrease of intake intensity within subsequent experimental sessions. Using 2 SA days - 1 day off protocol, it minimalized those negative variations. What is more, both models reveal individual differences in propensity to SA AMPH.
This study has been supported by research grant UMO-2015-/19/B/NZ7/03610 from the National Science Center (Poland).

20. Antidepressant-like effect of GPR39 agonist (TC-G 1008) in comparison to imipramine, ZnCl2 or MK-801

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GPR39 is a zinc receptor which seems to play an important role in the pathogenesis of depression. Here we examined the effectiveness of antidepressant response following GPR39 agonist (TC-G 1008) administration in comparison to imipramine, ZnCl2 and MK-801. CD-1 mice received TC-G 1008, imipramine, ZnCl2 or MK-801 in a chronic or acute treatment (effect measured after 30 min, 3h, 6h and 24h). Behavioral response was evaluated in the forced swim test (FST) and locomotor activity test. Additionally, we measured BDNF in hippocampus following TC-G 1008 administration. TC-G 1008 induced antidepressant-like response at all points in time following acute treatment. Imipramine decreased immobility time after 30 min and 3h while ZnCl2 and MK-801 only after 30 min. Chronic treatment with all compounds decreased immobility time in the FST. TC-G 1008 induced fluctuation in BDNF protein level following acute but not chronic administration. GPR39 agonist causes fast and long-lasting antidepressant response. Our results suggest that GPR39 should be considered as a promising target in a development of new antidepressants. The study was supported by the Polish Ministry of Science and Higher Education, Iuventus Plus (project number: 0314/IP1/2015/73) and partially by the statutory funds of the Faculty of Pharmacy, Jagiellonian University Medical College.

BASIC NEUROSCIENCE

21. SRF controls miRNA expression during neuronal development in vitro

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Dendritic spines, the locus for excitatory synaptic transmission, are small, dynamically changing protrusions. Dendritic spines' shape changes from thin elongated filopodia-like structures to stable mushroom dendritic spines during brain development. Re-arrangement of neuronal connections plays an important role in proper circuitry formation. Serum Response Factor (SRF) is a major transcription factor in the brain plays a prominent role in regulating various programs of gene expression in the adult brain. In this study, we aimed to investigate a role of SRF in the regulation of structural plasticity and transcription during brain development. To analyse the role of SRF on spines formation we used mouse hippocampal neurons from SRF flox/flox mouse transfected by CRE recombinase in early stages of neuronal maturation. We analysed dendritic spines morphology at DIV21. We showed that the lack of SRF expression increases the percentage of immature, filopodial spines and decreases the spines density. To identify miRNAs regulated by SRF during neuronal development we used Exiqon microarrays. We identified four miRNAs (miR-129-5p, miR-132-3p, miR-212-3p, miR-222-3p) with significant changes in the expression between control and SRF depleted hippocampal neurons. These findings indicate that SRF regulates spines maturation and transcription of selected miRNAs during development.
The research was financed by Polish National Science Centre (NCN); decision No:2012/07/E/NZ3/01814.

22. Polypeptide complex yolkin from chicken egg yolk as a potential modulator of BDNF expression/secretion – a pilot study

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Brain-derived neurotrophic factor (BDNF) fulfills an important role in proper brain functioning. It regulates neuronal survival and outgrowth and influences synaptic plasticity and function. Furthermore, its expression level is decreased in patients with brain-related diseases. Polypeptide complex accompanying chicken immunoglobulin Y, named yolkin, possesses immunomodulatory activity and acts as a pro-survival factor in neuronal cell line PC12 treated with toxic amyloid protein. The aim was to study the effect of yolkin on expression and secretion of BDNF protein in neuronal cell line PC12 Tet On. Variations in the level of the intracellular BDNF protein and changes in phosphorylation of cAMP response element-binding protein (CREB) were determined via Western blotting. Whereas, the extracellular level of the BDNF protein was tested by ELISA assay. Yolkin showed neuroprotective properties through stimulation of neuronal PC12 cells to release significant amounts of mature BDNF, when added at concentrations higher than 10 μg/ml. This result was connected with an increased intracellular level of pro-BDNF. Moreover, it was correlated with activation of CREB protein responsible for the expression of BDNF and other proteins controlling survival of neurons and regulating intracellular transport of neurotrophins.

23. Early life growth retardation and increased fat metabolism in Tph2-deficient rats

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Serotonin is widely known as major player in the pathophysiology of a broad spectrum of psychiatric disorders. In recent years it has also been linked to fat metabolism. Genetic deletion of tryptophan hydroxylase 2 (TPH2), the rate limiting enzyme for serotonin synthesis in the central nervous system, results in lack of brain serotonin and a prominent growth retardation. The aim of our study is to elucidate the link between central serotonin depletion and growth retardation in Tph2-deficient rats. Body weight recording of Tph2-deficient and wildtype rat pups at different postnatal ages revealed first differences between the genotypes already 3-4 days after birth. This phenotype persists throughout the first postnatal weeks, however body weight and size are normalized later in life. The appearance of lacteals was normal demonstrating unaltered milk fat absorption in Tph2-deficient pups. Nevertheless, body composition analysis revealed that Tph2-deficient pups are not only smaller, but also have a decrease in body fat content in comparison to WT animals of the same age. Interestingly, 5-HTP treatment restored brain serotonin levels in Tph2-deficient pups, but did not affect their growth rate. We conclude that metabolic alterations, including increased energy consumption contribute to the growth retardation phenotype of Tph2-deficient rats.

24. Structural diversity of the ribbon synapses in the rat retina - a TEM imaging study

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Ribbon synapses are the peculiar and intriguing intercellular sensory connections located exclusively in the retina and in the organ of Corti. Despite the ongoing studies on unique morphological and biochemical properties on these structures their functions are not so far fully understood. Recent hypothesis suggests that the ribbon forms a reservoir of primed glutamate vesicles that are in very close contact with the presynaptic membrane. The pool of vesicles tethered to the ribbon facilitates the fast signal transduction in the sensory cells. In the current study we aim to describe the morphology of the rat eye ribbon synapses using transmission electron microscopy (TEM). The analysis was made using TEM Imaging software. Immediately after excision, the retinal samples were fixed in glutaraldehyde and subsequently were post-fixed in osmium tetroxide. After dehydration in alcohols and propylene oxide the samples were then infiltrated in propylene oxide/Epon 812 mixtures, embedded in Epon 812 epoxy resin then polymerized. Ultrathin sections were cut from with a diamond knife using a Reichert OmU-3 ultramicrotome,

mounted on 300-mesh copper grids, and stained with uranyl acetate. The grids were examined in a TECNAI G2 12 Spirit BioTWIN-TEM. We found a distinct structural diversity of ribbons located within the examined synaptic connections of the retinal plexiform layers. Interestingly, there were some differences both in the ribbon size and in the density of adjacent vesicle pool. The study does also reveal the subtle ultrastructure of the ribbons showing the RIBEYE protein localization.

25. New tool for integrative analysis of gene expression in specific cell types of complex tissues

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The immense computational power of the brain lies in the diversity of neural cells. This diversification has been a huge challenge for omics-based attempts to understand the roles of individual cells in brain networks. A handful of techniques were developed to "tag" and then purify nucleic acids from selected populations of cells in order to study their gene expression profiles by Next Generation Sequencing methods. With these techniques tissues can be rapidly frozen upon dissection, thereby minimizing artifactual changes to nucleic acids. We expanded this strategy by developing a Cre and Flp-dependent knock-in mice that combine four biochemical tools to study gene regulatory networks of the brain and other complex tissues. As a result, from specific cell populations of a single mouse, multiple biotypes of nucleic acids can be purified: 1) total RNA 2) translating mRNA, 3) miRNA and 4) chromatin. The system enables analysis of gene expression at multiple regulatory levels with optional RNA pulse labeling with synthetic uracil analogs.

26. A genetic approach to investigate neuron-glia interaction in health and disease

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Astrocytes and neurons represent the majority of brain cells, which together form complex networks. It is becoming increasingly clear that astrocytes and neuronal communication are crucial for sensory perception, decision-making and learning and memory processes. Malfunctions within the neuron-glia interactions are being recognized as fundamentally important in neurological and psychiatric diseases. To investigate the role of neurons and astrocytes in health and disease, we use recombinant adeno-associated viruses (rAAVs) for gene delivery and cell type-specific gene expression. We have developed genetic methods for cell type-specific optical activity imaging, circuit manipulation and inducible control of gene expression. My project is to investigate the role of astrocytes in synaptic plasticity and learning and memory. First, in acute brain slices, I will induce long-term potentiation with and without astrocytes or more specifically by also blocking astrocytic release machinery. Next aim will be to investigate the role of astrocyte function in the functional and anatomical organization of a tripartite synapse.

27. Glucocorticoid receptor-dependent alterations of metabolism in primary culture of astrocytes

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Stressful life events impact on memory, cognition and emotional responses and if prolonged are known to precipitate mood/anxiety disorders. Hypothalamic-Pituitary-Adrenal (HPA) axis is at the centre of stress response that is coordinated by glucocorticoids (GCs). The role of GCs on energy metabolism, immune system and negative regulation of the HPA axis are well characterized. However, little is known on how GCs regulate metabolism of the brain, particularly in astrocytes. It has already been shown that GCs treatment of astrocytes results in temporally dynamic transcriptome regulation in vitro and astrocyte-enriched mRNA changes in vivo. Here, we have exposed primary mouse astrocyte cell cultures to synthetic agonist of glucocorticoid receptor (GR), dexamethasone for 4h or 48h. To

evaluate the impact of GCs treatment on metabolic performance of astrocytes we used a series of readouts using Seahorse technology. We found that stimulation with GR agonist led to: change of glycolytic rate, alteration of mitochondrial oxidative phosphorylation, alterations of energy source used by astrocytes. Our data indicate that GCs exert a prominent effect on the energy metabolism in astrocytes. Understanding glucocorticoid metabolic regulation in astrocytes might help to understand the major factors involved in the dysfunctional brain circuits in stress-related disorders.

28. Neuronal factors regulate astroglial glycolysis

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It has been previously shown that neurons alter the expression of astrocytic metabolic enzymes by secretion of so far unknown molecule(s) into extracellular fluid. Our present study reveals that incubation of rat hippocampal astrocytes in neuronal conditioned medium (CM) elevates mRNA levels, protein abundance, and activity of glycolytic enzymes in astrocytes as compared to cells cultured in fresh neuronal medium (FM). We also present evidence that neurons release at least two types of metabolic modulators with distinct molecular mass. One of these regulators was identified as transthyretin, a 55 kDa protein. Transthyretin stimulates expression of regulatory enzymes of glycolysis (phosphofructokinase, pyruvate kinase) in astrocytes and increases the synthesis of ATP. This regulation is mediated by the cAMP/PKA-dependent pathway and is antagonized by the PI3K/Akt pathway. We also found that CM, but not transthyretin, stimulates expression of aldolase, but not phosphofructokinase and pyruvate kinase. This regulation is mediated by the PI3K/Akt pathway. Preliminary results show that this regulator is heat-unstable and has a molecular mass below 10 kDa. FM also stimulates expression of aldolase, but, after longer time of exposure than CM. This suggests that the 10 kDa regulator is also present in FM, albeit at lower concentration.

29. Muscle fructose-1,6-bisphosphatase is essential for LTP induction

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Fructose-1,6-bisphosphatase 2 (FBP2) hydrolyses a fructose-1,6-bisphosphate into fructose-6-phosphate and inorganic phosphate in the gluconeogenesis but the growing body of evidence suggests that FBP2 is engaged, via protein-protein interaction, in processes essential for cell survival. One of them is protection of mitochondria against calcium stress. It was demonstrated that FBP2 reduces the rate of calcium-induced mitochondrial swelling and interacts with mitochondrial proteins involved in energy and ion homeostasis. Calcium ions are indispensable for induction of neuroplasticity processes like long-term potentiation (LTP) and depression (LTD). The local calcium elevation in dendritic spines during potentiation affects mitochondria located in/nearby dendritic spines. To check if FBP2 is involved in mitochondrial calcium homeostasis, the ratio of FBP2-mitochondria co-localization during LTP and LTD induction in mouse hippocampal neurons culture was determined using the immunofluorescence microscopy. The effect of FBP2 on calcium-induced swelling was assayed spectrophotomerically in isolated neuronal mitochondria. Finally, to establish if FBP2 is essential for LTP induction, the expression of FBP2 in neurons was inhibited by antiFBP2-shRNA and the level of LTP marker proteins was observed using fluorescence microscopy. The results demonstrated that FBP2 is a crucial for LTP induction. It co-localizes with dendritic mitochondria during LTP induction and prevents calcium-induced mitochondrial swelling.

30. Electrochemical glutamate sensing strategies for neuronal cell cultures

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Glutamate is the principal excitatory neurotransmitter in the mammalian central nervous system. It is related to Parkinson's disease, cognitive disturbances, epilepsy, schizophrenia, attention deficit hyperactivity disorder and drug abuse. It is also crucial for processes of synaptic plasticity (underlying learning and memory) and formation of specific types of dendritic spines (spine head protrusions). Glutamate is involved in neuro-glia interactions and

having in mind its excitotoxicity it is worth to remember that astrocytes play a fundamental role in its regulation and in metabolic functions. We are currently working on two distinct systems for glutamate sensing, one being a sensor based on ion-transfer and the other a layered biosensor. The layered biosensor based on glutamate oxidase and prussian blue enables detection of hydrogen peroxide produced in the enzymatic reaction. As the concentration of hydrogen peroxide is proportional to concentration of glutamate it is possible to indirectly quantify the amount of the substrate. In the other approach detection of glutamate is based on specific interactions between glutamate and a recognition molecule, an ionophore entrapped in the organic phase covering the sensor. Sensors developed by us gives the opportunity to accurately determine the concentration of the main excitatory neurotransmitter within synapses in primary neuronal cultures.

31. Correction of organic mercury cytotoxicity in human glioblasts (U-373 MG) with antioxidants

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Compounds of mercury, even in small concentrations, exert intense negative effects on the human body, on the nervous system in particular. We attempted to estimate the features of separate and combined use of Thiotriazolinum and Mildronatum against toxic effect of mercury (II) (10.9 μM) chloride on cultured in vitro cells of IMR-32 - human neuroblastoma (concentrations of 0.01-10.0 mg/ml). These cells were studied in an unstained wet mount preparations and counted on slides stained after May-Grünwald using hemocytometer with the standard magnification. The relative number of living cells (%) was determined in the following conditions: exposition to mercury, exposition to mercury plus each of the Antioxidants, and mercury plus combination of Antioxidants (12 wells of the assay for each condition). The mean number of living cells exposed to Thiotriazolinum in concentrations of 0.1 and 0.01 mg/ml was, on average, about 83.0% vs 54.7% in case of isolated effect of HgCl2. The mean number of living cells cultured in the medium containing HgCl2 with the addition of Mildronatum + Thiotriazolinum reached 87.0% of the control value taken as 100%. Therefore, under the toxic effect of HgCl2 on cultured neuroblastoma cells, the combination of Mildronatum and Thiotriazolinum have demonstrated significant protective effect.

32. Dopamine D2 short receptor interacts with bradykinin B2 receptor

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The involvement of dopamine receptor 2, including their short isoform (D2Rsh) in neurodegenerative diseases has been reported. An increasing interest in the role of bradykinin receptor 2 (B2R) in such disorders is also observed. These receptors, ubiquitous in nervous tissues, belong to the G-protein-coupled receptor superfamily within which functional and structural interactions have been reported. A recent study demonstrated an interaction between B2R and the long isoform of the dopamine receptor 2. This study was aimed to investigate the cooperation between B2R and D2Rsh. Plasmid vectors encoding D2Rsh fused with EYFP or mCherry fluorescent proteins were constructed by Overlap Extension PCR technique and their functionality were checked. Colocalization and dimer formation of B2R and D2Rsh were determined in HEK 293 cells co-transfected with plasmid vectors by confocal microscopy and FLIM-FRET techniques, respectively. The consequence of B2R-D2Rsh dimerization was studied by monitoring secondary messengers, such as intracellular Ca2+ and cAMP concentration. The obtained results indicate on B2R-D2Rsh dimer formation at the cell membrane, that might modulate cellular action of the studied receptors. These observations enrich the knowledge about the function of these receptors, what may contribute to a better understanding of neurodegenerative pathologies.

33. Complex effect of benzodiazepines on GABAA receptor mechanism of activation

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GABAA receptors play a crucial role in mediating inhibition in the adult brain and are sensitive to many pharmacological modulators such as benzodiazepines whose mechanisms have not been fully elucidated. In particular, whether or not BDZ affect GABAAR gating remains a matter of debate. We examined the mechanism of flurazepam modulation of α1β2γ2L GABAARs, both wild-type and mutated at α1F64 residue, which has been shown to be involved in the receptor preactivation. We used patch-clamp technique with ultrafast perfusion system and single-channel recordings. We observed that α1F64 mutation strongly increases the spontaneous activity and flurazepam enhances it both in wild-type and mutated receptors by prolonging single-channel open times. Interestingly, flurazepam increased GABAAR current responses to a saturating partial agonist, P4S in wild-type receptor and enhanced responses to the saturating [GABA] in α1F64A and α1F64C mutants. This effect was associated with an acceleration of the macroscopic desensitization. Quantitative data analysis based on model simulations indicated that flurazepam affected both desensitization and preactivation transitions. Homology modeling combined with ligand docking revealed a very slow unbinding of flurazepam explaining very slow deactivation of spontaneous activity upon removal of this modulator.
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34. Long-Term Plasticity of inhibitory synaptic transmission in hippocampus strongly depends on the activity of MMP-3

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It is well established that matrix metalloproteinases (MMPs) play a crucial role in excitatory plasticity, learning and memory. Recently, we have shown that MMP-9 is involved in t-LTP in the barrel cortex of mouse (Lebida and Mozrzymas, 2016) and that MMP-3 supports NMDA-dependent LTP in hippocampus (Brzdak et al., 2017). Nevertheless, inhibitory synapses exhibit numerous forms of long-term plasticity but the contribution of MMPs in these processes is still unknown. To check the impact of the MMPs on the inhibitory long-term potentiation (iLTP) in the Sch-CA1 hippocampal projection we induced i-LTP using NMDA treatment (3 min, 20M) in control conditions and in the presence of MMPs inhibitors: FN-439 (180μM), SB3-CT (10μM) and UK356618 (2 μM). We have found that pharmacological blockade of MMPs activity by a broad spectrum MMP inhibitor (FN-439) prevented the induction of iLTP (CTR: 122±6%, n = 8; FN-439: 98±6%, n = 7; $p<0.05$). Interestingly, bath application of UK356618 (mainly blocking MMP-3) also completely abolished induction of iLTP (94±5%; n = 11, $p<0.05$). However, blockade of gelatinases by SB3-CT has no effect on i-LTP (121%±10%, n = 6, $p>0.05$). In conclusion, our data indicate that hippocampal iLTP in this model strongly relies on the activity of MMP-3.
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35. The influence of altered GSK-3β activity on dendritic spine morphology and excitatory synaptic transmission

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Glycogen synthase kinase-3 beta (GSK-3β) is a serine/threonine kinase regulating functional and structural synaptic plasticity in the hippocampus, mostly because of its role in excitatory synaptic transmission or development of neuronal morphology. Improper changes in the morphology of dendrites and synapses are associated with different neuropsychiatric and neurodegenerative disorders. How GSK-3β contributes to dendritic spine architecture and to the pathogenesis of these diseases is not fully understood. To understand the relationship between aberrant GSK-3 activity and structural plasticity of dendritic spines we developed primary hippocampal cell culture from mice with overexpression of GSK3β. Furthermore, we constructed two vectors expressing GSK-3β under synapsin I promoter: human GSK-3β[S9A] (active form) and GSK-3β[K85A] (inactive form) and following transfection of mouse primary hippocampal neuronal cultures, we are analyzing their activity by western blot and ELISA methods. The relation of GSK-3β to dendritic spine morphology and excitatory synaptic transmission is now studied by microscopic and electrophysiological methods in hippocampal neurons transfected by the designed constructs as well as in neurons derived from GSK-3β overexpressing mice. In further experiments we will investigate molecular mechanism of GSK-3β action in synaptic plasticity in our models of aberrant GSK-3β activity.

36. *Identification of signaling pathways activated by the addition of PDE10A inhibitor in the striatal neurons in vitro*

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Phosphodiesterase 10a (PDE10a) is a dual-specific enzyme that can hydrolyze both cAMP and cGMP. It is highly expressed in striatal medium spiny neurons. Activity of PDE10a modulates corticostriatal and nigrostriatal transmissions which are affected in schizophrenia. The aim of our study was to characterize new PDE10A inhibitor that can be potentially used as a drug in psychotic disorders. In the present study we analyzed signaling pathway modulated by CPL-500-036-02, a novel PDE10a inhibitor. We used three weeks old, primary striatal rat cultures. Neurons treated with the inhibitors were analyzed by Western Blot. PDE10a inhibition led to increased phosphorylation of proteins like AMPA receptor subunit GluR1 and extracellular signal–regulated kinases, ERK1 and 2. Since both D1 and D2 neurons express high level of PDE10A, we used striatal cultures from transgenic mice (drd1a-tdTomato and drd2-GFP) to compare the effects of PDE10A inhibition in both type of striatal neurons. Using immunofluorescence staining we monitored level of histone 3 phosphorylation in response to stimulation. Our preliminary results show that after PDE10A inhibition higher level of histone 3 phosphorylation occurred in D2 neurons. The results indicate that administration of PDE10A inhibitor increased phosphorylation of proteins by affecting cAMP signaling pathways in D1 and D2 neurons.

37. *The influence of transcranial direct current stimulation on elemental and molecular composition in the brains of obese rats*

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Recent evidence highlights that high-caloric diet not only induce obesity in terms of simple excess of calories intake, but also may change the electric activity in the brain areas responsible for appetite and carrving control results generating food addiction. Therefore, the main aim of our study is to determine the behavioral, biochemical (on lipid and protein secondary structure) and elemental levels influence of transcranial direct current stimulation (tDCS) used to change the brain electric activity of obese rats. The brains of electrically- and sham-stimulated animals on high-caloric diet were thinly sliced and raster-scanned. Micro-imaging was performed by Fourier transform infrared (FTIR) and synchrotron X-ray fluorescence (SRXRF) spectroscopies. From the SRXRF data, it could be drawn that anodal-type tDCS had a somewhat stronger effect in terms of the brain's essential elements triggering its electric activity: Na+, Cl-, K+, Ca++. The treatment also affected S, Fe, Cu and Zn brain levels. By using FTIR, it could be found that tDCS came up with significant lipid and protein secondary structure changes. The study also demonstrates that tDCS significantly decrease rat's desire for food. The results suggest that tDCS is an efficient mean for modulating cortical excitability in appetite control. Acknowledgment: Grant number DEC-2013/09/B/NZ4/02539.

38. *Examination of adenosine A 1 /A 2A receptor antagonists with MAOB inhibitory properties in antiparkinsonian tests*

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Drugs that act at multiple targets have been proposed to be advantageous for the treatment of neurodegenerative diseases like Parkinson's (PD) and Alzheimer's (AD) disease. Triple active compounds that inhibit the monoamine

oxidase B, block adenosine A 2A and A 1 receptors are expected to show synergistic effects in such conditions. In our efforts annelated derivatives of 1,3-dibutyl- and 1,3-dipropylxanthines bearing dopamine moiety were designed and synthesized. Compounds were evaluated for their activity against A 1, A 2A ARs. A 1 /A 2A AR ligands KD-396 and KD-397 with Ki values in nanomolar concentration range were identified. Moreover, these compounds showed MAO B inhibitory properties with IC 50 at human MAO-B in the 150-170 nM range. In the in vivo studies KD-396 and KD-397 reversed haloperidol-induced catalepsy. Two tests were used: bar test and cross leg position test. From the results of present studies, it may be concluded that antiparkinsonian effects of the examined compounds correlate with their triple activity A 1 /A 2A ARs antagonistic effects and MAOB inhibitory properties.
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39. Neuronal biomechanics in development and disease: understanding neuronal responses to physiological strain amplitudes

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Our brain consists of billions of neurons that form over a trillion of synaptic connections. To enhance our understanding of both healthy development of the brain and the impact of disease, the interest increases in how this complex system is regulated and how numerous connections with specific targets are formed. Recent studies on cerebral biomechanics emphasize a central role of mechanical forces in neuronal development. Thus, besides chemical cues mechanical stimuli are involved in neuronal maturation, pathfinding and development. We constructed an in-vitro system to assess neuronal responses to mechanical strain by cultivating primary rat neurons on elastomer chambers. The effect of mechanical forces during outgrowth and development was studied by subjecting neurons to cyclic strain after the cell adherence. Cytoskeletal proteins were stained by immunofluorescence and the cell morphology was analyzed. With uniaxial strain we could steer the direction of neuronal outgrowth. Further, stretched neurons showed an enhanced length growth and formation of nascent branches, suggesting that cyclic strain has a growth enhancing effect on cortical cells. Our results suggest adaptive mechanisms of neurons to mechanical stimuli. Cyclic mechanical strain may therefore play a key role in neuronal development and may constitute an essential parameter for neuronal cell regeneration.

LINGUISTIC PROCESSES

40. Human-analogue lexical processing hierarchy in the dog brain

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Human brains process lexical-meaning separately from acoustics-based of speech. Lexical-meaning processing takes place at a higher level of the processing hierarchy with hemispheric asymmetry. Whether this speech processing hierarchy is human-specific is unknown. Earlier we found hemispheric asymmetry for lexical-meaning processing in dogs, but the involved cortical regions and the similarity level of speech processing mechanisms in dogs and humans remained unexplored. In humans, fMRI adaptation designs have been used successfully to identify brain areas involved in speech processing, but adaptation effects have never been explored in awake dogs. To localize lexical-meaning processing brain areas and to explore whether lexical processing in dog brains follows a human-analogue processing hierarchy, we measured fMRI adaptation in awake family dogs. In an event-related design, dogs listened to lexically and intonationally marked and unmarked sound sequences. Short-term fMRI adaptation reflected intonation sensitivity in the bilateral auditory thalamus, and long-term fMRI adaptation reflected lexical-meaning sensitivity in the right auditory cortex. This multi-level fMRI adaptation in dogs reveals a human-analogue speech processing hierarchy, with temporally and anatomically distinct levels for acoustics-based and lexical representations, suggesting that the human lexical processing hierarchy is partially based upon ancient brain mechanisms that are also present in a non-primate species.

41. *The human mental lexicon representation of morphologically complex numerals - evidence from masked-morphological priming*

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The processing of morphologically complex words has been subject to considerable debate in recent years. At the heart of the controversy is the question of whether words such as singer possess their own entries in the human mental lexicon, or whether they are decomposed into their morphological constituents during word recognition, with only stems (e.g. sing) and affixes (e.g. –er) possessing lexical entries. In the present study, we address this question with regard to complex numerals, a class of words which has only rarely been looked at from this perspective. Just as singer, numerals such as sixty possess a word-internal grammatical structure. In a masked-morphological priming experiment with 33 native German speakers, we investigated the processing of German numerals such as fünfzig (50). The results show similar, significant priming effects for number-word pairs such as fünfzig-fünf (50-5) and for other morphologically related word pairs such as Wahrheit-wahr (truth-true). The results from matched orthographic and semantic control conditions suggest that these priming effects cannot entirely be due to semantic or orthographic similarities between prime and target. We conclude that complex numerals are represented in the mental lexicon in a similar way as other complex words, and are decomposed during word recognition.

42. *What are the origins of second language after-effects on native language? Electrophysiological correlates of language competition in picture naming task*

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Naming pictures in L1 considerably slows down after performing the same task in L2. Thisphenomenon is known as L2 after-effect and can be observed on behavioural and ERP level. However, its mechanism is still not established: the slow-down may either reflect the effort related to change of task (L2 to L1) or be a consequence of inhibition of L1 during previous L2 task. 33 native speakers of Polish (L1) learners of English (L2) named a set of pictures in L1 in 3 conditions: after naming pictures in L1, after naming pictures in L2 and after performing a non-linguistic task (NLT). The experiment allowed to assess effects of mere task change (L1-after- NLT) and previously performed L2 task (L1-after- L2) on L1. On behavioural level, we observed L1 slow-down only in L1- after-L2 suggesting that L2 after-effect is a consequence of inhibition occurring in the preceding L2 block rather than mere task change. On ERP level, we found an early fronto-central positivity (150- 250 ms). Its amplitude increased with order of trials across all blocks which possibly reflects substantial training effect in naming pictures. Interestingly, the effect did not occur in L1-after- NLT suggesting that training effect was disrupted by the change of task.

43. *Functional lateralization of tool-sound and action-word processing is influenced by bilingual experience*

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The impact of bilingualism on lateralized brain functions such as praxis– the control of skilled actions, and language representations themselves, particularly in the auditory domain, is still largely unknown. Recent studies suggest that bilingualism affects both basic (fundamental frequency) sound and action-related speech processing. Whether it can impact non-verbal action sound processing is a question of debate. Here we examined twenty bilinguals using a dichotic listening paradigm, in which in addition to repeating the just heard action words, participants named –in Polish or English– one of two simultaneously presented tool sounds from attended ears. The results were compared

with data from these same participants tested with reading the same words in a visual-half field paradigm. In contrast to typical outcomes from monolinguals, the laterality indices of action-related sound processing (verbal and non-verbal) were not left lateralized but hemispherically balanced. Notably, despite similar organization of tool- and action-word sound processing, their auditory (balanced) and visual-language (left-lateralized) representations must be independent because there were no significant correlations between any of their laterality indices. This indicates that bilingualism might involve unpredictable reshuffling/reorganization of typically lateralized brain functions and such plasticity will have consequences for second language learning strategies, as well as for neurorehabilitation.

44. Effects of orthographic transparency and reading proficiency on the brain networks processing print

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Shallow or medium-deep orthographies (e.g. Polish) are acquired more easily than opaque orthographies with a high proportion of inconsistent spellings (e.g. English). Even though language networks identified in subjects reading in different languages are similar, brain response for print is characterized by subtle differences depending on the script. In the current study we aim to compare language networks of young monolingual readers of Polish and English matched for reading skill, IQ, SES and age (5-9 y.o.) who processed print in the fMRI task. We wanted to explore effects of the orthographic transparency and reading proficiency found in the networks processing print. Polish children, when processing print, activated dorsal and anterior networks related to phonological processing, while American children relay more on the ventral (orthographic) stream. When brain response for print was correlated with reading skill, positive correlation was found in the broader network of language-related regions in the Polish group, while in better readers of English - in the left IFG. This finding suggests that phonological processing in the anterior and dorsal stream is more accessible for shallow orthography readers, while readers of opaque English, especially at the beginning of reading acquisition, rely on visuo-orthographic characteristics of the script.

45. Biochemical correlates of dyslexia

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Concentration of metabolites i.e. glutamic acid (Glu), choline (Cho), and gamma-aminobutyric acid (GABA) were hypothesized biomarkers of developmental dyslexia. The aim of this study was to determine if dyslexia is associated with poor phase synchronization (phase-locking) in low frequency bands (theta and delta), which corresponds to Glu and Cho concentration. Alternatively, if dyslexia is caused by poor synchronization in the gamma band (30-40 Hz), reading skills should be correlated with the concentration of GABA. 57 children as well as 36 adults tested for the dyslexia were scanned with MEGA-PRESS single voxel spectroscopy in ROIs placed in the occipital cortex and temporoparietal cortex. LCModel was used for automatic quantification of metabolites with an extension of Gannet Toolbox in case of GABA. Concentrations of choline in visual cortex of dyslexic children is lower by 5.8% ($p<0.05$). Additionally, interaction between adult and children group was detected ($p<0.01$) in both ROIs showing changing role of choline with ageing. Glutamic acid is lower in dyslexic adults by 6.4% ($p<0.005$) but not in the children group. Interestingly there were no significant differences in GABA concentration in neither of the groups. Our results, for the first time, show the changes in choline in two different age groups.

46. Executive and attentional functions in dyslexia

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Dyslexia is characterized by an unexpected reading difficulty in children who otherwise possess intelligence,

motivation and educational potentials. It is evidenced that attention problems and dyslexia co-occur frequently that also might affect performance of executive function tasks and working memory. Here we investigated visual working memory and task switching in children with dyslexia. 18 dyslexic children and 18 their age and IQ match typically developed children (age 8-11 years old for both groups) participated in our experiments. Participants performed Wisconsin Card Sorting Test (WCST), visual n-back test and serial search tasks. We found that performance of WCST was low for both groups, although dyslexic children were worst compare to their age match typically developed children. In serial search task there were no significant differences in accuracy of performance but reaction times for dyslexic children were higher. We found no differences in performance of working memory task for two groups. Our results show that deficits in executive functions and attention in dyslexic children might not be due to dyslexia but ongoing developmental processes in children in general.

47. Letter and speech sound integration in emerging readers with familial risk of dyslexia

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Learning letter-speech sound (LS) association is the first and critical step for reading development. At the neural level, LS integration is related to left superior temporal cortex (STC) activity and its disruption was previously observed in dyslexia. Whether this disruption is a cause of reading impairment or a consequence of decreased exposure to print remains unclear. We compared brain activity for letters, speech sounds and LS integration in emerging readers with (FHD+, N=50) and without (FHD-, N=35) familial history of dyslexia, out of whom 17 developed dyslexia two years later. FHD+ and FHD- groups showed opposite pattern of activation in left STC – in FHD- children it was higher for incongruent compared to congruent, whereas in FHD+ it was higher for congruent LS pairs. Higher activation to congruent LS pairs was also characteristic of future dyslexics. The magnitude of incongruency effect in left STC was positively related to early reading skills, but only in FHD- children and (retrospectively in) typical readers. We conclude that neural disruption in LS integration can be identified at initial stages of reading acquisition, suggesting a causal involvement in dyslexia.

48. Neural systems underlying audio-visual Polish and Polish Sign Language comprehension in hearing late-learners of sign language

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Research on sign languages (SL) has provided new perspectives into the nature of human languages. Although SL differ from spoken languages in perceptual and articulatory systems, striking parallels are also present – including both formal linguistic aspects and overlapping neural substrates. Previous fMRI studies comparing SL to audio-visual (AV) speech have shown recruitment of common perisilvian network for both SL and AV, and specific for SL activity in occipito-parietal cortex. However, these findings were based on comparisons between native proficient users of both languages – little is known how these networks develop in hearing late learners of SL. In the present study using fMRI we directly compared brain activity during Polish Sign Language (PJM) and AV Polish comprehension in 21 hearing participants, who finished 8-months course of PJM. PJM>AV contrast revealed greater activation in bilateral frontal, parietal and occipital network. AV>PJM comparison revealed clusters in bilateral superior temporal gyrus.

The conjunction analysis showed that both languages engaged bilateral inferior frontal gyri and superior/middle temporal cortex, suggesting a modality-invariant language system. Our findings suggest that late-learners of SL activate similar modality-dependent and -independent language networks to native deaf and hearing users of SL, despite the late acquisition and low proficiency.

49. Various aspects of compensatory plasticity during resting-state in early deaf adults

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In the absence of one sense, deprived brain areas become engaged in the processing of the sensory input from remaining modalities. Here, we studied this phenomenon called compensatory plasticity by comparing resting-state functional connectivity in 21 early deaf and 21 hearing subjects. The aim of our study was to provide comprehensive description of neuroplastic changes following early deafness both on the local level of auditory regions connectivity and on the global level of large-scale network topological organization. We found decreased functional connectivity in early deaf adults between somatomotor regions and auditory areas (especially Superior Temporal Gyrus and right Planum Temporale). Edge-wise analysis confirmed the existence of weakened connections between auditory and somatomotor networks. Whole-brain network analysis revealed that deafness was related to altered structure of large-scale brain systems and decreased functional segregation. In deaf participants salience network was clustered with fronto-parietal system while in hearing controls it was a part of a large multi-system cluster. These findings indicate that compensatory plasticity is potentially more complex phenomenon not solely limited to alterations within auditory areas and involves reorganized interplay between large-scale brain networks.

50. Multi-modal MRI investigation of brain plasticity during prolonged Braille learning in sighted subjects – voxel- based morphometry (VBM) and quantitative T1-mapping approach

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Despite major progress in the field, our knowledge about the processes governing use-dependent brain plasticity is limited. Previous studies showed brain plasticity changes in local brain volume and cortical thickness, but failed to assess their neurobiological underpinnings. Quantitative MRI offers a unique insight into microstructural brain anatomy changes associated with learning such as myelination. The goal of our study was to investigate grey matter volume and brain tissue property changes related to Braille reading learning in sighted individuals. The combined approach will help us to disambiguate morphometrics from learning-associated brain tissue property changes. 28 right–handed females underwent 8-months tactile Braille reading course with MRI sessions conducted every 2.5 months and a follow-up study. MRI included T1-weighted images and T1-relaxation maps. VBM analysis showed that during training, gray matter volume increases in early visual, cuneal, premotor, motor and somatosensory cortices. The quantitative T1-map analysis demonstrated that tissue property changes occur in the left sensory-motor cortex and right middle frontal gyrus. Our morphometrics and T1-maps results provide complementary information about brain microstructure reorganization associated with improvement of Braille reading abilities. We conclude that combining different MRI methods may lead to broader understanding of neural processes underlying brain plasticity.

51. Orthographic priming for tactile Braille alphabet in the ventral Occipito-Temporal cortex of congenitally blind

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When blind subjects read Braille, they activate the same brain area as in the sighted reading, the Visual Word Form Area in the ventral visual cortex. The blinds' visual cortex, however, is also massively activated by memory and spoken language tasks and it remains unclear whether the vOT of the blind is indeed deeply similar to the VWFA of the sighted, or whether this similarity is superficial. The strongest evidence for the role of the VWFA in reading in the sighted comes from repetition suppression studies. To determine the role of the VWFA in the blind, we tested 15 congenitally blind adults with a repetition suppression paradigm with pairs of auditory and Braille's pseudo-words. Our results reveal orthographic priming in the left vOT cortex of the blind in the tactile modality, with no priming to auditory stimuli. While we do not dispute the evidence showing weaker selectivity for tactile reading (Kim et al., 2016) and more sensitivity to linguistic information in the blind's vOT, our finding of orthographic priming in that region suggests that the function of the vOT in the blind, although not identical, nevertheless overlaps to a large extent with the function of the sighteds' VWFA.

52. Auditory cortex activation for tactile rhythms perception in blind– preliminary study

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Previous studies on blind and deaf subjects show that sensory deprived cortices may switch processing modality without changing their function through cross modal plasticity. It remains unclear, however, to what extent this effect can be considered a general principle of brain cross-modal reorganization, concerning regions outside the deprived cortices. Here we show results of a pilot fMRI study of two congenitally blind subjects and one sighted subject who discriminated rhythms presented in the auditory and in and additional unusual tactile modality. Participants were asked to compare between rhythmic sequences presented tactily as series of finger tips stimulations, or auditorily as series of sounds. As control they discriminated between sound pitch, or stimulated fingers in tactile condition. We observed recruitment of bilateral auditory regions (superior temporal gyrus) for tactile rhythmical task when compared to the tactile control condition in both blind subjects and not in sighted subject. Importantly, the overlapping region has been activated for auditory rhythms comparing to auditory control condition in blind, suggesting the auditory recruitment to be task-specific.If confirmed, these results could suggest that through brain reorganisation in congenitally blindness, regions outside sensory-deprived cortices may switch processing modality and preserve its particular function corresponding to rhythm perception.

MEDICAL NEUROSCIENCE

53. Immunomodulatory Effects of Autologous Bone Marrow-Derived Mesenchymal Stem Cell Therapy in Symptomatic Epilepsy

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Background: There is growing evidence for autoimmune mechanisms in the pathogenesis of some epilepsy

syndromes. It was discovered that implantation of autologous mesenchymal stems cells (MSC) results in stabilization of the local microenvironment by secretion of neuroprotective and immunomodulatory molecular cues. The ongoing research aims to explore mechanisms by which MSC affect immune cells. Methods: An experimental group includes 20 patients receiving antiepileptic drugs supplemented with single intravenous administration of undifferentiated autologous MSC, followed by a single endolumbar injection of neurally induced autologous MSC. A normal control group includes 20 individuals without history of neurologic disorders. The immunological status was assessed by the combination of monoclonal antibodies to CD3, CD4, CD8, CD19, CD25, CD38, CD56, CD57, CD95, HLA-DR, TcRγδ. Results: High level of cytotoxic T-cells, NK-cells, CD4+CD8+ cells, TcRγδ+CD4+ T-cells, activated CD19+CD38+ B-cells was revealed in patients with epilepsy. After the MSC transplantation, decrease in the level of activated CD19+CD38+ B-cells, CD3+CD8+, CD4+CD8+ cells, and NK-cells was revealed ($p<0.05$). The level of TcRγδ+CD4+ T-cells remained at an initially high level that suggests recent or current chronic antigenic stimulation in patients with epilepsy. Conclusion: MSC possess unique immunomodulatory properties that contribute to positive outcome of MSC treatment in patients with epilepsy.

54. The clinical image of cognitive disorders in a school-aged child with autoimmune epilepsy: Effects of neuropsychological therapy

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Background: The aim of this study was to identify specific aspects of the cognitive and socioemotional functioning of a school-age child with autoimmune-resistant epilepsy and to describe the effects of annual neuropsychological therapy. Material and methods: A battery of neuropsychological tests, clinical trials, interviews, observational data, and EEG results were used to neuropsychologically diagnose the child in two ways: before and after the annual neuropsychological therapy. Results: Intellectual functions have significantly improved: in 2017, the quotient of fluid intelligence ranged from light intellectual disability to lower than average intelligence. Currently, the child's IQ is in the range from lower than average intelligence to average intelligence. An improvement also took place in socioemotional processes and neurocognitive functions, such as motor praxis, direct auditory memory, visual-motor coordination, and some executive and visual- spatial functions. Other cognitive processes did not show any change, but there was some difficulty in using optimal strategies in acting and in correcting mistakes. Conclusions: Neuropsychological therapy proved both valuable and effective. Referring to the current diagnosis, the research results, and the theory of the microgenetic symptoms based on knowledge of the mechanisms of plasticity, it can be assumed that neuropsychological therapy should be continued while establishing new goals.

55. Simultaneous EEG-fMRI study of patients with primary generalized epilepsy

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Introduction: Primary generalized epilepsy is characterized by the occurrence of generalized spikes and waves discharges (GSWDs) lasting up to several seconds without or with minimal movement manifestation. Because of the poor clinical manifestation (short-term episodes of unconsciousness or limbs or eyelid myoclonus), these patients often remain undiagnosed for a long period of time and diagnosis is often established after an accidental EEG exam. The aim of the study is to investigate changes of the regional blood flow in the brain and functional connectivity of the thalamus during the epileptic discharges. Methods: 5 epileptic patients participated in the study. Subjects were scanned simultaneously using MRI scanner (GE Discovery MR750w) and 64-channel EEG (Neuroscan). Three 10 min resting state runs were acquired. GSWD events in EEG signal were manually detected by experienced neurologist. All GSWD events detected in three runs were used in fMRI analysis using General Linear Model (GLM) in SPM12 neuroimaging software package. Results: Analysis revealed significant bilateral activation i.e. in the thalamus, middle frontal gyri, premotor supplementary area and middle temporal gyri and the functional connectivity pattern of thalamus seems to be disturbed. The results of the study may contribute to the understanding of the pathomechanisms of generalized epilepsy.

56. *Employment as an important factor in maintaining quality of life and cognitive functions in patients with multiple sclerosis*

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Unemployment is a serious issue among patients with MS, as the disease affects people in the peak of productive years and leads to depression, fatigue and cognitive dysfunctions, resulting in decreased QoL. Thirty-two patients with MS were assessed twice, at baseline and after one year, using a self-created quality of life questionnaire, Beck depression inventory (BDI), fatigue assessment scale (FAS) and cognitive tests: RAVLT, ROCFT, SDMT, CWIT, TMT, DST. Mean age of patients was 37.06 years (SD=10.36), length of the disease 11.39 years(SD=8.83), EDSS 3.30(SD=2.06). Employees and non-employed patients did not differ significantly in these parameters (p=0.5679, p=0.5992,p=0.2076 respectively). Nineteen patients were employed (59.38%) on first assessment and sixteen (50%) after one year. In the second examination we observed that employees had significantly higher results than non-employed patients of SDMT (the difference of means is 13.86, 95%CI=3.62-24.13, p=0.0167), and CWIT (15.38, 95%CI=7.08-23.67, p=0.0013). Employees had lower scores in BDI (6.31, 95%CI=1.76-10.87, p=0.0056) and FAS (11.38, 95%CI=0.93-21.82, p=0.0302). Satisfaction of work was in correlation with sense of support from family (R=0.88, p<0.002) and friends (R=0.78, p<0.002). We propose to highlight the importance of maintaining a steady employment after diagnosis of MS as it is associated with lower fatigue/depression rates and better cognitive functions.

57. *Intellectual screening in supratentorial brain tumors before neurosurgery treatment: assessment of executive and cognitive domains deterioration*

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Background: Cognitive deficits in brain tumors are thought to be relatively mild and non-specific. The aim of the study was to investigate neuropsychological assessment of the intellectual deficits in patients with brain tumors with particular emphasis on the impact of location on executive function and other cognitive processes. Methods: The prospective study consisted of 28 patients (13 female; 46,42%), diagnosed with supratentorial lesions. In the preoperative assessment we used Addenbrooke's Cognitive Assessment (ACE III) and Trail Making Test A and B (TMT). Results: The average score of ACE III was 81.96 points, below the assumed cut-off (82.00) for the dementia. Lower results were recorded in the memory (70.73%), fluency (67.86%) domain. There were trends suggesting patients that undergone awake craniotomy were more likely to gain greater scores in ACEIII and TMT. The significant correlation was also found between the temporal-located(n=10) and tumors located elsewhere in time of TMT-A (63,83s vs.111,5s ; p = 0.02). Conclusions: Our findings suggest that patients with temporal lobes lesions demonstrate significant impairment of cognitive and executive functioning at the time of diagnosis. However, the analysis of datas indicates more on partial cognitive deficits than on global decline.

58. *The results of using implantable loop recorder devices in cryptogenic stroke survivors for stroke etiology determination in Pauls Stradins Clinical University Hospital from 2014 to 2017*

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Cryptogenic stroke is a stroke for which no probable cause is identified. Identifying atrial fibrillation (AF) is relevant as AF-related strokes are associated with an increased risk of disability and death, and they tend to recur when anticoagulation is not implemented. However, conventional HR monitoring methods are sometimes insufficient to rule out possible AF because of its asymptomatic, paroxysmal nature. Therefore, implantable loop recorders (ILR)

have taken an important role in revealing AF. Aim. To evaluate the incidence of AF among cryptogenic stroke survivors using implantable loop recorders. Materials and methods: Retrospective study included cryptogenic stroke survivors who had ILR implanted between the years 2014 and 2017. The data was collected from electronic database and via phone. The analysis of data was carried out using IBM SPSS 23.0. Results: The study included 22 patients aged from 42 to 74 (mean 55.18) years. In 7 (31.82%) patients AF was found, time ranges from 2 to 8 months (mean 4.86). Conclusion: Among patients with cryptogenic stroke, AF was detected in 31.82%. These results suggest that the ILR is an effective way of finding subclinical AF.

59. Acute post – stroke/TIA depression is associated with worse clinical outcome after 3 and 12 months

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Post – stroke depression (PSD) is common in patients with cerebrovascular diseases. It is associated with lower quality of life and worse cognitive functioning after stroke or transient ischemic attack (TIA). The aim of this study was to evaluate association between acute post – stroke or TIA depression symptoms and clinical outcome after 3 and 12 months after stroke or TIA. The consecutive patients admitted to the Stroke Unit, Department of Neurology, University Hospital, Krakow, with supratentorial stroke or TIA were included in the study. Depression symptoms was assessed 7-10 days after admission with The Patient Health Questionnaire-9 (PHQ-9). Clinical outcome after 3 and 12 months was measured with modified Rankin Scale (mRS). 460 patients performed PHQ – 9 and depression symptoms were diagnosed in 54,8% (n= 252). The results in mRS after 3 and 12 months were higher in patients with depression symptoms compared to patients without depression symptoms. In conclusion, acute post – stroke or TIA depression symptoms are associated with worse clinical outcome after 3 and 12 months after stroke/TIA.

60. Severity of depressive symptoms, gender and lesion location in acute phase of stroke and transient ischemic attack

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The results of previous research on relationship between post–stroke depression and right– and left–sided lesion location proved to be varied and inconsistent. The question about the possible mediating role of gender in that relationship have not been clearly answered yet. The aim of this study was to identify the impact of lesion location and gender on severity of depressive symptoms in patients with acute cerebrovascular diseases. Data from 523 patients admitted to the Stroke Unit, Department of Neurology, University Hospital, Krakow, with ischemic stroke, hemorrhagic stroke or transient ischemic attack were analyzed. Severity of depressive symptoms was assessed 7–10 days after admission with the Patient Health Questionnaire–9 (PHQ–9). The assessment of lesion location was based on CT or MRI and neurological examination. The following lesion locations were distinguished: right hemisphere, left hemisphere, posterior fossa and more than one location. In male no significant differences in severity of depressive symptoms between different location were found, whereas in female severity of depressive symptoms was greater in patients with lesions in right hemisphere in comparison to patients with lesions in left hemisphere. In conclusion, the pattern of relationship between lesion location and severity of depressive symptoms appeared to be dependent on patients' gender.

61. Association between chronotypes and bipolarity, schizotypy, seasonality, and affective temperament

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Background: Chronotype is a construct describing individual circadian preference. Diurnal rhythms disturbances are linked to mental disorders. This study aimed to investigate the associations between chronotype and bipolarity, schizotypy and affective temperaments' traits, seasonality. Methods: The study was conducted as an online survey. 1449 participants completed self-report questionnaires: the Composite Scale of Morningness (CSM), the Mood Disorder Questionnaire (MDQ), the Hypomania Checklist (HCL-32), the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE), the Munich ChronoType Questionnaire (MCTQ), the Sleep Wake Pattern Assessment Questionnaire (SWPAQ), the Temperament Evaluation of Memphis, Pisa, Paris and San Diego-autoquestionnaire version (TEMPS-A). Participants were divided into three groups of circadian preference according to CSM scores: morningness, intermediate, eveningness. Results: Eveningness cluster showed highest scores on bipolarity and schizotypy, misalignment of biological and social rhythms, increased seasonal variation of functioning, anxious, cyclothymic and irritable temperamental features. Morningness group was characterized by lowest scores on bipolarity and schizotypy, good allegiance between biological and social rhythms, little seasonal variation of functioning and increased hyperthymic temperamental traits. Conclusions: The results of this study indicate that circadian preferences relate to psychosocial functioning and affective temperament. Eveningness was associated with increased bipolarity, schizotypy and anxious, cyclothymic and irritable affectives temperaments' traits.

62. *Affective temperament in inflammatory bowel diseases: another brick in the wall of differentiation*

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Background: Psychiatric disorders are significantly common complications among patients suffering from inflammatory bowel diseases(IBD). The assessment of affective temperament can convey useful information about patients' vulnerability to mood disorders in autoimmune diseases. We aimed to evaluate affective temperament in patients suffering from Crohn's disease(CD) and ulcerative colitis(UC) in relations to the intensity of depressive symptoms and clinical severity of both diseases. Due to our knowledge this is the first study of this kind. Methods: The study enrolled 130 patients with IBD, including 68 with CD and 62 with UC. We used TEMPS-A to evaluate affective temperament and HADS scales to assess the intensity of depressive and anxiety symptoms. Harvey Bradshaw scale, Crohn's Disease Activity Index (CDAI) and Mayo Score were used to evaluate clinical severity of the diseases. Results: We observed higher prevalence of depressive, cyclothymic and anxiety temperaments in CD patients compared to the control group. Harvey Bradshaw scale, CDAI and Mayo Self Report showed significant positive correlations with depressive, cyclothymic and anxiety subscales of TEMPS-A, and negative correlation with the hyperthymic temperament in CD subjects. Conclusions: Our findings indicate significant differences between CD and UC due to temperament traits, and suggest distinct pathogenesis of mood disorders in IBD.

63. *Vertebral artery dissection and cerebrovascular insufficiency following cervical spine fracture in ankylosing spondylitis patient – case report*

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Background: Spinal fractures in patients with ankylosing spondylitis often lead to severe damage of the spinal cord. About 70% of blunt cerebrovascular injuries (BCVI) are associated with cervical spine fractures. However, they are rarely reported to cause significant intracranial complications. Case report: The patient is a 55-year old male who sustained head and neck injury after a fall. He initially presented limited contact and tetraplegia. CT and MRI revealed C5-C6 tricolumnar fracture with transverse spinal cord injury, characteristics of ankylosing spondylitis and no intracranial pathology. During preparation for a surgery the patient went into a cardiac arrest episode. Anterior cervical spine stabilization and spinal cord decompression were performed. On the 3rd day episodes of bradycardy and hipotension occured. Control CT revealed cerebellum ischemic stroke, infratentorial oedema and active hydrocephalus. Angio-CT visualized a lack of flow in left vertebral artery with features of dissection above. Despite stabilizing intracranial pressure with external ventricular drainage the patient showed no improvement and died. Conclusions: Initially asymptomatic BCVI may lead to serious and life threatening complications including ischemic stroke and intracranial hypertension with cardiovascular insufficiency. Trauma patients with ankylosing spondylitis should be a group in which additional attention is paid to a vertebrobasilar circulation assessment.

64. CO*MT Val158Met and DAT1 in executive functioning*

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Background: DAT1 and COMT genes regulate the levels of dopamine in the brain, and are considered in the development of obesity- the disease which is associated with neurocognitive vunerabilities. The aim of our study was to evaluate the impact of genes associated with dopaminergic neurotransmission on the prefrontal cortex functioning. Methods: 375 patients were enrolled to the study and went biometric analyses and neuropsychological assessment. We utilized The Wisconsin Card Sorting Test(WCST) to evaluate executive functions. Genetic evaluation comprised DAT1 and COMT genes polymorphisms from the blood samples. Results: Both DAT1 and COMT Val158Met significantly correlated with WCST parameters. DAT1 S allele homozygotes showed the worst scores in WCST, while L allele homozygotes gained the best results. S/S individuals presented the highest weight and L/L showed the lowest BMI. BMI values significantly correlated with worse WCST scores. COMT heterozygotes showed the highest WCST performance in comparison to homozygotes. Conclusions: Dopaminergic transmission significantly affects prefrontal cortex activity, however COMT Val158Met polymorphisms seems to influence it in indirect manner. DAT1 S allele homozygotes showed the poorest cognitive performance and the greatest BMI values, suggesting that obesity and lower subcortical dopamine concentration deteriorated executive functions.

65. Differences of cognitive functioning in self complaining, MCI and healthy control groups

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Objective: The aim of the present study was to investigate individuals with subjective cognitive complaints (SCC) in terms of their cognitive functioning evaluated with objective measures as well as demographic (i.e.: age, education, sex, and occupation) and emotional (depression) characteristics. The comparison between SCCs and MCI patients in the context of neuropsychological test performance has been performed. Material and Methods: 408 individuals performed Neuropsychological Test Battery (NTB). The cohort has been divided into three groups, cognitive complaining group without any diagnosis (CoG), the mild cognitive impairment group (MCI), the healthy control group (ConG). The NTB consisted of the Turkish adaptations of the neuropsychological test battery, Beck Depression Inventory (BDI) and Geriatric Depression Scale (GDS) has been used. Results: The GCFI was different between the SCC clusters. The study demonstrates significant differences between SCC group and healthy Controls group, as well as between MCI and healthy controls. Conclusions: The present study demonstrates the cognitive functioning of the SCC individuals is very heterogeneous. The most distinctive differences observed in the domains of verbal attention, abstract thinking, verbal fluency and naming. General cognitive functioning of the SCC patients did not differ from MCI patients.

66. Drug abuse in children and adolescents

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In recent years worldwide has been observed a significant increase in the number of minors reaching for psychoactive substances. The purpose of the study is to evaluate the drug abuse in children and adolescents in Cracow. We analyse 279 cases of children treated as inpatients at the University Children's Hospital (USD) in Cracow from 2007 through 2017 suspected for poisoning with psychoactive substances. The analysis included the gender and age of patients, the type of substance ingested, clinical symptoms, the circumstances of drug intake and the family situation of the patients. The analysis indicate a decrease in the age of drug intake initiation 2009 mean age: 13,17 versus 14,78 at 2017). Statistically significant female dominance was found for ingestion of drugs - 36 boys (31.03%) versus 80 girls (68.97%). The number of patients hospitalized due to suspicion of poisoning with psychoactive substances was much higher than the number of confirmed poisonings (116 patients). It could be related to new kind of drugs, so called legal highs, difficult to determine them using laboratory tests. The study showed that the problem of psychoactive substance abuse among children and adolescents in Poland is growing.

67. Cerebellar stimulation is helpful for children with overactive bladder

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50 children suffered from middle severity of overactive (neurogenic) bladder were observed. Uroflowmetric data were used for the evaluation of the aerodynamic of low urinary tract (LUT). Transcranial magnetic stimulations (TMS) were delivered to left prefrontal area (group I) and to cerebellar surface (group II). Sessions were conducted five times per week with TMS at 1,0 Hz, 80% of motor threshold, 200 pulses/session, for 4 weeks. Uroflowmetric measurements after treatment revealed significant reduction of average velocity of urine flowing in both group I and II – by 30,5% and 27,0% correspondently pertained to the initial values of the indices. The time of voiding increased by 37,0 and 42,0%, and the volume of urine also increased by 36 and 39,3% pertained to the corresponded indices registered before TMS. In group II the reduction of maximal velocity of urine flowing (Qmax) was also significantly reduced (by 25,0%), while the period of the achievement of Qmax was enlarged by 31,6%, while in the group I stimulation such changes were not observed. Hence, gained data demonstrate the improvement of autonomic neural regulation of bladder activity with TMS of prefrontal cortex and cerebellum with more pronounced effects in case of cerebellar TMS.

68. Kinetics of inflammation resolution in neonatal hypoxic-ischemic encephalopathy

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Hypoxic-ischemic encephalopathy is a serious untreatable disease that may lead to severe neurological and cognitive impairment or even death. Novel approaches to cure HIE include hypothermia and stem cells transplantations. In case of the latter, understanding kinetics of inflammation resolution may define successful therapeutic window to enhance efficient stem cells engraftment and thus neurological improvement. Aim of this study was to determine pattern of ongoing neuroinflammation in mice model of HIE. We evaluated brain samples obtained from mice model of HIE. After histopathological confirmation of HIE induction, staining for immune cells' response was performed. Subsequently, RNA was isolated from paraffin-embedded tissues and qPCR analyses were performed to assess genes' expression for pro-inflammatory and anti-inflammatory factors. Then, in significant time points, microglia activation phenotypes were determined by flow cytometry analyses. Our results show altered pro-inflammatory and anti-inflammatory genes' expression in different time points from HIE induction. We believe that our results provide insight into resolution of inflammation that can be crucial in case of HIE treatment.

69. *Is there a relationship between subjective assessment of sensory modalities using the VARK questionnaire and teaching methods in medical students?*

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Learning preferences depict subjective assessment of most effective methods of knowledge acquisition. Medical students are a group heavily burdened with the amount of education, which makes them very liable to the development of individual complex learning systems. A total of 523 students from six Polish medical universities completed self-prepared survey along with the VARK (Visual, Aural, Read/write, Kinesthetic) questionnaire. According to the VARK results students most often chose K- 6,23 and least often R answers- 5,5. 75,7% of students represented multimodal schemes, and 25% had the all-four VARK profile. Students with a single dominant feature usually represented A(33,0%) and R(23,6%) modalities. From four suggested, 49% of students (Gr.1) chose simulations as the most and 16% (Gr.2) as the least interesting classes. Regardless of this difference, K answers were the most popular in both groups. However, Gr.2 significantly more often chose R answers (6,04 vs 5,07; p=0,001). As the dominant modality, students with the average grade >4.5 more often had V and R, and those interested in rather surgical specializations- V and K. Conclusions: Medical students represent really various learning preferences. Kinesthetic answers were the most popular. Describing preferences of students may be helpful in achieving a full didactic success.

70. *Reorganization of large scale functional networks during low frequency electrical stimulation of the cortical surface*

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In the present study we investigated the physiological and epileptic functional network reorganization caused by low frequency electrical stimulation of the healthy and epileptic tissue. 16 presurgery epileptic patients were analyzed with subdural grid positions. Dynamic functional connectivity analysis and Minimum Spanning Tree graph parameters were applied to express the changes in synchronization and network topology after current injection. Electrical stimulation resulted in the centralization of the physiological functional network topology compared to the baseline. The centralization was increased in early responses compared to late responses, suggesting increased number of direct neural links between the stimulation site and distant brain regions in early responses. A more extensive synchronization and a more centralized topology was observed when the current injected into the epileptic zone, supporting the idea of abnormal balance between inhibition and excitation mechanisms in the epileptic networks. Moreover, the seizure frequency showed positive correlation with the centralization of the epileptic network topology, which may reflect deleterious long-term effects of seizures on network reorganization. This study showed that tracking the propagation of the injected current by dynamic functional connectivity analysis can be a tool for mapping physiological and epileptic activation patterns of the brain networks.

POSTER SESSION III

LEARNING AND MEMORY

1. The long-term effect of repeated epileptic seizure activity on learning processes

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Epileptic seizures can cause changes in both synaptic neuronal activity and higher operating levels too. In our experiments, we used 4-aminopyridine (4-AP), a potassium channel blocker, to evoke epileptic seizures. Our aim was to investigate the effect of epilepsy-related acute and chronic changes on general behaviour, learning- and memory processes. Rats were treated for twelve consecutive days to provoke epileptic seizures. To examine learning and memory processes, eight-arm radial maze (RAM) and novel object recognition tests (NOR) were used. Besides this, locomotor activity was also investigated in open field test (OF). Electrophysiological measurements were performed on surviving hippocampal brain slices. During the OF and RAM tests there was no difference between the control and the treated group. However, in the NOR tests, treated rats spent significantly less time with the novel object than the control animals. Long term potentiation (LTP) studies revealed that in both 4-AP treated groups the efficacy of LTP induction was moderately higher than in the corresponding control group. Based on the results obtained, the repeated epileptic seizures induced changes in the hippocampus at the electrophysiological level immediately after the treatments, which persist on the long term to a certain extent but do not affect spatial learning.

2. Effects of febrile seizures on behaviour and memory processes in rats

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Epileptic discharges may cause modifications in neuronal activity both on synaptic and network level, which often lead to learning and memory deficits. Febrile seizure (FS) is the most frequent seizure type during childhood. It could play significant role in developing temporal lobe epilepsy, the most common epilepsy type in adulthood. Our goal was to investigate the long-term behavioural and memory effects of FSs in young age. In our present experiments, rat pups were heated with an infrared lamp to induce hyperthermic seizures on postnatal days 11, 14 and 17. Three month after treatments, learning and memory processes were examined with 8-arm radial maze and novel object recognition tests. In addition, anxiety and locomotor activity were also investigated in open field test. Open field tests showed that the treated animals were less active than control ones and FS rats spent less time with the novel object than the control animals. In the radial maze test the treated animals had mildly impaired performance. The results suggest that FSs, which occurred in a fairly vulnerable life stage caused such alterations in behaviour and memory processes that 3 months were not sufficient to repair the probably damaged neuronal networks, or the changes are permanent.

3. Impact of environmental enrichment on anxiety and learning in the rat model of epilepsy induced by electrical stimulation of the amygdala

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Environment plays an influential role in the development of many brain disorders, however its role in modulation of epilepsy phenotype has not been studied in details. The aim of this study was to investigate whether environmental enrichment impacts anxiety and learning in experimental model of epilepsy. Rats were allocated to either environmentally enriched (EE; n=13) or standard housing condition (SH; n=13). Epilepsy was induced by SE (Status epilepticus) evoked by electrical stimulation of the amygdala. Following tests were conducted to assess the behavior of animals: behavioral hyperexcitability, open field, new object recognition, elevated plus maze, social interactions, and Morris water maze. Blood was withdrawn at the end of experiment to assess cortisol levels. Environmental enrichment significantly reduced anxiety levels. We observed a reduced mobility in the open field test ($p \leq 0{,}0001$) or decreased touch-response test in the behavioral hyperexcitability test ($p \leq 0{,}0001$). SH animals showed impaired spatial memory and learning compared to EE animals. Moreover, SH rats showed hyperactivity and thigmotaxis. Blood analysis demonstrated that SH rats had significantly higher level of cortisol compared to EE rats ($p \leq 0{,}01$). The present study indicates that environmental enrichment had beneficial effects on anxiety, learning, and memory, which may be caused by lower stress hormone levels.

4. Behavioural response of house cricket (Acheta domesticus) to virtual reality environment

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Virtual reality (VR) systems presents the unprecedented possibility to shape experimental setups such as mazes or arenas beyond the limitations of the physical world. Additionally, as an emerging technology, VR draws increasing public attention and, in consequence, interest in its eventual effects on human brain and mind. Most of the contemporary VR setups provide a degree of immersiveness regarding only single modality - the visual one. Thus the brain receives inconsistent, conflicting stimuli. Although, in order to fully understand how VR experience is processed the comparative approach, employing animal models, is necessary. Insects from family Grylloidea are extensively utilized in the studies of sensory integration as their behaviour is guided by tactile, acoustic and visual modalities. The presented study assesses differences in behavioural responses of freely behaving house cricket (Acheta domesticus) in VR setup in comparison with analogous, physical environment.

5. Pro-cognitive effects of a dual 5-HT6/5-HT2A receptor ligands in the novel object recognition test in rats

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Antagonists of the serotonin 5-HT6 receptor improve the cognitive functions. In addition, the subtype 2A of serotonin receptor (5-HT2AR) is a target of many atypical antipsychotics like aripiprazole, olanzapine and ziprasidone. These findings led to the synthesis of 5-HT6/5- HT2AR ligands, which are investigated as possible therapeutics for Alzheimer's disease and cognitive impairments associated with schizophrenia. The aim of present study was to evaluate the effects of a dual 5-HT6/5- HT2AR ligand, compound PKSN-279, on phencyclidine-induced deficits in the novel object recognition (NOR) test in rats. The acute administration of phencyclidine attenuated recognition learning and this was reversed by co-administration of compound PKSN-279. This effect was similar to the effects of Lu AE58054 compound, whose efficacy was demonstrated already in phencyclidine-induced learning impairment in rats. The present study supports the observations that dual activity at 5-HT6 and 5-HT2A receptors might exhibit pro-cognitive effects in animal models of learning impairments associated with psychoses. This study was supported by the National Center for Research and Development Grant No PBS3/B7/20/2015 "New non-amyloid therapy of cognitive disorders" and by the Statutory Funds of the Institute of Pharmacology, Polish Academy of Sciences.

6. *Who is at the top of the heap? - fully automated dominance assessment in rodents*

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For most species of rodents maintaining the stability of social structure in a group is fundamental to their survival. Understanding that social dynamics in studies involving animal models is essential to properly establish links between behavior and its neural correlates. During the classical behavioral assay, animals are exposed to stressful conditions such as repeated confrontations, that in the natural conditions could probably be easily avoided, an influence of experimenter and poor habituation procedure. All of these factors can induce high anxiety and masking of natural behavior. In order to avoid these problems, we designed a new, fully automated and ecologically relevant dominance test, based on RFID system and competition for sucrose reward. We conducted series of experiments using three different strains of female mice - C57BL/6, FVB, and Swiss Webster. From the results obtained from each experimental group, we were able to determine dominant mouse and observed dynamic changes in the rest of social structure levels, stable over repetitions. We were also able to establish how sociability of investigated strains changes over time. In conclusion, we claim that our tool could be a valid and reliable method to assess social hierarchy in a group of mice, without invoking unnecessary stress.

7. *Reinforcement learning without a rush*

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Reinforcement learning (RL) is a cognitive process essential for adaptive behaviour. RL in humans and rodents is mostly consistent with theoretical models based on reward prediction error. Thus far this required testing long sequences of choices in quick succession. Here, we model RL in a task with possibly superior ethological validity. C57Bl/6N mice were tested in a probabilistic reversal learning task in IntelliCage, where individual choices had no time limits. Animals could freely enter two small compartments with bottles containing sweetened water. The bottles were accessed through doors, which had 90% or 30% opening probability (changing every 48h). We note that mice preferred visiting the compartment where the probability of receiving the reward was greater. Moreover, mice were more likely to select the previously rewarded compartment again (win-stay ratio). Computational models based on the reward prediction error were fitted to the observed sequences of choices. We considered models based on single or dual learning rates, choice bias also including an update of the expected value of the non-selected choice and potential effects of time intervals between choices. Further research will aim at finding an optimal approach to take into account the effect of the intervals between choices.

8. *The HexMaze task for studying acquisition and updating of knowledge-networks in rodents*

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Learning new information rarely happens in isolation from existing memories. Instead, new experiences are usually incorporated into existing knowledge-structures. Studying such processes requires a controllable yet complex environment for examination of gradual emergence and subsequent updating of long-term memories. To address this challenge, we developed the Hex-Maze task for rodents: a novel, complex maze consisting of interconnected, adjustable blocks of hexagonally-arranged pathways. Systematic training on the maze and manipulation of its structure and reward sites allows examination of navigational behavior emerging from acquisition and updating of long-term memories. We show the effectiveness of such a training paradigm in a pilot study with mice. On each trial, the mouse was placed at varying starting positions, and allowed to find food located in one fixed location

(counterbalanced across animals). The trial ended when the animal started eating the food. The mice showed (i) increased frequency of direct runs to the food, (ii) reduced difference between the paths taken and the shortest possible path, (iii) and statistically significant increase in dwell time at the food location during probe trials when food was removed. We next plan to examine updating of such memories resulting from changes to the maze structure and the reward location.

9. Rats can transfer information about the localization of the food via social interaction

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Rats can socially transfer information about the palatability of novel foods via breath odors. We tested if they are also able to transmit information about food localization. We used modified place preference test. Cage consisted of two chambers, covered with two distinct smells allowing rats to distinguish between them. Two rats (observer and demonstrator) were habituated to the cage and then put on food restriction. During the test, the demonstrator was put in one of the chambers and ate a food pellet covered with the smell of that chamber. It was then placed in a home cage with an observer for an interaction. Test cage was cleaned and observer was put inside. We measured time spent in the chamber where the food was eaten by the demonstrator. Rats in the control group were treated in the same way, except for the feeding took place in their home cages. We found that the observers in the experimental group spent significantly more time in the chamber where the food was eaten previously, whereas rats in the control group did not consequently prefer any chamber. This result suggests that rats can transmit socially information about food localization, probably via odors sensed in the breath.

10. Involvement of the amygdala GABAergic neurons in appetitive and aversive learning

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Learning and memory formation are fundamental processes that contribute to the survival of a species in environment. One of the structures involved in regulation of learning is the amygdala. In our study we would like to verify whether inhibitory neurons are involved in appetitive and aversive learning in the amygdala. For this we used IntelliCage system (NewBehavior TSE Systems). Training was performed using transgenic mice expressing fluorescent protein under inhibitory neurons promoter (GAD-dtTomato). To analyze neuronal activation we used c-Fos immunostaining as a marker. Confocal images of brain sections covering amygdala were used to analyze colocalization of c-Fos with inhibitory neurons. Data that we obtained from IntelliCage shows that in appetitive and aversive training all animals learned required tasks effectively. We observed that c-Fos expression in the central amygdala was clearly enhanced by appetitively motivated behavior. Moreover, the number of c-Fos positive cells were changed in anterior-posterior axis of amygdala. Last, we have counted number of inhibitory neurons with c-Fos expression. Our results show that GABAergic neurons are activated during learning process in amygdala. Interestingly, only a small fraction of c-Fos positive cells are also GABAergic. To what extend GABAergic neurons contribute to appetitive and aversive remains to be examined.

NEUROPHYSIOLOGY

11. Motor stimulation affects the level of synaptic proteins, expression of DmMANF neurotrophic factor and lifespan of Drosophila melanogaster

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Studies on rodents and human have reported a positive influence of physical activity on health. However, less is known about the synergistic action of the circadian clock and physical activity time on the nervous system. The aim of

study was to investigate the effect of motor stimulation on lifespan and on the level of synaptic proteins and DmMANF neurotrophic factor in the brain. Flies were forced to high locomotor activity in four different times, in the morning or in the evening, when flies show two peaks of activity, or in the middle of the day or night when they sleep. The results showed that everyday locomotor stimulation prolongs the lifespan and increases the level of DmMANF but only when the stimulation is applied in the morning. In turn, the level of synaptic proteins was altered in flies which were stimulated both in the morning or in the evening. This effect was not the same, however, in case of different synaptic proteins. Our data showed that increased locomotor activity affects several processes in the brain of D. melanogaster, however, these effects are correlated with the exact time of locomotor stimulation.
This work was supported by NCN grant number 2014/15/B/NZ3/04754 to EP.

12. Ecdysteroids receptors and enzymes of the biosynthesis pathways of them in central nervous system in spider females Parasteatoda tepidariorum (Araneae, Theridiidae)

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Ecdysteroids are probably the most important neurocompounds in the regulation of development processes in arthropods. However, knowledge about ecdysteroids in spiders is rudimentary, although the hypothetical model of ecdysteroids synthesis in the molting organ is known. In this study, we investigated the presence of genes encoding enzymes of the biosynthesis pathway of ecdysteroids (disembodied – dib, shadow – sad, shade – shd) and receptors of these hormones (ecdysone receptor protein – EcR and ultraspiracle protein – USP) in the central nervous system with the neuroendocrine system and in the whole body of females of the model species of spider Parasteatoda tepidariorum. Moreover, we determined the expression profile of these genes during the crucial stages of spider female ontogenesis. Here we show by using the qPCR the presence of genes: dib, sad, shd, EcR and USP in P. tepidariorum. Expression of these genes were tissue and time-specific. It should be noted that not all tested genes are expressed in the central nervous system. It seems that our results can negate the model of ecdysteroids synthesis in the molting organ.
This work was financed by the PRELUDIUM Grant from NCN, no. 2014/15/N/NZ4/04505.

13. The visual system and food intake - oxyntomodulin activates the thalamo-cortical neurons in the rat dorsal lateral geniculate nucleus

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The oxyntomodulin (OXM) is an anorexigenic factor secreted postprandially in gut that modulates glucose metabolism and energy expenditure. In the brain, OXM is produced by the nucleus of the solitary tract as a signal of satiety that may even lead to nausea, stress and increase in sympathetic outflow. The OXM binds both to glucagon-like 1 receptor (GLP1R) and glucagon receptor (GCGR).The dorsal lateral geniculate nucleus (DLG) is a relay thalamic centre for the visual system. Its thalamo-cortical (TC) neurons convey photic information from the retina to the primary visual cortex. The aim of our study was to evaluate if DLG TC neurons respond to OXM administration. Whole-cell patch clamp electrophysiological method was used on acute brain slices (250 μm thick) extracted from young (13-19 days old) male Wistar rats. We observed depolarising effect of OXM (1μM) on the DLG TC neurons varying across the anterior-posterior axis-more frequent in the anterior DLG division. We hypothesise that the activatory action of satiety cues on the visual pathway may signal excessive food intake and play a role in interceptive stress or taste aversion. Our research may suggest a possible direct link between the visual system and food intake.
Research supported by grant OPUS13 obtained from National Science Center, 2017/25/B/NZ4/01433.

14. Relative expression of genes encoding allatoregulatory neuropeptides in spider Parasteatoda tepidariorum (Araneae, Theridiidae)

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The knowledge about the structure of the nervous and neuroendocrine system of spiders gives an opportunity to get to know the physiological processes that occur in these arthropods. So far, any substances that are synthesized and

secreted by neurosecretory cells and processes controlled by them have not been shown. There is also no data whether the allatoregulatory neuropeptides belong to the primary substances secreted by tissues of spiders. The main aim of the research was to verify the presence of allatoregulatory neuropeptides (allatostatin A, allatostatin B, allatostatin C and allatotropin) in the tissues of Parasteatoda tepidariorum females, determine the site of their synthesis and recognise the tissues which are under allatoregulatory control. For this purpose, the expression of genes encoding allatoregulatory neuropeptides and their receptors was measured by qPCR methods. This study demonstrated that allatostatin A, allatostatin C, and allatotropin may be present in P. tepidariorum females, whereas allatostatin B has not been confirmed. The nervous and neuroendocrine systems have also been reported to be the main site of the synthesis of these compounds, whereas digestive tract and ovaries were primarily affected by allatoregulatory control. These results allow to fill the gap in basic knowledge about spider biology.
The research was funded by PRELUDIUM grant (National Centre of Science) no. 2014/15/N/NZ4/01931.

15. A new model of gestational diabetes in mice and its consequences to the central nervous system of the offspring

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The aim of this study was to establish a new model of GDM in mice and evaluate effects on the cognition of the offspring in adulthood. Swiss mice (12 weeks, 25 to 40g) were mated. Females received either saline or S961 (30nmol/kg/day,s.c.) starting on the 7th gestational day until delivery. Fasting glycemia and glucose tolerance test (GTT) were performed 7 days after starting the treatment, and dams which received S961 presented higher values. S961 group showed elevated water consumption. S961 treatment did not cause differences in maternal behavior, physical and reflex development of the pups, and neither in locomotion or the anxious profile. Offspring received a high-fat diet (HFD) or standard diet between P60 and P90 and locomotion and anxious profile were re-evaluated, but did not present statistical differences. Males and females offspring submitted to HFD presented higher body mass values. Just males revealed cognitive impairment at hippocampal memory task. Hippocampus were collected from the males for western blot and results suggested an increased inflammatory profile. A new model of GDM was described. Offspring had normal behavior when evaluated in adulthood, but responded exaggeratedly when exposed to HFD, developing obesity and early cognitive impairment.

16. Neuron- and microglia-dependent actions of fractalkine on neurons activity in the rat basolateral amygdala

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Chemokines, together with neurotransmitters and hormones, are signaling molecules playing a key role in the maintenance of neuro-immune-endocrine system homeostasis. One of their member, fractalkine, is a critical mediator in neuron-microglia crosstalk. Yet, recognition and characterization of chemokine effects on neurophysiology are still lacking. Therefore, this study aimed to evaluate the effects of fractalkine on basal membrane neurons properties, their excitability and synaptic transmission in the rat basolateral amygdala. Whole-cell patch clamp recordings were made from principal neurons in the rat basolateral amygdala using acute brain slices (300μm). After recording a baseline, fractalkine (2nM) was bath-applied and basal membrane properties and postsynaptic excitatory and inhibitory currents were measured. To assess the specificity of observed effects some slices were incubated with CX3CR1 antibody or minocycline (inhibitor of microglial activation). Fractalkine application leads to receptor- and microglial-dependent neuron depolarization, decreased membrane resistance and excitability as well as it modulated both excitatory and inhibitory synaptic transmission in the BLA. Our results suggest multifaceted effects of fractalkine application in the basolateral amygdala, indicating that this protein can be an active modulator of neuronal activity in the fear-related response circuitry, which may have significant scientific and therapeutic implications.
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17. *Effects of flaxseed on the pathophysiology of obesity and Behavioral disorders following a high fructose diet in wistar rats*

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This study aims to evaluate the impact of flax seeds on the emotionality, cognition and metabolism in Wistar rats that received a high fructose diet (23%). Month-old wistar rats were divided into four groups of 8 rats: control group (30ml tap water + 30g standard food), control group + flaxseed (7g of flax seeds + 23g of standard food + 30ml of tap water), fructose group (23% of fructose + 7g of flax seeds + 23g of standard food), fructose group + flaxseed (23% of fructose 7g of flaxseed + 23g of standard food). High calorie diet and flaxseed was administered 2 months. Afterwards behavioral tests to evaluate the affective and cognitive, and biochemical analysis of blood glucose, cholesterol (HDL), Low Density Lipoprotein (LDL) cholesterol and triglycerides were conducted. As for behavioral tests the flax seeds have anxiogenic and antidepressant effects. In addition, flax seeds act on memory, they have differences in learning and reference memory. However, there was a significant main effect in working memory. Moreover, the flax seeds correct the lipid profile.

18. *The influence of tryptophan food supplementation in rats on their body weight and basic behaviours*

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Serotonin is present in the brain and body where it regulates many fundamental aspects of physiology and behaviours. Biochemically, serotonin is derived from tryptophan – an indispensable amino acid, which is transferred with consumed food into the intestines. In our research, we checked if diet enrichment in tryptophan changes rats eating habits, body weight and basic behaviours. We conducted an experiment on 18 rats housed individually with free access to food and water. In the beginning, during two weeks, we analysed food intake of standard food pellets. Then, we changed standard pellets in 9 rats into modified ones, containing 15 000 mg of tryptophan per kg (three times more than the standard). Despite daily food consumption being almost at the same level, animal body weight decreased significantly after one week in comparison to rats with the standard diet. In turn, locomotor activity analysed on the fifth day in an actometer (40x40 cm box) was higher after tryptophan supplementation. In further analysis, we would like also to investigate social behaviours on the tenth day and anxiety on the fifteenth day of the procedure.
This project has been financed by Polish National Science Centre grant (2014/15/N/NZ4/04844).

19. *Downregulation of DmMANF in clock neurons influences rhythmic behaviour of Drosophila melanogaster*

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DmMANF (Drosophila melanogaster mesencephalic astrocyte-derived neurotrophic factor) is a neurotrophic factor required for the maintenance of dopaminergic neurons and involved in tissue repair mechanisms. Since DmMANF is present in the Drosophila clock neurons the aim of this study was to investigate if silencing of DmMANF gene expression in the circadian pacemaker neurons, affects locomotor activity rhythm, sleep and morphology of these cells. Using GAL4/UAS system we induced silencing of DmMANF in different subpopulations of clock neurons, including TIM- PER-, PDF- or CRY-positive cells. The results showed that after silencing of DmMANF in the clock neurons the period of locomotor activity was lengthened. Moreover, in all experimental groups sleep duration in light phase of 12h:12h light:dark cycle was increased, while normally sleep occurs primarily at night. The most prominent effect was observed in flies with silenced expression in TIM-positive subpopulation of clock neurons in which almost 90% of flies were arrhythmic and morphology of PDF-positive neurons in the dorsal part of the brain was changed comparing with the control group. Our results showed an involvement of DmMANF in the regulation of the fruit fly circadian rhythms and clock neurons. This work was supported by NCN grant number 2014/15/B/NZ3/04754 to EP.

20. The effect of receptor-selective dopaminergic and noradrenergic drugs on the wake-sleep states

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Sleep is homeostatically regulated suggesting a restorative function. Sleep deprivation is compensated by an increase in length and intensity of sleep. In this study, suppression of sleep was induced pharmacologically in freely moving rats by drugs related to the dopaminergic and noradrenergic systems, which are basic elements of the arousal systems. All drugs were administered in three different doses. Measurements lasted for 24 hours after drug application and local field potentials were recorded during the experiments. All drugs caused non-rapid eye movement (NREM) sleep loss followed by different compensatory processes. In case of the nonselective dopaminergic agonist apomorphine and the selective D1 agonist SKF-38393 the strong – but shorter lasting - suppression of sleep was followed by an intense recovery. On the other hand, the D2 receptor antagonist sulpiride and the alfa-2 receptor antagonist yohimbine caused a long-lasting suppression of NREM sleep, but the following recovery was absent. It seems that the different ascending activating systems play different roles in the homeostatic regulation of sleep, and among them the dopaminergic system may be more important than previously suggested.

21. Short wavelength spectral sensitivity of the rat lateral geniculate nucleus

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Rodents see and use light in the ultraviolet spectrum to communicate, identify food or, as recently proved, to synchronise their circadian rhythms to the solar cycle. Their retina possesses 0.12% of UV-sensitive cones (UVS-cones) among all photoreceptors. The lateral geniculate nucleus (LGN) of the rat thalamus is a complex structure receiving information about the ambient light from all photoreceptors and using it to control image and non-image forming visual functions. Interestingly, the contribution of UV light upon the LGN activity in rats is still missing. To addressed this issue, we examined light-induced responses within the LGN triggered by high-irradiance stimuli of different wavelengths in the range between 340 and 490nm (10nm step, 3s pulses). Multielectrode recordings in vivo were performed in 3 Long-Evans rats under isoflurane anaesthesia. High-irradiance light in the UV range elicited responses in 56% of light-sensitive neurons within three LGN subdivisions: the dorso- (n=7), the ventro-lateral geniculate nucleus (n=2) and the intergeniculate leaflet (n=5). They exhibited both tonic and phasic excitation in response to UV light. Our results show that all parts of the rat LGN receive input from UVS-cones and confirm involvement of UV light to both image and non-image forming visual functions.
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22. Norepinephrine affects activity of the rat intergeniculate leaflet neurons of the thalamus

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The circadian rhythmicity can be influenced by light, as well as many non-photic (light-unrelated) stimuli. The non-photic cues are delivered to the circadian system via the non-specific projections of the brainstem, one of which is the norepinephrine system from the locus coeruleus. All the information which might have an influence on the sleep-wake cycle is integrated within a small thalamic nucleus, called the intergeniculate leaflet (IGL). In this project, we investigated the effect of norepinephrine (NE) on the rat IGL neurons, in order to add a piece towards understanding the whole web driving the circadian rhythms. For this purpose, we performed electrophysiological recordings in vitro (patch clamp) in the current clamp mode on rat brain slices. It was found out, that the vast majority of recorded cells were depolarized after norepinephrine application, however some cells were hyperpolarized or showed no response, which suggests possible variety of impacts this neuromodulator has on different types of cells (and perhaps on different connections arising from the IGL). These results are most probably due to presence of different types of receptors for NE, but the details remain to be determined.

23. *Hypothalamic dopamine neurons as a potential source of sex differences in food intake control governed by the rat nucleus incertus*

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Relaxin-3, synthesised in brainstem nucleus incertus (NI), controlling feeding, stress response and behavioural arousal, increases food intake in a sex-specific manner. Dopamine D2 receptors in the NI mediate decrease in food intake and locomotion, as indicated by intra-NI injections of their agonist - quinpirole. Thus, the NI connection with dopamine-synthesising neurons is worth investigating. This study aimed at exploring tyrosine-hydroxylase (TH)–immunoreactive fibres in the NI and uncovering their source. Rats were perfused and immunohistochemical staining against TH and relaxin-3 was performed. Neural tract-tracing with a retrograde-tracer FluoroGreen and subsequent staining was conducted to locate the source of TH-immunoreactivity in the NI. A map of TH-positive fibres within the NI was prepared and FluoroGreen- and TH- double labelled neurons were counted. The NI is rich in TH-immunoreactive fibres, in apposition to relaxin-3-cells. Posterodorsal hypothalamus and medial zona incerta (A11 and A13 dopamine cell areas) contain TH- and FluoroGreen-double labelled neurons. Hypothalamic dopamine neurons, implicated in sensorimotor and arousal control (A11), as well as defensive behaviour, paradoxical sleep control and feeding (A13), innervate the NI. Importantly, A13 area responds to gonadal steroids. These regions may modulate behavioural activation through the NI and contribute to sex differences in functions regulated by the NI.

24. *Age dependent effects of orexin A on the neuronal activity in the rat dorsal lateral geniculate nucleus*

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Orexins (OX-A, -B) are hypothalamic peptides playing crucial role in arousal, feeding, social and reward-related behaviours. The recent patch clamp study on juvenile rats suggested their involvement in vision modulation, due to their direct, excitatory action on the dorsal lateral geniculate (dLGN) neurons. Moreover, immunohistochemical stainings showed sparse, circadially modulated orexinergic innervation of the dLGN. We aimed to verify whether similar action of OX-A can be observed in adulthood. Thus, we performed in vivo electrophysiological recordings on urethane-anaesthetised Wistar rats across the light-dark cycle and combined them with light stimulations and EEG recordings. Correspondingly, patch clamp study was conducted. During the day, OX-A excited approximately 15% of dLGN neurons in both, in vivo and in vitro preparations. The effect was slow and long-lasting. Similar number of cells were sensitive to OX-A during the night, however two different types of responses were observed: excitation and inhibition, respectively. Interestingly, the responding cells were randomly located in the dLGN and did not show any common properties. In contrast to previously published data, we show that minority of dLGN neurons are sensitive to OX-A in adulthood, suggesting its involvement in visual system development, rather than visual processing. Supported by National Science Center grant: 2013/09/B/NZ4/00541.

25. *Influence of carbachol on electrical activity of midbrain dopaminergic neurons – in vivo studies on urethane anaesthetized mice*

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Dopamine (DA) plays a key role in control of behaviors and motor functions. Synaptic release of the transmitter depends on firing pattern of dopaminergic neurons, which is continuum between regular and bursting mode of activity. Functional NMDA receptors are considered being crucial to evoke DA neurons' bursts of action potentials. Whether other neurotransmitters can also evoke this type of activity remains an opened question. The aim of the

study was to determine the effects of cholinergic agonists on electrical activity of dopaminergic cells. We have used NR1DATCreERT2 mice with selective, inducible deletion of NR1 subunit of NMDA receptor on dopaminergic neurons. We conducted extracellular recordings of midbrain dopaminergic cells' activity in urethane anaesthetized mice, combined with iontophoretic drug application. Loss of NMDA receptors on DA neurons decreased basal firing rate, attenuated bursting and abolished responsivity to NMDA. Nevertheless, after application of cholinergic agonist, some of the DA neurons, developed slow, oscillatory changes in firing rate, which in some cases transformed into robust, complex bursts of action potentials. These results suggest that cholinergic agonists can modulate level of firing as well as switch DA neurons to bursting mode of activity via NMDA-independent mechanism.
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26. Neuronal and intestinal effects of the mycotoxin zearalenon on rats after subchronic administration

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Zearalenon (ZEA) is a non-steroidal oestrogenic mycotoxin produced by Fusarium species mostly in temperate and warm areas. It can be detected in crops and processed food as well, presenting health risks to farm animals and humans. It is known that ZEA may interfere with sexual maturation and reproductive functions in humans but we have less information about how it affects neuronal network functions. Adult Wistar rats of both sexes were treated intragastrically with 2 different ZEA doses (20 and 200 microg/kg) for 28 days. After treatment, electrophysiological recordings were carried out on hippocampal and cortical brain slices. Electrically evoked and epileptiform spontaneous field potentials were analyzed. In addition, the motility and pharmacological sensitivity of isolated ileum segments was studied. Our results show that ZEA does not have any impact on the neuronal networks in female rats, but in males it may cause an excitatory effect. The toxin increased evoked potential amplitude and changed burst pattern. Data analysis of ileum recordings is still in progress. In conclusion, subchronic exposure to ZEA may have significant excitatory effects on brain functions. Due to climate changes, fungal infections represent an increasing health risk in Europe. Supported by National Research, Development and Innovation Fund: NVKP_16-1-2016-0016.

27. Neuronal and intestinal effects of the mycotoxin fumonisin B1 on rats after subchronic administration

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Microscopic fungi, like Fusarium species infecting agricultural crops can produce different toxic secondary metabolites, so called mycotoxins, such as fumonisin B1 (FB1). This toxin is chemically stable so it may be found in processed food as well and through the inhibition of ceramide synthesis, it may cause adverse impacts on animal and human health. Neurotoxicity of FB1 has been demonstrated in vitro, but we have less information about effects on mature neuronal networks in vivo. Adult Wistar rats of both sexes were treated intragastrically with 2 different FB1 doses (50 and 500 microg/kg) for 28 days. After treatment, electrophysiological recordings were carried out on hippocampal and cortical brain slices. Electrically evoked and epileptiform spontaneous field potentials were analyzed. In addition, the motility and pharmacological sensitivity of isolated ileum segments was studied. Both doses of FB1 caused an increase in evoked potential amplitude and alterations in epileptiform burst pattern. Effects were more predominant in male rats. Data analysis of ileum recordings is still in progress. In conclusion, subchronic exposure to FB1 may have significant excitatory effects on brain functions. Due to climate changes, fungal infections represent an increasing health risk in Europe. Supported by National Research, Development and Innovation Fund: NVKP_16-1-2016-0016.

28. Neurotoxicity of acrylamide changes the level and the circadian pattern of locomotor activity of Drosophila melanogaster

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The goal of our study was to examine the behavioral response of Drosophila circadian clock to chronic exposure to the dietary neurotoxin, acrylamide (ACR). The typical pattern of activity of Drosophila is bimodal in day-night (Light-Dark, LD) conditions. Flies display two peaks of activity at the beginning and at the end of the day, and this rhythmicity is maintained also in constant darkness conditions (DD). Recordings of daily locomotor activity (actograms) of wild type flies (Canton-S) kept on medium containing 80 μg/g of ACR revealed changes in both the level and their circadian (~24h) pattern of flies activity. Their activity was significantly elevated during the night (showed the "nocturnal" phenotype) in LD and flies were frequently arrhythmic in DD. Interestingly, such alterations in the pattern of locomotor activity were reported to indicate the hyperexcitation of the circadian clock neurons (ventral lateral neurons, LNvs) that modulate arousal and sleep in D. melanogaster (Shang et al., 2009; Sheeba et al., 2008). Therefore we conclude that chronic exposure to ACR may induce hyperexcitation of the clock (LNv) neurons.
The studies were supported by the grant K/ZDS/007356 in the Institute of Zoology and Biomedical Research.

29. Influence of activation of D1 and D2 dopamine receptors on activity of nucleus incertus neurons – electrophysiological and immunohistochemical studies in rats

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Nucleus incertus (NI) is a stress-sensitive brainstem structure and a main source of relaxin-3 in the brain. Since dopaminergic receptors were described in this structure, possible modulator of NI neurons activity is dopamine, but the source of dopamine in the NI remained unknown. Using track-tracing technique and immunohistochemical staining we indicated A11 and A13 (parts of periventricular nucleus and zona incerta, respectively) as sources of tyrosine hydroxylase (TH) immunoreactive fibers in the NI. Moreover, whole-cell patch-clamp recordings showed that NI neurons express both D1 and D2 dopamine receptors. Bath application of D1R agonist SKF-81297 (10 μM) caused depolarization of NI cells by 5.01 ± 0.75 mV (mean change ± SEM). Activation of D2R with quinpirole (20 μM) exerted both inhibitory (increase in outward current by 12.63 ± 5.27 pA and decrease in action potentials firing frequency by 2.78 ± 1.54 Hz) and excitatory effects (increase in inward current: 12.32 ± 4.12 pA and mean depolarization by 0.88 mV). Similarly, in tetrodotoxin and GABAergic and glutamatergic receptors blockers, application of quinpirole causes both excitation and inhibition. Possibly, NI neurons differently sensitive to activation of dopaminergic receptors control different processes, such as alertness or sensorimotor response to salient stimuli.

30. Direct influence of dynorphin-A on nucleus incertus activity - implications for motivation and feeding control

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The nucleus incertus (NI) of the brainstem is situated in the dorsal tegmentum at the floor of the 4th ventricle. The (NI) is the primary source of the highly-conserved neuropeptide, relaxin-3 (RLN3), involved in stress response and food intake control. The NI has a reciprocal connection with the lateral hypothalamus where neurons co-expressing the excitatory neuropeptides, orexin and dynorphin-A (DynA) are situated. DynA is one of the main endogenous opioid peptides that exert inhibitory influence on neuronal activity of brain structures involved in arousal and associated homeostasis. Therefore, we assessed the relationship between these hypothalamic peptidergic systems and rat NI, by investigating the neurophysiological effects of DynA within NI using whole-cell patch-clamp in vitro recordings. We observed both hyperpolarizing, and depolarizing effect of dynA on NI neurons. Importantly, the inhibitory effect of DynA persisted in the presence of GABA and glutamate-receptors antagonist and tetrodotoxin, what indicates direct, postsynaptic effect of DynA in the NI. Our findings identify direct DynA influence on NI neurons which provides a particular impulse to research exploring the role of opioid signaling in this structure. Particularly, DynA sensitivity of NI neurons may be involved in governing stress induced overeating, process under a strong of relaxin-3 peptide.

31. Neck restraint stress-induced changes in LTP are not mediated by Akt/mTOR pathway

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Repeated neck restraint stress impairs dentate gyrus (DG) long-term potentiation (LTP) after 3 daily repetitions but enhances it after 14 and 21 repetitions. To study mechanisms involved in these phenomena we investigated whether changes in LTP are mediated by the Akt/mTOR pathway. We also investigated the effects of repeated neck restraint on cognitive performance using the object location test (OLT). C57BL/6 male mice were exposed to 1, 3, 7, 14 or 21 daily neck restraint sessions (10 minutes per day). Electrophysiological (LTP recordings), biochemical (Akt, p-Akt, mTOR and p-mTOR immunodetection in isolated hippocampi) or behavioral (OLT) experiments were carried out 1 day after the last restraint. One hour before each of 3 or 14 restraint sessions some animals were intraperitoneally injected with the mTOR inhibitor, ridaforolimus. Behavioral analysis showed that neck restraint repeated for 3 times impaired cognitive performance in the OLT but improved it after 14 and 21 repetitions. Administration of ridaforolimus before each of 3 or 14 restraint sessions did not reverse the effects of neck restraint stress on LTP. Restraint stress affect neither the levels of Akt and mTOR protein levels nor their phosphorylated forms (p-Akt and p-mTOR). Supported by: Polish National Science Center grant no. 2013/09/D/NZ4/00592.

32. Two forms of adaptation act as a powerful spatiotemporal filter of visual responses in the rodent collicular neurons

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Adaptation of visual responses enhances visual information processing mainly by preserving the full dynamic range of neuronal responses during changing light conditions and it is found throughout the whole visual system. Although adaptation in the primate superior colliculus neurons has received much attention little is known about quantitative properties of such adaptation in rodents, an increasingly important model in vision research. By employing single unit recordings, we demonstrate that in the rat collicular neurons visual responses are shaped by at least two forms of adaptation. When visual stimuli were repeatedly presented in the same location, visual responses were reduced in the majority of single units. However, when the adaptor stimulus was outside a small diameter receptive field (RF), ON but not OFF responses to visual stimuli in RF were enhanced in the majority of units. OFF responses were reduced less and recovered faster than ON responses and the effect was limited to a fraction of RF area. Simulations showed that such adaptation acted as a powerful spatiotemporal filter and could explain several tuning properties of collicular neurons. These results demonstrate that in rodents the adaption of visual responses has a complex spatiotemporal structure and can profoundly shape visual information processing.

EPILEPSY

33. The role of kainate receptors in epileptic discharges during entorhinal cortex development, an ex vivo study

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Kainate receptors (KARs) have important role in the modulation of physiological and pathophysiological oscillatory mechanisms, like epileptic discharges. We aimed to characterize epileptic discharges provoked by magnesium-free ACSF in different developmental terms and to define how KARs are involved in these processes by the use of GluK1/2 antagonist UBP-296. Combined hippocampal-entorhinal rat brain slices from different ages (P14, P21, P28, young, and old adult animals) were tested. Electrophysiological signals were recorded by multi electrode arrays. Parameters of field potential and single cell activity were analysed. The highest seizure frequencies were detected at P14 while the lowest at P28. Burst length was the longest at P28 animals. The effect of the antagonist was the most powerful in young adult group in the level of field potential, but changes were significant in all age-groups except in P21. We examined cellular activity and found that length of active window in layer II/III was very similar to burst length in field potential, while in layer V we could not find any difference between age-groups.Based on our results from different age groups we can summarize that KARs participate mainly in the propagation of seizures activity, and KAR antagonists could strongly decrease the length of epileptic bursts.

34. Cerebellar suppression of pentylenetetrazol (PTZ) -kindled seizures is increased by tyrosine-kinase inhibition

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The aim of work was to investigate seizures induced in kindled rats with PTZ (30,0 mg/kg, i.p.) after treatment with axitinib (20,0 mg/kg, p.o.) and electrical stimulation (ES), (100 Hz, 20 trials) of paleocerebellar cortex (VIth lobula). In separate groups only ES or axitinib (20,0 mg/kg, i.p. – both as a single and daily - ten adminisitrations) were delivered. In two other groups axitinib was delivered in 30,0 min before ES, and daily during 10 days also before ES. Gained data revealed that ES was followed by reduction of PTZ-induced seizures by 25,0% pertained to seizures severity in control kindled rats (P<0,05). Axitinib in single dosage reduced the severity of kindled seizures by 20,0% (P<0,05), with the increase of reduction after 10 days of administration – up to 40,0% (P<0,05). Seizure severity in rats with single axitinib administration and ES were reduced by 20,0% (P<0,05) while seizures induced after ES delivered to kindled rats treated with axitinib during 10 days were reduced by 72,0% (P<0,05) with complete prevention of generalized clonic-tonic seizures. Hence, gained data are in favor for the increasing of antiseizure effects of cerebellar ES under conditions of inhibition of tyrosine-kinase in PTZ kindled rats.

35. TTYH1 overexpression influences spine formation and kindling susceptibility

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TTYH1 (Tweety homolog1) protein is a presumed volume-regulated Cl− channel and may be involved in neuronal function. We aimed to examine morphogenesis of CA1 and CA3 neurons following TTYH1 overexpression and influence of increased TTYH1 expression on PTZ-induced epileptogenesis. Rat organotypic hippocampal slices were co-transfected with TTYH1-GFP-Synapsin and RFP-β-actin constructs, using biolistic transfection. L-measure was used for morphometric analysis of CA1 and CA3 neuronal reconstructions. Spine morphology was studied with SpineMagick!. Transgenic rats with TTYH1 overexpression and non-transgenic littermates were subjected to PTZ induced epileptogenesis three times a week. TTYH1 overexpression resulted in increased number of stubby spines on CA1 neurons (apical-proximal and distal dendrites: P<0.01; basal dendrites: P<0.05) and CA3 neurons (apical-proximal dendrites: P<0.05). TTYH1 overexpression led to decreased percentage of mushroom spines (CA3 apical-proximal dendrites: P<0.01; CA3 basal dendrites: P<0.05) and long spines on CA1 neurons (apical-proximal and distal dendrites: P<0.01) and CA3 neurons (apical-proximal dendrites: P<0.05). Transgenic rats with TTYH1 overexpression showed a tendency to increased latency to the onset of stage-5-seizures and kindling acquisition. TTYH1 protein may be involved in neuronal plasticity and participate in susceptibility for epileptogenesis and seizure propagation. Supported by Polish National Science Centre Grant: 2011/03/NZ4/00302 and 2015/19/N/NZ3/03268.

36. Effects of ketogenic diet on susceptibility to electroshock-induced seizures

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Ketogenic diet has been proven to reduce frequency and severity of seizures in patients suffering from epilepsy refractory to antiepileptic drugs. The ameliorating effects of the dietary treatment have already been confirmed experimentally but using animal models. In this study, we present the effects of the ketogenic diet on susceptibility to seizures induced with repeated electrical stimulation. Forty-seven male 60-day-old Wistar rats were fed either ketogenic or control, non-ketogenic standard diets, and the food intake was measured. The body mass and blood level of ketone bodies were recorded weekly. At the age of 85 days, the dietary treatments were modified according to different schedules and the rats were subjected to 21 daily electrical stimulations to evoke seizures. Tonic and clonic seizures were distinguished from each other and their severity was evaluated using separate scales. Generally, groups remaining on the ketogenic diet had a significantly increased susceptibility to seizures following electroshocks. Our previous studies using the pilocarpine epilepsy model showed an opposite experimental relation, i.e. reduced susceptibility to seizures in animals treated with ketogenic diet. These data, taken together, suggest the existence of different mechanisms underlying effects of the ketogenic diet depending on the experimental seizure model.

37. Behavioral characteristic as a biomarker of development and phenotype of epilepsy in the temporal lobe epilepsy induced by electrical stimulation of the amygdala in rats

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Non-invasive biomarkers of epileptogenesis and epilepsy in experimental models would allow fast and easy evaluation of disease development and impact of treatments aiming at modification of disease development or progress. The project was conducted to test the hypothesis that there are differences in the results of behavioral tests depending on (I) time to develop epilepsy and (II) intensity of epilepsy. Epilepsy was evoked by status epilepticus using electrical stimulation of the amygdala (25min, 400μA, 60Hz, delivered every 0.5s). EEG was used to classify rats into groups with short (<20 days, n=7) and long (>20 days, n=8) latency and groups with low (SE_L:62±64.5, n=7) and high (SE_H:456±185, n=8) seizure number. We applied several behavioral tests. No difference was observed in the anxiety, activity and learning between all experimental groups. However, we observed increased anxiety, measured by number of imputes to the closed arms, in group with high seizures in elevated plus maze carried out in 26 week compared to animals with low seizures (SE_H:35±13.6, SE_L:15.14±8.9, $p<0.01$). Our studies showed that analysis of basic behavioral parameters in animals kept in enriched environment shows no difference between control and stimulated animals.
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38. The peculiarities of the development of pentylenetetrazole kindling in rats of different ages

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Aim of the study was to investigate the differences in the generalization of convulsive activity during classic pentylenetetrazole (PTZ) kindling in rats of different ages under different intervals of PTZ. Experiments were carried out on 220 albino rats. The PTZ kindling protocol with injections of convulsant every 24 or 48 hours in 5- and 8-week-, 3- and 6-month-old rats was provided. The ED16 for induction of clonic seizures was used as the kindling doze. The kindling showed an age-dependent decrease in kindling doze of PTZ from 42 to 22 mg/kg. Our studies have shown that the development of severe clonic-tonic seizures at the lowest percentage of animals in the groups of 3- and 6-month-old rats was registered. Among the 3- month-old rats the variants of seizure generalization were recorded: in 40 % - earlier than at in other term of the occurrence of clonic-tonic seizures, 40 % - complete generalization of seizures after the last injection and the absence of severe seizures in 20 %. In the group of 6-month-old animals development of severe seizures were recorded in 60 % after the last covulsant`s injection, in others - such seizures were not generated. Data may indicate a different stage of involvement of pro- and anticonvulsant mechanisms in rats of different ages with different conditions of administration of PTZ.

39. Subchronic exposure to cannabinoid agonist R(+)WIN55,212-2 alters spike-wave discharge duration and termination in rat

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WAG/Rij rats, a genetic model of absence epilepsy, exhibit 7-10Hz spike-wave discharges (SWDs) in their EEG. Single exposure to cannabinoid agonist R(+)WIN55,212-2 (WIN) reduces seizure incidence during 3 hours after injection, followed by an increase in SWD duration. Since drug effects of repeated use are of utmost relevance clinically, we studied the effects of subchronic administration of R(+)WIN55,212-2 on SWDs. 16 adult male rats were treated with WIN (6 mg/kg in 3 mg/ml olive oil, s.c.) or olive oil (controls), 6 times in 2 weeks. 24-hour EEGs were recorded before treatment, after first treatment, and after 2 weeks. SWDs were quantified: incidence, duration, distribution and hazard rates were calculated. SWD incidence was not affected, but the mean SWD duration in WIN-treated animals was longer than that of controls. Hazard rates were lower at SWD lengths in the 5-25s range, which points to lower probability of SWDs to terminate. All effects occurred after first treatment and were stable over the duration of

the experiment. These results suggest that the endocannabinoid system is involved in modulating SWD termination, which is believed to be controlled by the reticular thalamic nucleus.

COGNITIVE PROCESSES

40. Task-based functional network changes following 6-week working memory training

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Human brain is a complex network which constantly undergoes plastic changes in response to changing environment. We investigated effects of intensive 6-week working memory training on task-based functional network reorganization. Thirty-nine participants (age range: 18–26) were scanned in the functional magnetic resonance imaging (fMRI) four times - before and after 2, 4, and 6 weeks of intensive working memory training. After the first fMRI scan, participants were randomly assigned to one of the group: (1) an experimental group, trained with a dual n-back task with increasing level of difficulty; and (2) an active control group performing single n-back task with no increasing cognitive demands. We found that only experimental group exhibited significant behavioural improvement during the dual 2-back task across all fMRI sessions. Moreover, change of the whole-network modularity from 1-back to 2-back at first fMRI scan predicted training progress measured during the whole course of training (18 sessions). Edge-wise network analysis revealed significant group differences especially in default mode and frontoparietal subnetworks. These results may facilitate our understanding of the mechanisms behind human learning and task automatization. This project is supported by the National Science Centre, Poland (2015/17/N/HS6/03549; 2017/24/T/HS6/00105).

41. New approaches to studying cognitive changes

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Changes in the spatial memory and navigation functioning affect the quality of life and are considered to be first signs of dementia (Vlacek, 2011). Finding abnormality in them is a difficult task, due to general cognitive decline in the elderly, as well as lack of standard tools for the navigation diagnosis (Iachini, 2009). The aim of this study was to check which memory aspects are relevant in the navigation process and allow classifying into the age groups. The study was performed using standard (Cantab tests and BVRT) and non-standard (navigation in the building with gait measurement) tasks. In the study 39 women divided into groups: youth (under 25), younger seniors (65-72 years) and older seniors (72-80) participated. The results verified the legitimacy of gait monitoring, which can measure indirectly cognitive functioning. Moreover, it was demonstrated that associative and working memory are involved in navigation process ($p<0,05$). The discriminant analysis showed that memorizing paths, associative memory, spatial span and step counts are indicators of changes in healthy aging ($p<0,01$), allowing classification. In summary, there are subtle differences between older people which can be omitted without the non-standard feature's inclusion. Results confirmed the validity of similar measurements in people with dementia.

42. Gait parameters as an indicator of navigation skills

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Gait is an important component of the navigation process, it is a source of information about position in the space but also the number of stops on the route and chaotic movements are considered to be the indicators of the navigation task executing (Koenig et al., 2009). The main aim of our study was to test navigation skills at healthy elderly woman (n=20). The task was conducted in a building and was divided into four phases during which participants were asked to: remember the predefined path (learning phase), retrace the path (memory phase), recall 10 objects location seen on the path (objects location test), reach some objects from the path with using the shortest way (delayed phase). During the task, participants were equipped with the gait sensors which let us monitor gait parameters. Results from the study showed that the number of steps made during the particular phases of the task was related to the ability of recalling object locations during the location objects test ($p<0,05$). Obtained results can support the assumption about relation between gait and cognitive state, in particular for the gait parameters as an indicator of navigation skills.

43. Hallucinogen use is related to greater volume in brain regions known for object recognition

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Structural MRI and questionnaire data from 1206 people were downloaded from the openly available dataset of the Human Connectome Project and then analysed with the use of FreeSurfer. Self-reported data on hallucinogen use were collected with the Semi-Structured Assessment for the Genetics of Alcoholism questionnaire. By means of massive univariate approach, the biggest difference between hallucinogen users and non-users was found in bilateral fusiform gyrus, lateral occipital sulcus and left inferior temporal gyrus (all $p_{corr} < .001$). In general, hallucinogen users had greater volume in enlisted brain regions. Interestingly, the same analysis conducted for cocaine, opiates, sedatives, alcohol and stimulants use did not yield any significant results. Note, that all the areas of interest are thought to be the part of ventral visual pathway known for engagement in object processing. However, it is not possible to infer simple causal connection between volume of brain regions and hallucinogen use, at least two explanations can be taken into account. Firstly, it was shown that hallucinogens, to some extent, can cause neurogenesis. The other plausible explanation is that people with higher capabilities of seeing patterns are more likely to take hallucinogenic drugs since they are seeking for more imagery-related stimulation.

44. Can neurofeedback improve mental rotation process? A Beta-band ERD Study

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Kosslyn's visual imagery model contains attention shifting system which plays crucial role in this process. Previous studies indicate that parietal beta ERD is connected with mental rotation process. The purpose of our studies was to estimate the impact of acoustic neurofeedback on the process of mental rotation of 3D objects. Thirty-three subjects were randomly divided into two groups performing the classic Shepard & Metzler's mental rotation task. The experimental group received sound stimuli whenever the level of their concentration dropped below the threshold specified individually for each subject on the basis of engagement index [$\beta/(\alpha+\Theta)$]. The acoustic neurofeedback was used in order to improve attentional engagement. The concentration level of the control group was not stimulated. In experimental group beta suppression (18-24 Hz) was stronger than in control group. This effect occurred over the left and right parietal cortex. Only in experimental group the beta-ERD differences between high (140°, 160°, 180°), medium (80°, 100°, 120°) levels of depth rotation angle and control condition (0° or no rotation), over the right parietal and central areas were observed. Results indicate that acoustic neurofeedback can improve mental rotation process.

45. Number line estimation strategies used by children with dyscalculia and healthy controls

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We investigated the number line estimation for symbolic and non-symbolic format in children with low numeracy skills compared to healthy controls. Twenty children with diagnosis of dyscalculia and 27 normally developing children participated in the study. All children revealed the greatest estimation error (EE) for numbers located in the middle of number line, but the effect was more pronounced in dyscalculic group. Moreover, groups manifested similar range of the overestimation value, but they differ in the value of underestimation error. Children with dyscalculia showed a greater left bias than control group in case of almost all number magnitudes. The exploration of EEs measured for each number enabled to describe the estimation strategy used in dyscalculic and healthy group. It seems that children with dyscalculia tend to assess the number line segments starting from a left end point, and even setting an anchor in the center of number line ("5") does not help them to estimate position of "4" and "6" correctly. All children showed also greater EE for non-symbolic format, especially in case of the right end of number line, what is interpreted as the manifestation of a position estimation error as well as the incorrectness in dot counting.

46. Correlation between mathematical competencies and intelligence in children

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The research attempts to answer the question of whether there is a connection between the level of specific components of intelligence and the level of different basic mathematical skills as well as to indicate the mathematical competencies that most strongly correlate with the intelligence quotient. For this purpose, the correlational analyses have been conducted for IQ obtained in Wechsler Intelligence Scale for Children (WISC-R) and basic mathematical abilities (e.g. number comparison, numerosity and number line estimation) measured using the computer test (Prokalkulia 6-9). Eighty-two participants took part in the study, both normally developing and children with dyscalculia. It has been shown that there is no homogeneous WISC-R results profile that would characterize the group with mathematical disabilities. These results are consistent with previous knowledge that suggests the complexity of cognitive profile observed in different types of mathematical deficiencies. However, according to the obtained results, these deficits occur primarily in such basic mathematical abilities as comparing numbers in different formats (processing of mental representations of numbers), number line estimation (processing of numerical and spatial relations). They are highly correlated with the following WISC-R subscales: messages, arithmetic and verbal understanding as well as patterns from blocks, puzzle and coding.

47. The effect of cognitive and cognitive-motor training with the use of mathematical computer game "Kalkulilo" on the number line estimation and number magnitude comparison

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Studies confirm the benefits of a positive effect of cognitive training using modern technology in education on the level of mathematical skills. The aim of the study was to examine the effect of cognitive training with computer math game "Kalkulilo" in the development of such skills. In the study, sixty-eight children (aged 7-10) were divided into 3

groups: 1st group was training with „Kalkulilo" game on a laptop, 2nd group was training with the "Kalkulilo" and Kinect sensor of movement and the 3rd group was the passive control. Training took 5h and was divided into 10 sessions. Before and after training we measured the level of mathematical skills of participants using the computer test. The results indicate the effect of training on spatial representations of numbers development because it improved the accuracy of number line estimation. This effect is particularly pronounced in the 2nd group of participants, which further suggests that this type of motor-cognitive training is more effective than a standard training. It could be concluded that the use of mathematical game training may be a valuable tool not only in math education but also it could be helpful in overcoming the cognitive deficits observed in dyscalculia.

48. Is communicative intentions processing automatic or volitional? ERP study

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The ability to comprehend communicative intentions seems to be of crucial importance as it enables people to engage in social interactions. However, the role of reflexive and reflective social cognitive processes in communicative intentions processing still remains unclear. The aim of the present study was to examine the temporal dynamics of communicative intentions processing and, consequently, to elucidate whether it can be considered as automatic or volitional. Given its excellent temporal resolution, the Event Related Potential (ERP) method was used in the study. The task has been presented to the participants while their brain activity was recorded with 64-channel EEG. In each trial participant observed an animation presenting either point-light display (PLD) of actor (performing communicative gesture or non-communicative action) or scrambled non-biological motion and had to decide whether PLD was presented. Early (N170; 120-200ms) and late (Late Positive Potential - LPP; 800-2000ms) ERP components were analysed. PLD presentation elicited more negative N170 and more positive LPP. Furthermore, an interaction effect was observed with communicative actions eliciting larger LPP than other types of displays. Since LPP is believed to reflect processes of maintained attention, these results suggests that observation of communicative intentions is associated with automatic attentional engagement.

49. Prolonged blue light blockade affects sustained attention but not working memory

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The influence of light on human functioning is linked to retinal ganglion cells that are sensitive to blue light (BL). Behavioral and neuroimaging studies demonstrated that exposure to BL directly enhances alertness and performance. However, due to aging, the ocular lens become more yellow, reducing the BL transmission. Longitudinal changes in behavior while blocking BL exposure were investigated. We examined 19 young volunteers wearing BL-blocking contact lenses (BLB) and 19 controls wearing only UV-blocking lenses (CTRL) at baseline session and for 4 consecutive weeks of wearing the lenses. Participants performed a psycho-vigilance task, widely used test of sustained attention (SA) as well as n-back task as a working memory (WM) measure. The results show increasing reaction time in consecutive sessions only for BLB ($p<0.05$) and a stable measure in CTRL group in SA task. In WM task, neither accuracy nor reaction time showed difference between groups. The findings of this experiment show that continuous reduction of blue light exposure affects the human functioning only in attention domain. Working memory is not affected. This may suggest that BL acts on neuronal system linked to attention and arousal but not on prefrontal cortex, responsible for higher cognitive functions.

50. The recovery processes following a period of chronic partial sleep deprivation. An EEG study

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Sleep deprivation is an important societal problem that affects millions of people around the world. However, it is typically studied in terms of its 'total' rather than 'chronic' state. Our study aimed to examine recovery processes following a period of chronic partial sleep deprivation. The study run over 21 consecutive days, divided into 3 periods: 4 baseline days, 10 days of partial sleep deprivation, 7 days of recovery. Each day, participants took part in an EEG experiment in which they performed a classic Stroop test. Moreover, over the 21-day period, participants' spontaneous locomotor activity was measured with the use of actigraphs, which record periods of rest and activity. We have found behavioural and neural changes associated with different time periods. The 10-day period of partial sleep deprivation was linked with poorer performance on the Stroop test and an attenuated P300 neural response, compared to the baseline. This was followed by the observation of slow and gradual return in the period of recovery, which has, surprisingly, never fully returned back to the baseline levels. Chronic partial sleep deprivation has detrimental, long-term consequences on both behavioural and neural levels, which are difficult to overcome even after a period of normal sleep patterns.

51. Exploring working memory modalities - functional network alterations due to increasing demands of visuospatial and auditory working memory tasks

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Studies show that functional network reorganizes from more segregated to more integrated pattern when demands of a cognitive task increase. However, differences in network reorganization during a working memory task engaging different modalities were so far not investigated. We examined forty-seven healthy subjects (aged 18-26) using functional magnetic resonance imaging during resting-state and while they were performing visuospatial and auditory n-back tasks at increasing levels of difficulty (1-back and 2-back). We obtained correlation matrices for each participant, task type, and task condition for two types of brain parcellation. We calculated global connectivity measures and compared the strength of individual edges using network-based statistic. We showed that the brain becomes more integrated while switching from the lower- to the higher-demand task for both modalities. NBS showed that for both auditory and visuospatial conditions most weakened network edges belong to the default mode network (DMN) and the most edges in the strengthened network link DMN with other brain systems. We confirmed the previous findings that the brain adapts to increasing cognitive demands and extended these conclusions for different modalities.
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52. The effect of task difficulty on brain activation in auditory verbal working memory task in elderly adults: an fMRI study

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Working memory (WM) is a limited capacity system engaged in temporary maintenance and manipulation of information. While its neuronal basis has been widely described, few fMRI studies have explored auditory verbal processing in elderly. The study goal was to verify brain regions engaged in auditory WM in elderly, considering task difficulty assessed by the WM load. Participants were 19 healthy elderly (aged 62 – 79 years). They performed auditory verbal n-back task with different memory loads: 0-back (control condition), 1-back and 2-back (experimental conditions). Significant effect of task difficulty on response accuracy was obtained ($F(1{,}428, 25{,}713)=16{,}04$; $p<0{,}001$). It was accompanied by increased activations (FWE cluster-corrected at $p<0.05$) in parietal regions, prefrontal cortex (PFC), insula, right medial frontal gyrus and right cingulate gyrus (2-back vs. 1-back). Furthermore, the maintenance of information in WM (1-back vs. 0-back) activated right inferior parietal lobule, left superior frontal gyrus, left inferior frontal gyrus and bilateral middle frontal gyri. Although previous studies on auditory verbal n-back task indicated predominantly the engagement of the left prefrontal cortex, the bilateral activations of PFC reported here suggest greater involvement of inhibitory and attentional control processes in elderly due to higher executive demands. Supported by National Science Centre Grant 2015/17/B/HS6/04182.

53. Neuronal mechanisms of cross-modal transfer in healthy aging

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The study aimed at exploring neural and behavioural correlates of higher cognitive functions in the healthy elderly. 41 subjects took part in the study, out of which 27 met the inclusion criteria (over 65 yo, Mini-Mental State Examination scores within norm, lack of psychoneurological history, less than 10% excessive movement scans during the functional Magnetic Resonance Imaging [fMRI]). Each subject underwent both neuropsychological and fMRI assessment, the latter during performing the Paced Auditory Serial Addition Test (PASAT). The task was blocked-design with two alternating conditions of "repeating digits" and "serial addition". The fMRI data was processed in Freesurfer software in the surface-based stream. Preprocessed data was analyzed within the General Linear Model framework. Additional regressors included motion correction vectors, as well as outlier scans identified by the Artifact Detection toolbox. The contrast "addition-vs-repeating" was investigated with neuropsychological variables as model's covariates. Out of tested ones, only the visual component of the working memory raised significant results after accounting for multiple comparisons. The better subject's visual memory was, the more extensive was the involvement of the visual cortex of both hemispheres in the processing of the fMRI auditory working memory task. The results indicate a cross-modal transfer in the study group.

54. A Comparison of Visual Working Memory and Episodic Memory Performance in Younger and Older Adults

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Previous studies showed that both working memory and episodic memory decline with age. However, as working memory and episodic memory are typically studied separately, it is largely unknown whether age-associated differences are similar for working memory and episodic memory and how they relate. A task design was developed in which visual working memory and episodic memory performances were measured using the same stimuli, with both tasks involving context binding. A 2-back working memory task was followed by a surprise subsequent recognition memory task that assessed incidental encoding of object locations of the 2-back task. The study compared performance of younger (N=30; Mage=23.5, SDage=2.9, range 20-29) and older adults (N=29; Mage=72.1, SDage=6.8, range 62-90). Older adults performed worse than younger adults on both tasks. There was no interaction between task and age-group. In younger, but not in older adults, performance on the two tasks was related. Furthermore, the number of errors on lure trials was the same in both age groups. We conclude that although age differences (Young & Older) are similar in the visual working memory and incidental associative memory tasks, the relationship between the two memory systems differs as a function of age group. Longitudinal research is needed to investigate life-span changes in the relationship between working and episodic memory. As some neurodegenerative diseases are characterized by specific types of memory impairment, it is important to have a profile of functioning of memory subsystems for unimpaired older adults.

55. *How doing nothing is related to memory performance*

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Researchers utilize electroencephalography (EEG) to answer their research question focus on task-related brain activity. However, even the EEG at rest can be related to person's cognition and can be used to predict person's performance on a task. When analysing a resting state EEG, one can look at different frequencies of brain oscillations, including delta (.5-4 Hz), theta (4-7 Hz), alpha (7-13 Hz), beta (13-30 Hz), and gamma (30-100 Hz). Oscillations in certain frequency bands have been linked to specific cognitive processes. Specifically, task-related theta oscillations have been linked to memory processes, like subjectively perceived memory confidence. However, it is still unclear how theta oscillations at rest are related to memory processes. To this end, we recorded resting state EEG from our participants before they encoded stimuli, between the encoding and retrieval of stimuli, and after the retrieval of the stimuli. We show that theta oscillations at rest are negatively correlated with subjectively perceived memory confidence. This mirrors current findings of the positive relation between task-related theta oscillations and subjectively perceived memory confidence. This suggest that the modulation of theta oscillations during rest and task-related activity is closely associated with the level of subjectively perceived memory confidence.

56. *Effects of emotional congruency and basic emotions on memory for emotional words within communicative context*

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Information congruent with prior knowledge is remembered better than incongruent information. At the same time, emotionally charged items are often remembered better, but emotional associations -worse. We investigated how emotional congruency and basic emotions influence associative memory for words in communicative context of faces. 18 females (age 22-29) took part in fMRI study. Stimuli included emotional words and faces (disgusting/fearful/neutral) from standardized datasets. During encoding sessions, words were presented with faces, emotionally congruent or incongruent. Subjects were instructed to memorize these pairs and imagine as messages and senders. During retrieval sessions, old and new words were shown, and participants indicated what was the emotion of accompanying faces. Behavioural analyses showed interaction between emotion and congruency – disgust was remembered better than fear when congruent, but not incongruent. During correct encoding, we observed that left parahippocampal gyrus was more active for incongruent than congruent pairs, while right hippocampus was more active for disgust than fear. Correct encoding of congruent disgust was specifically related to activation of right amygdala and hippocampus. During correct retrieval, right parahippocampal gyrus was more active for congruent than incongruent pairs and also for disgust than fear. Retrieval of congruent disgust activated specifically left hippocampus and medial prefrontal cortex.

57. *How disgust and fear influences long-term memory of verbal unitizations – measuring encoding-retrieval similarity with fMRI*

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Emotion-memory interactions are present from encoding to long-term retrieval. However, little is known about the influence of specific basic emotions on the reinstatement of encoding-related activity during retrieval. 52 subjects (29 female; age 20-33) took part in two fMRI sessions: encoding and retrieval, with stimuli selected from the Nencki Affective Word List (NAWL). During encoding session, they were presented with word pairs (disgusting/fearful/neutral), and instructed to imagine them unitized. After 2-3 weeks, during the recognition session, they were presented with old pairs from encoding and new lures, and asked to determine if a word pair was old or new. Behavioral analyses showed the main effect of emotion. Specifically, emotional stimuli were better remembered than neutral, and disgusting better than fearful. At the neuronal level, correct compared to incorrect recognition of word pairs was related to a higher index of encoding-retrieval similarity of brain activation patterns in the left middle temporal gyrus. The activation of left amygdala during encoding significantly modulated brain activation during recognition in the right hippocampus and right inferior frontal gyrus. Finally, we found that the level of encoding-retrieval similarity was correlated with left amygdala activation during encoding of disgusting compared to fearful word pairs.

BRAIN STATES

58. Recognizing cortical and deep sources of human brain activity from resting-state EEG spectral fingerprints

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During rest different brain structures are connected into distinguishable networks (Damoiseaux et al. 2008, Bola & Sabel 2015). Each region of interest (ROI) tends to preserve its own natural frequency (Rosanova et al. 2009). We want to develop a reliable method which allow us to access milliseconds-level dynamic features of brain networks from EEG signal, so called EEG brain fingerprint. Keitel and Gross (2016) proposed a method of clustering each ROI's MEG source-reconstructed activity. It turned out that spectral fingerprints representation enables accurate ROIs classification. Moreover, using only functional data, the algorithm linked ROI to clusters that correspond well to large-scale anatomical parcellations of the cortex. We have recreated and adapted this method to analyse resting-state EEG signal from two different datasets (each one N=22). Results show that despite it is hard to differentiate between ROI using EEG data still performance is well above the chance level. Each ROI EEG activity is characterized by less number of clusters than ROI MEG activity and ROI similarities forms less clear image of brain networks. Nevertheless, method is still promising and further development could lead us to founding new and reliable tool useful in scientific and clinical practice.

59. Informativeness of auditory stimuli does not affect EEG signal diversity

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Cortical signal diversity constitutes a robust marker of global states of consciousness, as it is decreased during unconscious states, and increased during psychedelic states. The aim of the present study was testing whether neuronal diversity corresponds to the temporal diversity of subjective experience. We hypothesized that greater information rate processed by subjects within a time interval will be related to more differentiated experience and, consequently, to greater EEG signal diversity. To test this hypothesis, we manipulated the information rate by presenting speech recordings (audiobooks) at five different speeds, and we also included backwards (unintelligible) speech and a resting-state (no auditory stimulation) as control conditions. We tested 19 healthy subjects and used the Lempel-Ziv algorithm (LZs) to evaluate diversity of the recorded EEG signals (64 channels). Our hypothesis was not confirmed, as we found no significant effect of the information rate on LZs ($F(4)=3.49$, $p=0.47$). Unexpectedly, greater LZs was observed during the resting state than during listening to meaningful ($Z(18)=3.0$, $p=0.002$) or

unintelligible speech (Z(18)=2.37, p=0.035), with most pronounced differences over centro-parietal and frontal electrodes. We speculate that greater variety of experiences during an unconstrained resting-state, including mind-wandering and spontaneous attention switching between stimuli and modalities, might cause greater signal diversity.

60. Short latency intracortical inhibition in the angular gyrus characterized by paired-pulse TMS and EEG co-registration

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Short-latency intracortical inhibition (SICI), showing local inhibition mediated by GABAA receptors, is commonly measured using motor evoked potentials (MEPs) induced by transcranial magnetic stimulation (TMS) from the primary motor cortex. Nowadays, the TMS-compatible EEG allows to measure TMS-evoked brain potentials (TEPs) from non-motor areas. Our aim was to characterize SICI in one of these areas, the angular gyrus (AG), using a combined TMS-EEG protocol and thus investigate the function of local GABAergic circuits. 10 healthy volunteers participated in six blocks of TMS stimulation with EEG co-registration. Both single and paired-pulse TMS were applied over the left AG. In the paired-pulse trials, two intensities of both testing and conditioning stimuli were examined with the inter-stimulus interval of 2.5 ms. Each condition was tested 80 times while different stimuli were delivered in randomized order. Furthermore, the SICI in the left primary motor cortex was measured using MEPs recorded from the contralateral hand. Our preliminary results suggest that it is possible to use TEPs to study SICI in the AG in terms of changes in amplitude of short latency deflections in TEPs. The paired-pulse TMS protocol could therefore serve as a new non-invasive tool for assessment of GABAA receptor-mediated neurotransmission in non-motor areas.

61. Nuclear magnetic resonance thermography

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Introduction: Currently, our ability to measure brain temperature in vivo is limited. Techniques for estimating temperature in vivo could improve our understanding about mechanisms of thermoregulation inside the brain and help with diagnosis of brain trauma and tumors. The aim of this study was to develop program that would allow us to calculate temperature from spectra obtained during MRS acquisitions in vivo. Methods: Two phantoms across two MRI scanners (GE Discovery MR 750w and Bruker Biospec) was studied. Fiber optic temperature probe (OSENSA) was inserted into the phantoms. One phantom was put inside Bruker MRI scanner and heated (31,4°C to 40°C) using water circulating around the phantom. Second one was heated (up to 42,1°C) and put inside GE MRI scanner where it would cool off (down 34,0°C). On both phantoms MRS sequence PRESS was run every time the temperature probe inside showed approximately 1°C change compared to the prior scan. Results: Developed program created 2 calibrations for in vivo brain temperature measurements. Calibrations acquired from literature and those created were then used to measure temperature inside in vivo human and cat brain. Results showed that when using MRS thermometry it is better to use calibration created on the same scanner.

62. Parcellation of the human amygdala based on the intrinsic dynamics of the BOLD signal

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Understanding the functional organization of the amygdala largely depends on development of the reliable parcellation method of this structure. As the previous methods of the amygdala parcellations yielded inconsistent results, the aim of our study was to develop a new method based on the intrinsic dynamics of the BOLD signal. We adapted the method previously used to analyze nonlinear dynamical systems - Recurrence Quantification Analysis

(RQA). It allows representing the behavior of a dynamical system with few parameters. We applied several RQA measures to each time series from amygdala voxels in resting-state fMRI data from 84 subjects (Siemens Verio 3T, TR = 1.4s., voxel size = 2x2x2mm) and established that the measure of Determinism (DET) is the most promising. DET could describe differences in signal predictability across distinct parts of the amygdala. On that basis, we have parcellated the amygdala into two subdivisions using hierarchical clustering. Our results converge with parcellation based on structural connectivity patterns estimated from diffusion-weighted imaging. This suggests that technique based on RQA is promising for analyzing fMRI data and delineating functional subdivisions of the human amygdala. The study was supported by a grant from the National Science Centre (Poland) based on decision number DEC-2014/15/B/HS6/03658.

63. Statistical power of non-parametric tests: EEG signal analysis of event related activity in the time- and frequency domain

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The correlates of brain's response to stimuli can be manifested in EEG signal in two different ways: phase-locked and non-phase locked activity. In classical approach, by averaging EEG signals, the phase-locked activity is clearly visible as event-related potential (ERP). On the contrary, a measure of event-related brain dynamics induced by, but not phase-locked to, the onset of the stimuli is cancelled out from the average. The analysis of time-frequency distributions of signal energy allows exploring fully phase-locked and non-phase-locked stimulus-induced oscillations. This study presents nonparametric method used for finding statistically structures on time-frequency maps. This study also shows that this method controls an error of the first kind, associated with false rejection of the null hypothesis (EEG-simulated data in different experimental conditions are equal) and an error of the second kind, when the false acceptance of the null hypothesis occurs (false discovery of statistically significant objects in EEG-simulated data). The data was generated using autoregressive model. Results obtained from the simulation will be presented at the conference.

64. Distinguishing between physiological and epiphenomenal phase amplitude cross-frequency coupling

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Coupling between low- and high-frequency brain rhythms provides valuable information on cognitive processing in humans. However, there are signals which have a waveform, e.g. sharp transients, that results in spurious PAC. Therefore, it's not always clear whether detected coupling has a physiological origin. The purpose of this study was to present a novel method of assessment of phase to amplitude cross-frequency coupling in terms of a distinction between physiological and epiphenomenal PAC. The proposed method is based on analysis of time-frequency representation of signals aligned to a given phase in the low-frequency band. Low-frequency wave is obtained with Matching Pursuit algorithm by selecting waveforms of interest. The time-frequency representation of signal’s energy density is derived from continuous wavelet transform and normalized at each frequency relative to its average value in the baseline period. Next, the representation is thresholded at values obtained from surrogate data. The resulting maps are used to compute comodulograms. The effects presented in the comodulograms are validated with extreme values statistics. The method is tested on synthetic and real data. We present that proposed approach correctly detects proper PAC and allows the user to infer the origin of the cross-frequency coupling as physiological or epiphenomenal.

BRAIN STRUCTURE

65. Cortical thinning in adult cigarette smokers: a large-scale (n=513) structural MRI study

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While the impact of cigarette smoking on cancer and respiratory disease is well established, there is no consensus on its impact on the brain. Some studies indicate that prolonged exposure to toxic chemicals in cigarette smoke could cause numerous negative effects, including poorer scores in cognitive tests, increased risk of dementia in old age or decrease of gray matter volume. However, most of these were done either on aged subjects, or on small subject populations. On the other hand, some studies suggest than nicotine could play a neuroprotective role. Here we analyze a large sample of MRI T1-weighted scans of healthy young adults (18 - 40 years old, 200 smokers 7.6 cigarettes/day average, 313 non-smokers). In a preliminary analysis, we extracted cortical gray matter (GM), white matter (WM) and subcortical nuclei volumes using FreeSurfer. The multiple regression model was used to correct for age, sex and weight. Relative to non-smokers, we found a significant reduction in total volume of GM (2.5%, p=2x10-4) and WM (2%, p=3x10-2) in smokers. We conclude that smoking is associated with cortical thinning in young adults. Our next step will be determining the association between years of smoking and structural changes in the brain.

66. The impact of geometric distortion correction on the results of population MRI study

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Introduction: Images of brain acquired using MRI are the basis for computational morphometry – studies of shape and size of brain structures. Precise and accurate measurements can be used to assess progress of neurodegenerative disorders. Nevertheless, geometric distortion (GD) of MR images decreases the accuracy of morphometry. Phantom measurements can precisely capture and correct GDs. The aim of this study was to investigate the impact of ADNI phantom-based geometric correction on brain morphometry results. Methods: T1-weighted images of brain were obtained from 26 healthy volunteers (13 female, mean age 30.4±8.2 years) and corrected for GD using an ADNI phantom. Voxel-based (VBM) and surface-based morphometry (SBM) analyses of the T1 images were conducted. Results: The results show differences in grey matter volume (GMV) and cortical thickness (CT) between measurements obtained before and after correction. GMV was significantly increased in the parietal lobe and reduced bilaterally in temporal lobes. CT was significantly increased in the parietal lobe and reduced mostly in frontal, parietal and temporal regions. Conclusions: This is the first VBM and SBM study to show differences in brain morphometry after GD correction. The results indicate that this correction results in changes in both GMV and CT even for one-site study.

67. An efficient recovery of diffusion tensor imaging biomarkers using the compressed sensing principle

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Diffusion magnetic resonance imaging (dMRI) is an emerging technique that enables to probe the microstructural properties of the tissues in a non-invasive way. However, dMRI suffers from a long acquisition time and is particularly sensitive to subject motion artifacts. Reduction in examination time is therefore a key element to minimize the confounding factors related to the acquisition process. In this study, we propose and evaluate an

efficient acquisition scheme of dMRI brain data using the compressed sensing (CS) principle and redundant multiple-channel receiver sources. The proposal allows to collect the data from non-uniformly subsampled trajectories and then recover the quantitative biomarkers from diffusion tensor imaging (DTI) using a sparse wavelet domain representation. For 1.7-fold acceleration ratio of the acquisition process (about 60% of the data collected) we obtain the relative error (RE) being 2.67%/-1.66% for fractional anisotropy (FA)/mean diffusivity (MD) in the corpus callosum (CC) area regarding to fully-sampled acquisition, while for 2.5-fold acceleration the REs equal 5.53%/-4.25% for FA/MD. The results underlie that the reduction in acquisition time for dMRI examination can be effortlessly achieved using the CS technique with negligible alterations to the DTI-based biomarkers in CC area.

MULTISENSORY PROCESSES

68. Unimodal and crossmodal extinction of nociceptive stimuli in healthy volunteers

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Nociception, the physiological mechanisms specifically processing information about noxious and potentially painful stimuli, has the function to warn the brain about potential body damages (interoception) and about the stimuli that might cause of such damages (exteroception). The exteroceptive function of nociception is thought to rely on multisensory processes integrating the perception of the body with that of the space surrounding it. To support this hypothesis, we exploited the extinction phenomenon usually observed in patients with lesion to one cortical hemisphere. In this vein, we conducted two experiments with healthy subjects to show that the perception of a nociceptive stimulus applied on one hand can also be extinguished in healthy volunteers, as compared to single presentation, by the simultaneous application of a nociceptive stimulus on the contralateral hand, and also by the presentation of a visual stimulus near the contralateral hand. In addition, we observed that visual stimuli presented near the stimulated hand facilitated the perception of nociceptive stimuli applied on that hand. This suggests that the perception of nociceptive events does not only depend on the anatomical and functional integrity of the nociceptive pathways but is also influenced by other sensory experiences about the body and the space around it.

69. Decoding Across Senses Representations of Everyday Objects from the Lateral Occipital Complex

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Visual paradigms highlight the role of the lateral occipital complex (LOC) in the representation of everyday objects, but objects are perceived by different senses in life. Our aim was to determine if it is possible to decode everyday object in LOC independently of the sensory system used. We used a multisensory paradigm in which we presented carrots, bread, apples, and marshmallows, in independent runs of visual, olfactory, gustatory and tactile modalities (8 runs for each sense, n = 10). Functional images were acquired on a 3-T scanner (TR/TE = 2000/27 ms). A multivoxel pattern analysis and full-brain searchlight were performed. The results showed that the only region with predictions above chance ($p < 0.05$) for all senses was LOC, we also test others multimodal regions (prefrontal cortex and precuneus) but without predictions above of chance to all senses. In conclusion, we found that LOC contains category-specific patterns (not sensory-specific patterns) of BOLD activity; suggesting that LOC encodes high-level characteristics of the stimulus independent of the sensory modality of presentation. Our results suggest that representations of everyday objects in LOC are not exclusively visual, rather are integrative representations. However, it is unknown if mental representations in LOC are amodal or multimodal.

70. Decoding Shape, Texture and Weight in the Somatosensory System

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Previously we found that the activity patterns of the parietal cortex could predict the category of an object explored through touch, this suggested that the parietal cortex have specialized groups of neurons that encode high-level characteristics of objects. However, the perception of an object through the somatosensory system is built from different low-level properties of the object. Our aim was to test if a parietal region can encode more than one low-level characteristic of the same stimulus. We acquired functional resonance images of participants (n=8) while they explored objects that differed in three properties: weight, shape, and texture. We analyzed the whole brain (using MVPA) and tested which region's activity could decode the tested properties. We found that the activity in the anterior intraparietal sulcus (AIPs) could predict above chance ($p < 0.01$) the texture and shape of the objects. However, the same region could predict the identity of the object (which can only be done by considering the three properties at the same time). These results suggest that the AIPs not only process low-level characteristics of an object (texture and shape) but it also functions as an integration node. This highlight the integrative role of the parietal cortex.

71. 40 Hz Auditory Steady-State Response: is handedness important?

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Auditory Steady-State Responses (aSSRs) are periodic brain responses to a periodic stimulation. As 40 Hz aSSRs has been previously reported to be asymmetric between hemispheres and handedness is associated with different brain asymmetry, we wanted to assess how handedness could affect the ASSRs. We enrolled 22 young healthy right-handers and 22 left-handers. Each group consisted of equal number of males and females. 64-channel EEG recording was performed during auditory stimulation with 500 ms click trains at 40 Hz presented to right ear, left ear and binaurally in a random order. Phase-locking index (PLI) and event-related spectral perturbation (ERSP) of the response were calculated. The results revealed handedness interaction with sex affecting processing of 40 Hz stimulation: lower phase-locking and strength of 40 Hz aSSRs were found in left-handed females compared to left-handed males, although no differences were observed in right-handers. The effect was independent from the ear stimulated. Also, PLI and ERSP were lower in left-handed than right-handed females, but no such differences were observed in males. We conclude that both handedness and sex modulate processing of 40 Hz auditory stimulation. Acknowledgements: the research was supported by the Project No. CH-3-ŠMM-02/03.

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