

NEURONUS 2016 IBRO & IRUN NEUROSCIENCE FORUM

APRIL 22-24 2016, KRAKOW, POLAND

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Website design

Szymon Jeziorko http://szymonjeziorko.com

Poster and booklet graphic design

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APRIL 22, 2016 (Friday) 12.00 **Registration opens** - Large Aula A -13.15 **Opening Ceremony** - Large Aula A -**Opening Lecture:** 13.30 -**Christian Büchel** 14.30 How memory guides decision making (University Medical Center Hamburg-Eppendorf, Germany) - Large Aula A -14.30 -FlashTalks (see p. 15) 15.15 15.15 -**Refreshment Break** 15.30 - Medium Aula A -- Medium Aula B -- Large Aula A -**Affective Neuroscience** <u>Neurology</u> Neurode(re)generation chaired by: Gilles chaired by: **Tomasz** chaired by: Walker Dziedzic Pourtois (Ghent University, Jackson (German Center for Belgium) (Jagiellonian University Neurodegenerative Diseases, Medical College, Krakow, Bonn, Germany) 1. Paul Whalen: The Poland) 15.30 -Surprising Utility of 1. Walker Jackson: 17.00 Surprise 1. Natalia Gawron: Older Selective vulnerability to age along with lower CD4 neurodegenerative cell count nadir, diseases: the curious case 2. Monika Riegel : Wolf in education, and social of Prion Protein sheep's clothing or wolf in support are associated wolf's clothing? Effects of 2. Lech Kaczmarczyk: with cognitive decline in emotional congruency and The "Grabber" - a knock-in men aging with HIV basic emotions on mouse line developed for infection associative memory in

	 in vivo, cell-type specific, multi-level gene expression analysis of the brain 3. Lukasz Szewczyk: Myelin impairment and axonal degeneration in ST8SIA2-deficient mice, a genetic model for schizophrenia research 4. Marcelina Szczerba: Neural differentiation of neural epithelial-like stem cells derived from Alzheimer's disease patient pluripotent stem cells 	communicativ fMRI prelimin 3. Didier Gra Neuronal dyn between amyr orbitofrontal emotion perce 4. Matthias W Disentangling mechanisms of predictable an unpredictable frequency-tag approach	nary results ndjean: amics gdalae and regions in eption Vieser: attentional during nd e threat: A	 2. Ahnjili ZhuParris: Experienced Drug Users Report the Nootropic Properties of Subperceptual Dosages of Psychedelic Drugs: A Web-Based Survey 3. Jan Miodoński: Modern instrument to transect peripheral nerves and soft tissues - knife coated in bioactive nanolayer 4. Zofia Ślosarek: Neurosurgical treatment of brain metastases from lung cancer – analysis of benefits 5. Magdalena Doręgowska: DBS-STN surgery for Parkinson's disease patients - results of 10 years experience
17.00 - 17.30	Coffee Break			
17.30 - 18.45	- Exhibition Room Poster Session (see p. 42-63)		Comr	- Large Aula A - nercial Presentation: EEG/ERP signal recording (Elmiko)
18.45 - 19.45	- Large Aula A - Plenary Lecture: Miguel Maravall <i>Response heterogeneity and temporal encoding in the rodent whisker system</i> (University of Sussex, UK)			

0.00			
8.30	Registra	ation opens	
	- Large Aula A -	- Medium Aula -	
	<u>Neurophysiology</u>	Multisensory Integration, Body	
	chaired by: Karl Farrow	Representation and Pain	
9.00 - 10.30	(Neuro-Electronics Research Flanders VIB, KU Leuven, imec, Belgium)	chaired by: Tineke van Rijn (Radboud University Nijmegen, the Netherlands) & Emanuel Van den Broeke (Catholic	
	1. Karl Farrow: Dissecting neural circuits of the visual system	University of Louvain, Belgium)	
	2. Cagatay Aydin : Impact of locomotion on population activity of visual	1. Valéry Legrain: Mapping pain in a multisensory space	
10.50	thalamus and cortex	2. Elia Valentini: Representation of	
	3. Jan Bielecki : Vision made easy: Box jellyfish is a unique model for visual information processing	potentially noxious events in the brain: quest for a pre-attentive nociceptive sensory trace	
	4. Katalin Major : Investigation of epileptic seizures following chronic 4-aminopyridine treatment in entorhinal	3. Daniele Romano : Body representatio shapes responses to painful stimuli	
	cortex of rat brain slices using MEA (multi electrode array) system	4. Casper van Heck: Pain, empathy, and control; an ERP study	
	- Larg	e Aula A -	
	Plenary Lecture:		
10.45 -	Ghislaine Dehaene-Lambertz		
11.45 -	The infancy of the human brain:		
-	<i>brain imaging studies reveal the roots of human cognitive successes</i> (INSERM, Gif/Yvette, France)		

11.45 - 12.15	Coffee Break		
	- Large Aula A -	- Medium Aula A -	- Seminar Room -
	<u>NeuroGlia</u> chaired by: Antje	<u>Neuroeconomics</u>	Interactive Session of Medical Case Reports
	Grosche	chaired by: Barbara Fryzeł (Jagiellonian University,	chaired by: Marcin Wnuk
	(University of Regensburg, Germany)	Krakow, Poland)	(Jagiellonian University Medical College, Krakow,
	1. Antje Grosche: The	1. Tobias Kalenscher: Behavioral and neural basis	Poland) 1. Rafał Skowronek :
	Müller cell – the glial all- rounder of the retina	of inequity aversion in rats 2. Adam Schweda : The	Traumatic basal subarachnoid hemorrhage
	2. Mykhailo Batiuk:	effect of stress on thinking	or ruptured brain
	Unraveling astrocyte heterogeneity using	and decision making	aneurysm in 16-year-old boy? – case report
	single cell	3. Alexander Soutschek:	2. Patrycja Mołek:
	transcriptomics	How the perspective-taking brain turns the future self	Misleading CT findings in
	3. Ana Amaral:	into a stranger: role of the	patients with non-
12.15 -	Metabolic remodelling during oligodendrocyte precursor cell	temporo-parietal junction in delay gratification	convulsive status epilepticus
13.45	differentiation	4. Amber Heijne : Why we stay with our partners:	3. Kamila Miętkiewska : Recurrent myelitis with
	4. Justyna Janowska : Neonatal hypoxic- ischemic insult alters process of gliogenesis in rat brains	Psychological and neural mechanisms of stay/leave decision-making	fluctuating anti-aquaporin- 4 autoimmunity in the course of neuromyelitis optica spectrum disorders (NMOsd)
			4. Michał Fidera : Neuromyelitis optica and Sjogren Syndrome - pathophysiological relationship or comorbidity?
			5. Katarzyna Sawczyńska & Wojciech Bochenek: Fiction or reality – the image of neurological
			disorders in feature films and TV series

13.45 - 14.30	Lunch		
14.30 - 15.45	- Exhibition Room - Poster Session II (see p. 63-86)		
15.45 - 16.45	Meet Your Speaker at the Table / Coffee Break		
16.45 - 18.15	 - Large Aula A - Sleep & Circadian Rhythms Chaired by: Etienne Challet (INCI, CNRS & University of Strasbourg, France) 1. Etienne Challet: Circadian clocks, feeding and metabolism 2. Patrycja Orlowska- Feuer: Dissecting the role of melanopsin retinal ganglion cells in generation and modulation of infra-slow oscillatory activity in the mouse visual system 3. Jagoda Jęczmień: The dorsal lateral geniculate nucleus of the thalamus responses to light are modulated by sleep-like states – in vivo electrophysiological study on urethane-anesthetized rat 	 Medium Aula A - Rehabilitation After Acquired Brain-Injury Chaired by: Luciano Fasotti (Radboud University Nijmegen, the Netherlands) 1. Luciano Fasotti: Cognitive and Graded Activity Training for persistent fatigue after Stroke: A randomized controlled trial 2. Dirk Bertens: A randomized controlled trial of errorless Goal Management Training in persons with brain injury 3. Urszula Górska: Monitoring the auditory textures processing in human cortex to distinguish states of consciousness 4. Viona Wijnen: Resting state EEG during recovery to consciousness 	 - Medium Aula B - Psychophysiology of Higher Cognitive Functions Chaired by: Tytus Sosnowski (University of Warsaw, Poland) 1. Tytus Sosnowski: Patterns of brain and cardiovascular activation 2. Ewa Ratajczak: Heart- coded. Heart rate variability as a psychophysiological marker of cognitive performance and psychological functioning – an EEG-ECG study 3. Wojciech Zajkowski: Crucial role of right frontopolar cortex in directed exploration 4. Ewa Beldzik: Brain activations related to saccadic reaction time and response conflict

	4. Magdalena Smyk : Synchrony is the key: jet lag consequences in epileptic rats		5. Karolina Finc: Functional network reconfiguration related to increasing cognitive effort
	Robert Lucas Re-imagining vision following the discovery of new photoreceptors		
18.30 - 19.30			
		(University of Manchester, UK)	
	Social Event: Party for all participants		

APRIL 2	24, 2016 (Sunday)		
	- Large Aula A -		
9.30 -	Plenary Lecture:		
10.30	Benno Roozendaal		
	Stress and emotional arousal effects on memory		
	(Radboud University Nijmegen, the Netherlands)		
10.30 - 11.00	Coffee Break		
	- Large Aula A -	- Medium Aula -	
	<u>Neuropsychiatry</u> chaired by: Ingo Willuhn	Brain Networks and Brain Oscillations chaired by: Rob van der Lubbe	
11.00 - 12.30	(Institute of the Royal Netherlands Academy of Arts and Sciences, the Netherlands)	(University of Twente, the Netherlands)	
	1. Ingo Willhun: Striatal dopamine dynamics during flexible behavior and compulsive actions	1. Rob van der Lubbe: Are early ERP components the result of a phase reset of ongoing pre-stimulus oscillations?	

	2 Instrue Day sight Installed		
	2. Justyna Papciak : Investigating affective biases in Sprague Dawley rats using hormonal manipulations	2. Michał Bola : Loss of inner awareness is related to hyper-correlated brain activity	
	3. Justyna Barut : Regulation of gene transcription in response to depressive- like behavior induced by morphine abstinence	3. Amir Avnit : Normalization of Abnormal Frontal Lateralization in ADHD via Deep TMS	
	4. Joanna Danielewicz : Imipramine treatment partially reverses the effects of maternal separation stress on synaptic modification range in the rat	4. Bálint File: Resting state brain networks predict the characteristics of visual evoked potentials	
	lateral amygdala	5. István Sulykos: Electrophysiological correlates of visual search asymmetry; a visual mismatch negativity study	
12.30 - 13.15	Lunch		
	- Exhibition Room -		
13.15 - 14.30	Poster Session III (see p. 86-109)		
		,	
	- Large Aula A -	- Medium Aula -	
	Learning and Memory	<u>Neural Correlates of Motor Activity</u>	
	chaired by: Marta Moita	chaired by: Emilia Zabielska-Mendyk	
	(Champalimaud Centre for the Unknown, Lisbon, Portugal)	(John Paul II Catholic University of Lublin, Poland)	
14.30 - 16.00	1. Marta Moita: The study of defense behaviors as alarm cues	1. Weronika Potok: The temporal involvement of the left Supramarginal Gyrus in planning functional grasps	
	2. Karolina Rokosz : Neural circuits underlying emotional contagion	2. Christabel Chittick : Diminished	
	3. Davide Ciliberti : Closed-loop control of hippocampal memory processing in freely behaving rats	somatosensory perception of the affected hand in children with unilateral Cerebral Palsy – an Event-Related Potential study	
	4. Malgorzata Borczyk : Studying ultrastructure of stimulated synapses with 3D electron microscopy	3. Jesse Saris : Are mirror movements in children with unilateral cerebral palsy related to secondary degeneration of the posterior part of the corpus callosum?	

	4. Witold Sławko: Connectivity of the		
	primary motor cortex in bilateral upper		
	limb congenitally amputated patients: a		
	DTI study		
	5. Joanna Mencel : Decrease of total power		
	of the EEG after motor imagery training in		
	patient with bilateral upper limb		
	congenital transverse deficiency		
	- Large Aula A -		
	Large Hala H		
	Closing Lecture:		
16.00 -			
17.00	Karl Gegenfurtner		
	Vision and eye movements		
	(Giessen University, Germany)		
	- Large Aula A -		
17.00 -	Closing Domarks		
17.15	Closing Remarks		
	(with awards for the best oral and poster presentations)		

Index of the presenting authors can be found at p. 111-112.

April 22, 2016 (Friday)

OPENING LECTURE: 13.30 – 14.30

How memory guides decision making

Christian Büchel

Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Germany

FLASHTALKS 14.30 – 15.15 moderated by: Wioleta Walentowska & Michał Ślęzak

- 1) Kamil Pradel PS I-3
- 2) Lukasz Chrobok PS I-13
- 3) Magdalena Jatczak PS I-17
- 4) Katalin Sviatkó PS I-21
- 5) Diana Legutko PS I-27
- 6) Agnieszka Limiszewska PS I-28
- 7) Kacper Kondrakiewicz PS I-33
- 8) Urszula Skupio PS II-7
- 9) Robert Drozd PS II-15
- 10) Magdalena Ziolkowska PS II-21

- 11) Łukasz Bola PS I-37
- 12) Katarzyna Chyl PS I-42
- 13) Monika Riegel PS II-47
- 14) Małgorzata Wierzba PS II-48
- 15) Tomasz Ligeza PS II-51
- 16) Victoria Heng PS II-54
- 17) Magdalena Matyjek PS II-57
- 18) Joanna Watroba PS II-61
- 19) Roxane De Keyser PS III-35
- 20) Vincenzo Vizzari PS III-39

NEURODE(RE)GENERATION

15.30 – 17.00 chaired by: **Walker Jackson** (German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany)

1. Selective vulnerability to neurodegenerative diseases: the curious case of Prion Protein

Walker Jackson

German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany

Neurodegenerative diseases evoke tremendous suffering on the victims and their families. They cause a once normal, productive individual to decline into an incapacitated state by destroying specific parts of the central nervous system (CNS), eventually leading to premature death. The culprits in these dreadful diseases are misfolded protein conformers, which eventually clump into aggregates as the diseases progress. They occur late in life, generally after the age of 40, which is particularly interesting for the genetic diseases since the disease causing mutant protein is present throughout life. Another interesting feature is that the rogue molecules damage only specific parts of the CNS despite their ubiquitous distribution. Put another way, certain regions of the CNS can tolerate specific diseaseinducing proteins whereas others cannot. The simplest explanation for this selective targeting is that the disease inducing protein is most abundant in the parts of the brain affected the most. However this simple hypothesis is simply wrong. Therefore, much work is needed to delineate the mechanism(s) behind the selective vulnerability of specific CNS regions to degeneration. Such knowledge could be exploited for therapeutic purposes by transfer of neuroprotective genetic elements into vulnerable regions. To this end our lab is studying mouse models of three genetic and one acquired (infectious) neurodegenerative diseases to identify similarities and differences. Our most important analytical tools involve the study of gene-regulation in specific cell types from brains at different disease stages. This approach is enabling us to identify the cell types most vulnerable and how their selective vulnerability evolves during disease progression.

2. The "Grabber" - a knock-in mouse line developed for in vivo, cell-type specific, multi-level gene expression analysis of the brain

Lech Kaczmarczyk, Lars Dittrich, Melvin Schleif, Walker Jackson

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The brain is by far the most cellularly diversified organ. This complexity presents a huge challenge for gene expression studies, which usually require tissue homogenization. Such samples are a mixture of material from multiple cell types, which obfuscates data, and thus interpretations. To handle this issue, in recent years several methods were developed for cell type-specific isolation of RNA populations (mRNA, ncRNA, miRNA, etc.) or chromatin from crude tissue homogenates. These methods share the common theme of labeling biomolecules in specific cells and then using the introduced labels as baits, to affinity purify (or co-purify) desired material from homogenized specimens. With this strategy, tissues can be rapidly frozen, thereby maximally preserving the native (patho)physiological state of gene expression. Many of these tools employ Cre/LoxP system for activation, allowing extraction of material from cells based on their identity, developmental stage or activity state, determined by the Cre driver used. Alone, or followed by next generation sequencing (NGS), these tools are vastly improving gene regulation studies of the brain. However, the experimental conclusions are limited since only a certain level of gene expression (for example only miRNA regulation) is analyzed. We therefore developed the "Grabber": a knock-in mouse line expressing a Cre/LoxP dependent transgene simultaneously expressing four independent proteins, each designed to affinity purify a different population of cellular nucleic acids: 1) ribosome-bound mRNA, 2) competing endogenous and non-coding RNA, 3) miRNA and 4) chromatin. For the first time multiple levels of regulation of gene expression can be studied in defined cell populations of the same tissue specimen. Despite the brain's immense cellular complexity, the Grabber will help to dissect mechanisms of neurological diseases and make new insight into physiology of complex brain functions such as sleep, memory or mechanisms of drug addiction.

3. Myelin impairment and axonal degeneration in ST8SIA2-deficient mice, a genetic model for schizophrenia research

Lukasz M Szewczyk^{1,2,3}, Nikola Brozko¹, Andrzej Nagalski², Herbert Hildebrandt⁴, Jacek Kuznicki², Marta B Wisniewska^{1,2}

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¹ Center of New Technologies, University of Warsaw, Warsaw, Poland
 ² International Institute of Molecular and Cell Biology, Warsaw, Poland
 ³ Postgraduate School of Molecular Medicine, Warsaw, Poland
 ⁴ Hannover Medical School, Hannover, Germany

Polysialyltransferase II (ST8SIA2) is an enzyme that attaches polysialic acid to the extracellular domains of cell adhesion molecules NCAM1 and CADM1. Polysialylation is associated with brain development and ST8SIA2 is a candidate risk gene for schizophrenia. We report that St8sia2-/- mice show myelin deficits and axon degeneration, resembling white matter alterations in schizophrenia. Westernblot and histological examinations revealed hypomyelination of the cortex and other brain regions. Ultrastructure analysis in the corpus callosum showed smaller axons and thinner myelin sheath in adult St8sia2-/- mice. In older, eight-month-old mice, white matter lesions occurred. Immunohistochemistry showed lower number of OLIG2+ cells in the knockout mice, suggesting impairment in oligodendrocyte generation. St8sia2-/- mice-derived oligodendrocyte precursor cells (OPCs) displayed lower than controls levels of polysialylation, higher levels of PDGFR α and overactivity of PDGFR α downstream pathways - ERK and AKT. St8sia2-/- OPCs expressed lower than controls levels of Mbp, Plp1 and Mag transcripts for myelin proteins showing lower differentiation potential. We propose that impairment in the differentiation of ST8SIA2 deficient OPCs lead to insufficient production of myelin and developing with age white matter deterioration. Our study indicates that St8sia2-/- mice are a suitable model to investigate the mechanisms of myelin-related pathologies in schizophrenia.

4. Neural differentiation of neural epithelial-like stem cells derived from Alzheimer's disease patient pluripotent stem cells

Marcelina Szczerba¹, Harriet Rönnholm², Malin Kele², Anna Falk², Cezary Żekanowski³, Michalina Kosiorek^{3*}

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¹Faculty of Biology, University of Warsaw, Poland ²Anna Falk's Reprogramming and Disease Modeling Laboratory, Department of Neuroscience, Karolinska Institutet, Sweden ³Mossakowski Medical Research Centre, PAS, Warsaw, Poland

Our current understanding of sequence of molecular events leading to early-onset Alzheimer's disease (AD) is limited due to a lack of appropriate in vitro model. Therefore, a generation of patient-derived induced pluripotent stem (iPS) cells, further converted into neuroepithelial-like stem (NES) cells, and differentiated into neurons can offer an alternative approach. The aim of this study was differentiation of NES cells into nerve cells. For this purpose primary cell lines of skin fibroblasts derived from a patient with Alzheimer's disease carrying R307S mutation in PSEN1 were reprogrammed into iPS using Yamanaka factors. Subsequently iPS cells were subjected to neural induction into NES cells. Established NES cell lines were cultured and differentiated into neurons. After 6 days of culturing NES cells were converted into neurons, which were validated by immunocytochemical staining with neuronal markers and glial marker. In order to characterize the obtained neuronal subtypes, mRNA expression profile of different neural lineages was analyzed. The latter analysis revealed that this differentiation protocol gave rise to neurons of predominantly GABAergic phenotype with some glia. Summarizing, this study showed derivation steps of neurons from Alzheimer's patient and provided material for future studies on AD pathomechanism using "disease-in-a-dish" approach.

AFFECTIVE NEUROSCIENCE 15.30 – 17.00

chaired by: Gilles Pourtois (Ghent University, Belgium)

1. The Surprising Utility of Surprise

Paul J. Whalen

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Dartmouth College, Hanover, NH, USA

Information gleaned from the facial expressions of others allows us to concurrently determine the internal state of the expressor as well as learn valuable information about what their state might predict for us. Many facial expressions communicate a clear valence [e.g., angry (negative); happy (positive)], in part, because the outcomes predicted by these expressions have been rather consistent in our previous experience. Surprised expressions, on the other hand, are more ambiguous with respect to valence, in part, because they have predicted both positive and negative outcomes in the past. In this talk, I will present behavioral, psychophysiological and neural responses to the facial expression of surprise, highlighting the unique ways that this expression can be used to address emotional responding.

2. Wolf in sheep's clothing or wolf in wolf's clothing? Effects of emotional congruency and basic emotions on associative memory in communicative context – fMRI preliminary results

Monika Riegel¹, Marek Wypych¹, Małgorzata Wierzba¹, Michał Szczepanik¹, Katarzyna Jednoróg², Patrik Vuilleumier^{3,4}, Artur Marchewka¹

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² Laboratory of Psychophysiology, Department of Neurophysiology, Nencki Institute of Experimental Biology of PAS, Warsaw, Poland

³ Swiss Centre for Affective Sciences, University of Geneva, Switzerland

⁴ Laboratory for Neurology and Imaging of Cognition, Department of Neurosciences and Clinic of Neurology,

University Medical Centre, Geneva, Switzerland

How emotion influences associative memory of words within communicative context? What are specific effects related to memory of disgust and fear? What are the effects of emotional congruency or incongruency between an information and its context? We attempted to answer these questions in a preliminary fMRI study, using emotional words and faces selected from standardized datasets. During encoding sessions, words were shown paired with faces, forming emotionally congruent or incongruent conditions. The subjects were instructed to memorize them and to

imagine the words as communicates linked to facial expressions. During retrieval sessions, old and new words were shown and participants indicated if they had seen them in the context of face expressing disgust (D), fear (F), other (O) or the word is new (N). Analysis of correct responses showed that congruent disgust was retrieved better than other emotional pairs. At the neuronal level, we found a significant effects of correct retrieval of emotional material in the right and left hippocampus driven mainly by the difference between BOLD contrast estimate values for emotionally incongruent and neutral stimuli. Based on preliminary results, we hypothesized that emotion influences associative memory of verbal stimuli emotional congruency between item and communicative context.

3. Neuronal dynamics between amygdalae and orbitofrontal regions in emotion perception

Didier Grandjean

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Swiss Center for Affective Sciences, University of Geneva, Switzerland

Past brain imaging and brain lesioned patient studies have shown that the perception and the recognition of emotion involved a series of brain regions including, among others, the amygdalae and the orbito-frontal regions (OFC). However, the precise neuronal dynamics within and between these crucial brain regions in emotional processing have been poorly investigated. We recorded local field potentials within amygdalae and OFC regions simultaneously in patients suffering from pharmaco-resistant epilepsy. The neuronal dynamic analysis within each region revealed, firstly, an early gamma modulation in the amygdalae followed by later high frequency increases of energy in the OFC regions in response to angry stimuli compared to neutral ones. Furthermore, we showed that the phases of these two brain regions are synchronized in the alpha band during angry exposure, suggesting a dynamic cross-talk between the amygdala and OFC medial regions. The phase amplitude coupling (PAC) analysis between these two regions revealed that the gamma bursts occurring in the OFC are organized as a function of the low frequency phase of the signal generated in the amygdala, only for angry stimuli. Moreover, the reaction time of angry stimuli categorization is specifically decreased as a function of the strength of the PAC compared to neutral stimuli. The different functional contributions of these dynamic neuronal couplings between amygdalae and OFC areas will be discussed.

4. Disentangling attentional mechanisms during predictable and unpredictable threat: A frequency-tagging ssVEP approach

Matthias J. Wieser¹, Philipp Reicherts¹, Georgiana Juravle², Andreas von Leupoldt^{2,3}

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¹University of Würzburg, Department of Psychology, Germany ²UKE Hamburg Eppendorf, Germany ³University of Leuven, Department of Psychology, Belgium

Fear and anxiety are functionally different defense states mediated by distinct brain structures. Whereas fear is elicited by imminent threat and leads to a phasic fear reaction, anxiety is characterized by a sustained state of heightened vigilance due to temporally uncertain danger. In the present study we sought to investigate whether fear and anxiety are associated with different states of attentional vigilance as measured by visuocortical facilitation. To this end, we employed a NPU-paradigm together with ssVEPs and frequency-tagging methodology. We investigated ssVEPs across three context conditions (30 sec): no aversive events (N), predictable aversive events (P), and unpredictable aversive events (U) signaled by a grid of four peripheral objects. Short-duration cues (Gabor patches) were presented for 3 seconds several times in each condition. Aversive events were signaled by the cues in the P condition but were presented randomly in the U condition. Importantly, cues and context events were flickered at different frequencies (15 Hz vs. 20 Hz) in order to disentangle electrocortical responses to contexts and cues. As expected, the onset of the context elicited larger electrocortical responses for the U compared to the P context in the first 1000 ms. Conversely, P cues elicited larger electrocortical responses compared to the N and U cues. Interestingly, during the presence of the P cue, visuocortical processing of the concurrent context was also enhanced. The results support the notion of enhanced hypervigilance to unpredictable threat, while predictable cues show electrocortical enhancement of the cues themselves but additionally a boost of context processing.

1. Older age along with lower CD4 cell count nadir, education, and social support are associated with cognitive decline in men aging with HIV infection

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Background: The aim of the study was to examine risk factors of cognitive decline in HIV-positive men treated successfully with antiretroviral therapy.

Method: 97 HIV+ patients and 94 seronegative controls completed measures of visuospatial and verbal working memory, learning, fluid thinking, fine motor and executive skills. Medical, socioeconomic, and leisure data were also collected.

Results: A PCA revealed one global factor of cognitive functioning. Three groups were found. Twenty eight HIV+ participants had global cognitive performance below 1 SD from all sample mean (HIV+ low). Two other groups had average performance i.e. within 0.5 SD around the mean: 40 HIV+ participants and 38 controls. Group comparisons showed that HIV+ low participants were significantly older, less educated, and received less social, emotional, and instrumental support than other groups. No group differences were found for occupational complexity nor amount of physical activity. HIV+ low participants were infected longer than HIV+ with average cognitive functioning and had lower CD4 cells count nadir.

Conclusions: The results confirm previous findings that older age, level of immunodeficiency, and lower education increase the susceptibility to cognitive decline in HIV infection. Lack of social support may be an additional factor.

2. Experienced Drug Users Report the Nootropic Properties of Subperceptual Dosages of Psychedelic Drugs: A Web-Based Survey

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OBJECTIVE: Testimonials dating back to the 1960s have described the microdosing of Lysergic Acid Diethylamide (LSD) to have nootropic properties such as cognitive enhancement, physical boost, increased creativity and mindfulness. Microdosing refers to ingesting sub-perceptual amounts of psychedelic drugs. This study catalogued and examined 600 reports from subjects, on Reddit and Erowid, who microdosed on a regular basis. RESEARCH DESIGN AND METHODS: The drugs examined were Tryptamines (5-methoxy-N,N-dimethyltryptamine, Psilocybin), Ergolines (LSD), Phenethylamines (Mescaline, The 2C family, NBOMe derivative, 2,5-dimethoxy, 4-substituted amphetamines), Cannabinoids and Empathogens (Substituted methylenedioxy-phenthylamines). Reports of microdosing with prescribed nootropic drugs such as psychostimulants (methylphenidate and amphetamine) and wakefulness-promoting agents (modafinil) were also collected. The data includes dosage, form of administration, tolerance and tolerance duration. The physiological and cognitive changes were also recorded, this encompassed sleep, side effects, appetite, motivation, concentration, memory, physical energy.

RESULTS: 56% of the users choose Ergolines for microdosing, 32% with Tryptamines, and 12% with Phenetylamines, Empathogens and Psychostimulants. Users experienced a variety of effects such as emotional clarity, enhanced senses, increased concentration and stamina. There were several reports of reduced appetite, excessive sweating, reduced sleep, indigestion and warped time perception.

3. Modern instrument to transect peripheral nerves and soft tissues - knife coated in bioactive nanolayer

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Introduction: Current methods of peripheral nerve cutting are highly unsatisfactory. Imperfect cutting plane directly influences the effect of nerve anastomosis. For precise rejoining of cut nerve stumps directly, or to bridge large gap with autologous nerve graft, the surfaces of nerve stumps must be even and perfectly matching. We examined the in situ morphological properties of rat peripheral nerves cut with and innovative device: the carbon-metal coated blade (nanoblade) with bioactive surface mounted on the high-speed drill.

Methods: Rat sciatic nerves were transected with scissors, scalpel, or nanoblade. Rotational speed ranged from 15-35.000/min. Cutting nerve has been previously stabilized on a special platform. Immediately after transection serial transverse sections were subjected analysis of the plane surface with scanning electron microscope, H-E and Massontrichrome staining.

Results: Desribed method allowed to eliminate uneven and lacerate edges of epineurium and perineurium. We found that single axons were cut regularly and smoothly. With electron microscope we observed preserved parallel arrangement of fibers and their undisturbed microstructure. There were none thermical damage of the transection plane.

Conclusions: This technique holds a promise for the development of a minimally invasive alternative approach with cutting plane allowing for perfect matching of nerve stumps subjected for rejoining.

4. Neurosurgical treatment of brain metastases from lung cancer – analysis of benefits

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Background: Brain metastases (BM) are frequent complication in lung cancer, especially non-small-cell lung cancer (NSCLC). BM are found in 10% of patients and 40% of all lung cancer will spread to the brain. The standard treatment for BM is surgery and radiation. We aimed to define incidence and demographic features of BM, early effects and complications of surgery.

Methods: Between 2007-2013, 50patients were diagnosed with BM from lung cancer and underwent surgical treatment. 45 patients underwent surgical removal, 5patients underwent tumor biopsy to achieve sample of tissue. Location was: superficial (25/51%), middle (4/8%) and deep(20/41%). We evaluated clinical presentation with Karnofsky Scale (KPS), management and outcome.

Results: Of all patients 18(36%) were women. 31 had NSCLC and 11-SCLC. The mean age was 66(49-83). 24patients had on admission<70KPS. 8 patients (16%) had early complications. Average length of stay was 7 days. 13 patients (54%) had good outcome with improvement of KPS-score.

Conclusions: The incidence of BM was higher in younger patients (<60) and males in NSCLC. Incidence of BM in NSCLC categories was highest among adenomas cell patients. Most common localization was superficial. Most patients condition improved after surgery. We can conclude that surgery in progress of treatment BM is effective and should be considered with every patient with neurological syndromes.

5. DBS-STN surgery for Parkinson's disease patients - results of 10 years experience

Magdalena Doręgowska¹, Marta Brachmańska¹, Aleksandra Myszczuk¹, Beata Rzepka¹, Mateusz Toś¹, Joanna Siuda², Stanisław Kiwiek², Monika Rudzińska -Bar²

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Introduction: Deep Brain Stimulation of subthalamic nucleus (DBS-STN) is the neurosurgical therapy for Parkinson's disease (PD) patients with inadequate symptoms control with medications.

Aim: Evaluation of the incidence of surgical and clinical complications of DBS surgery.

Materials and methods: Data of 52 PD patients (age 57,5+8,3 yrs.) who had undergone a DBS-STN surgery between 2004 and 2015 have been analyzed. All records were reviewed to identify perioperative and long-term surgical complications. Clinical outcome: cognitive status (MMSE), mobility level (UPDRS part III), L-dopa daily dose, and patients weight before and after the DBS were also assessed.

Results: Average observation time was 68 months (5-120 months). Surgery complications included: intracranial hemorrhage in 7,7% of patients, stroke and seizures in 1,09%. Hardware-related complications: wound infections and dermal fistula occurred in 8,79% and 2,29% respectively. Stimulation complications, mainly mood disorders were reported in 4,39%, and far-off clinical adverse effects, weight gain and memory impairment were present in 7,69% and 2,19% respectively. Pharmacological therapy in conjunction with DBS-STN stimulation resulted in significant improvement of patients' mobility (p=0,007).

Conclusion: DBS-STN treatment improves mobility of PD patients in long-term observation, but is connected with some risk of complications.

PLENARY LECTURE: 18.45 – 19.45

Response heterogeneity and temporal encoding in the rodent whisker system

Miguel Maravall

School of Life Sciences, University of Sussex, Brighton, UK

To make sense of the world around us, the brain must discriminate stimuli that are structured in space and time. In the tactile system, information about the identity of a stimulus is collected as a series of events (contacts, vibrations...) concatenated over time. The ability to encode individual events faithfully and precisely is central to tactile function. Work from my lab investigates principles of sensory encoding that underlie these capacities, using the rodent whisker system as a model. Neurons in the whisker system are sensitive to features of whisker motion over time; at each stage in this sensory pathway, different neurons are selective to distinct features, giving rise to rich and diverse population codes. In the whisker primary somatosensory cortex, cells selective to different stimulus dynamical features are interspersed in space. Neuronal diversity underpins a robust collective representation of texture. These findings have implications for how temporally patterned sensory stimuli are processed. To explore this, we have recently developed a novel sequence discrimination task. We have found that mice as well as humans can distinguish between stimuli that differ only in their temporal patterning. In this talk I will give an overview of our work and detail these latest findings.

April 23, 2016 (Saturday)

Neurophysiology 9.00 - 10.30 chaired by: **Karl Farrow** (Neuro-Electronics Research Flanders VIB, KU Leuven, IMEC, Belgium)

1. Dissecting neural circuits of the visual system

Karl Farrow

Neuro-Electronics Research Flanders IMEC, Leuven, Belgium

What the brain knows about the visual world is derived solely from the activity of retinal ganglion cells, the output of the retina. Retinal ganglion cells are made up of \sim 35 subtypes that each responding best to a particular feature in the visual scene and send information to at least 20 distinct destinations in the brain. To understand how visual processing in the retina influences visually guided behavior we dissect both the pre-synaptic circuitry in the retina as well as the post-synaptic circuitry in the superior colliculus. The pre-synaptic circuits of identified retinal ganglion cells are investigated to understand how neural computations, such as the computation of direction, are performed in the retina, while post-synaptic circuitry in the superior colliculus is dissected to establish causal links between specific retinal ganglion cell subtypes and visually guided orientating behaviors.

2. Impact of locomotion on population activity of visual thalamus and cortex

Cagatay Aydin¹, João Couto², Karl Farrow^{1,2}, Michele Giugliano^{3,4,5}, Vincent Bonin^{1,2}

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Neuronal processing in sensory areas is affected by the behavioral state of the animal. In the mouse visual system, locomotion modulates the activity of neurons in the primary visual cortex (V1), however it is not known how the encoding of stimulus features are influenced by locomotion. In order to study the impact of locomotion on thalamic and cortical neuronal activity, we simultaneously recorded visual responses from dorsal lateral geniculate nucleus (dLGN) and V1 using multi-site extracellular recordings in awake head-restrained mice during a linear treadmill assay. We probed visual neurons using moving gratings of various temporal and spatial contrast frequencies and found that the firing rate of dLGN cells was significantly modulated by locomotion (n=9 mice;120/300 cells; 31%; mean increase); similarly to what was observed in V1 (76/116 cells, 49%; mean increase). In addition, locomotion increased signal amplitude while the variability of neuronal responses to repeated presentations of the same stimulus decreased in both regions. These effects led to an increase in signal-to-noise ratio without affecting the preferred temporal or spatial contrast frequencies of the neurons. In order to understand if locomotion affects shared variability between pairs of neurons, we computed pairwise correlations within and across regions. Shared variability was similar within dLGN and V1, as well as across these regions. Furthermore, a large part of the observed pairwise correlations could be attributed to changes in behavioral state. Our results provide further evidence that behavioral state strongly affects thalamic responses, in particular, that locomotion shapes thalamic processing of visual inputs.

3. Vision made easy: Box jellyfish is a unique model for visual information processing

Jan Bielecki

Department of Ecology, Evolution and Marine Biology, University of California, Santa Barbara, USA

One question has always been an enigma in visual systems neuroscience: How can we extract important visual information from an otherwise complex scene, disregard redundant information, and subsequently navigate accurately through our environment? Unfortunately, we have limited understanding of the neural circuits responsible for visual information processing due to the vast neural involvement of traditional model systems such as mice, zebrafish, and even fruit flies. However, the much simpler box jellyfish visual system offers a unique opportunity to resolve sensory information processing with cellular resolution. Box jellyfish possess eight camera type lens eyes, potentially able to receive large amounts of visual information, display a variety of elaborate behaviours to navigate their cluttered mangrove habitat, yet have only around 1000 processing neurons available in their brain. The brain is contained within a transparent structure on which the eyes are also situated and is sufficiently small (about 300 μ m cubed) for continuous live cell imaging of the entire brain. This model could lead to a systems level understanding of a complete processing network in response to specific visual stimuli. In addition, long term potentiation has never been observed in the box jellyfish CNS, indicating genetic encoding of the brain connectome, which then must be assumed relatively constant between individuals. A visual sensor modeling the box jellyfish CNS will perform image analysis with very limited circuits and could bridge neural network computational neuroscience with construction of fuzzy logic systems.

4. Investigation of epileptic seizures following chronic 4-aminopyridine treatment in entorhinal cortex of rat brain slices using MEA (multi electrode array) system

Katalin Major, P.Varró, S. Borbély, A. Gáspár, I.Világi

Eötvös Loránd University (ELTE) Department of Physiology and Neurobiology, Hungary

Epilepsy is characterized by high brain excitability and generation of synchronized discharges. Epileptic seizures could be evoked by several types of convulsants. We investigated the changes in entorhinal cortex –the main initiation area of temporal lobe epilepsy - after status epilepticus evoked by 4-aminopyridine (4-AP), a potassium channel blocker. Rats were treated with the convulsant for twelve consecutive days. Brain slices containing entorhinal cortex were prepared either immediately after the treatments (acute test) or following a longer time interval (chronic test). Multi electrode array (MEA) system was used to analyze the appearance and the horizontal and laminar propagation of spontaneous discharges developed in magnesium-free solution. Firing properties were compared in slices from normal and pretreated animals and connections between the active neurons were mapped in different cortical layers. We found that seizure frequency was higher in slices from 4-AP pretreated rats than in slices from control animals, and there was a decrease in burst amplitudes. Burst lengths were more variable in slices from acute animals. We observed layer-specific increase in firing rates in treated groups.

We can conclude, that epileptic seizures, evoked by 4-AP cause acute and prolonged changes both in field potential and single unit level in the rat entorhinal cortex.

Multisensory Integration, Body Representation and Pain

9.00 - 10.30

chaired by: **Tineke van Rijn** (Radboud University Nijmegen, the Netherlands) & **Emanuel Van den Broeke** (Catholic University of Louvain, Belgium)

1. Mapping pain in a multisensory space

Valéry Legrain

Institute of Neuroscience, Université catholique de Louvain, Brussels, Belgium

It is now acknowledged that the cortical network activated by nociceptive inputs is not specifically involved in the perception of pain, but instead in cognitive functions aimed to prioritize, localize and react to stimuli that are meaningful for body homeostasis. Among these functions, spatial perception is of primary importance. Indeed, when dealing with a noxious stimulus, that is, a stimulus having the potential to inflict tissue damages, it is important to locate on the skin surface which part of the body is being damaged, and also to locate the cause of the damage in external space. This implies the ability to coordinate the perception of both the somatic space and external space (e.g. visual space). In other words, the brain must be able to integrate sensory inputs from different modalities, i.e. somatic and non-somatic, in order to build a multisensory representation of the body extending slightly from corporeal boundaries to external proximal space. While it was largely shown that the spatial perception of touch uses such peripersonal mapping frames, research about pain still focuses on the somatotopic, i.e., anatomical, representation of nociception. However, recent experiments have demonstrated close interactions between nociceptive and proximal visual stimuli, suggesting that spatiotopic and peripersonal frames of reference are also used to map nociceptive stimuli on the body surface. In turns, it was shown that the position of a limb on which a nociceptive stimulus is applied can influence the perception of external space. This highlights the multisensory aspects of the functional role of nociception.

2. Representation of potentially noxious events in the brain: quest for a pre-attentive nociceptive sensory trace

Elia Valentini

Department of Psychology and Centre for Brain Science, University of Essex, UK

The mismatch negativity (MMN) has been advocated as a tool for assessing abnormal brain function in a large number of clinical conditions, except that for chronic pain conditions. To date, as a matter of fact, there is no clear understanding of how early memory representation of nociceptive stimuli takes place in the brain. Given the current quest for objective neural markers of pain sensitivity, it is surprising that a pre-attentive electrophysiological index of brain activity associated with potentially noxious sensory events has not been investigated. In this talk, I will illustrate experimental studies showing event-related potentials (ERPs) linked to the process of deviance detection and standard formation of nociceptive stimuli as compared to other sensory stimuli. Findings from these studies converge in showing that the role of attention in a MMN paradigm is crucial to discriminate the effect of automatic change detection mechanisms from the modulatory effect of attention, particularly for nociceptive processing.

3. Body representation shapes responses to painful stimuli

Daniele Romano^{1,2}

¹ Department of Psychology - Università degli studi di Milano-Bicocca, Milan, Italy ² NeuroMi – Milan Center for Neuroscience, Italy

Both body representation and pain experience relay on complex, multisensory factors. It is known that looking at one's own body induces analgesia (visual analgesia), but the cognitive mechanism that connect body representation and pain are largely unknown. With the idea that visual analgesia is due to an interaction between ongoing information from body representation and pain experience, the working hypothesis is that manipulations of the former, should affect the latter. This hypothesis was tested measuring physiological responses (Skin Conductance Response – SCR) to pain (needle pinprick) either in patients presenting with deranged body representation, and healthy participants following experimental multisensory-induced manipulations of body representation. Three main findings can be outlined: a) anticipatory responses to incoming pain are detectable when stimuli approaches the body, entering the peripersonal space; b) sense of ownership is crucial to properly monitor noxious stimuli approaching the body; c) visual changes of body impact physiological responses to pain. This set of results provides novel experimental evidence in support of the critical influence of body representation for the mapping of sensory experience, in particular of pain.

4. Pain, empathy, and control; an ERP study

Casper van Heck, Josi Driessen, Clementina M.van Rijn & Marijtje L.A. Jongsma

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Psychopathic traits are normally distributed in the general population. Psychopathy is often associated with low capacity of empathy. In addition, psychopaths tend to experience pain differently compared to non-psychopaths. We investigate whether psychopathic traits can be linked to the neuronal responses resulting from pain and empathy related processes. Participants filled out questionnaires (IRI, SRP) to determine empathic and psychopathic traits. Painful electrical stimulation was applied with two participants in parallel. All participants were exposed to four conditions, during which participants played the roles of both 'victim' (receiving pain) and 'observer'. Both roles could be either 'active' (having control) or 'passive' (not having control). EEG of both participants was recorded. Visual-(VEP), motor- (MEP), and pain-evoked potentials (SEP) were extracted. A more negative event-related negativity in the MEP for the active observer compared to the active victim, suggestive of more perceived conflict in the active condition. The P3 amplitude of the SEP was higher for the active victim when compared to the passive victim, which is likely due to attention directed towards the painful sensation. Psychopathic traits (SRP) negatively correlated with the P3 amplitude of the active victim, which is in line with research that showed that pain is perceived as less intense in psychopaths. Stimulus relevance, attention and social context are important modulators of empathy-related neuronal responses.

PLENARY LECTURE: 10.45 – 11.45

The infancy of the human brain: brain imaging studies reveal the roots of human cognitive successes

Ghislaine Dehaene-Lambertz

Cognitive Neuroimaging Unit, INSERM, Gif/Yvette, France

Whatever the historical period and culture, humans not only succeed to learn their cultural environment but are able to invent new solutions to old and new problems. The success of our species relies on its renewed inventiveness and children are the best examples of this fast and efficient learning. Although human brain development extends over two decades, the roots of its cognitive successes are already observed during infanthood. The development of brain imaging techniques have permitted to study the human brain from birth on to look for the reasons of these successes: I propose that the strong continuity between infant and adult brain organization with notably an early involvement of frontal regions, and an heterogeneous maturation might be the key elements to obtain the best from our environment.

NeuroGlia

12.15 – 13.45 chaired by: **Antje Grosche** (Institute of Human Genetics, University of Regensburg, Germany)

1. The Müller cell - the glial all-rounder of the retina

Antje Grosche¹, Thomas Pannicke², Frank W. Pfrieger³, Michal Slezak⁴, Philip G. Haydon⁵

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Müller cells are the dominant macroglial cells in all vertebrate retinae (in vascularized mammalian retinae, additionally astrocytes reside in the nerve fiber layer). They have a characteristic radial morphology and span nearly the entire retina. Myriads of fine processes enable their intimate contact with virtually every retinal neuron, with blood vessels, the vitreous, and with the subretinal space. Based on this central position, Müller cells fulfill a plethora of supportive and modulatory functions. During the last three decades light was shed on their complex functions including the maintenance of the retinal ion and volume homeostasis or neurotransmitter recycling. To this end, they are endowed with ion channels, receptors, and transport proteins that hitherto were thought to be exclusively

expressed by neurons. My presentation aims to feature this prototypic glial cell type and update congress participants on the latest insight in their development and function, but major focus will be set on the intimate cross-talk between Müller glia and retinal neurons. The question whether glial cells are capable to release transmitters via regulated exocytosis (gliotransmission) and thereby to modulate neuronal activity is still discussed controversially. I will present direct evidence for exocytotic and non-exocytotic glutamate release from Müller cells and for its physiological relevance based on new approaches to block exocytosis in vivo and to detect glutamate release ex vivo. Moreover, I can present data demonstrating a contribution of exocytotically released glial glutamate to excitotoxic neuronal cell death in an ischemia/reperfusion model. Summarizing the newest findings about Müller glia functions in the healthy and the diseased retina, I hope that I can raise the awareness of this fascinating glial cell type and stimulate young scientists to engage in research on this glial "all-rounder".

2. Unraveling astrocyte heterogeneity using single cell transcriptomics

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Astrocytes constitute up to 20% of glial cells in the brain. They perform many important functions, including potassium homeostasis, neurotransmitter uptake, synapse formation, regulation of the blood brain barrier and CNS development. Understanding astrocyte function is also important, as all CNS pathologies involve astrocytes. Astrocytes have traditionally been studied as a homogeneous set of cells. However, recent reports suggest that astrocytes are in fact a highly heterogeneous cell population. This raises the question of whether astrocyte heterogeneity at the level of gene expression profiling, using single cell transcriptomics. Running a C1 microfluidic system, we captured individual cells from a single cell suspension of mouse hippocampus. Single cell sequencing libraries were prepared using an adapted version of the Smart-Seq2 protocol that was followed by high-throughput sequencing. Astrocytes were identified based on their co-expression of well-established marker genes. Astrocytes subtypes were then predicted using iterative clustering analyses, identifying several subclasses of astrocytes in the hippocampus. These results were verified by multiplexed in situ hybridization for selected transcripts. Our results reveal a level of astrocyte heterogeneity previously unknown in the hippocampus.

3. Metabolic remodelling during oligodendrocyte precursor cell differentiation

Ana I Amaral¹, Joana M Tavares¹, Fanny Michel¹, Ursula Sonnewald^{2,3} and Mark R Kotter¹

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³ Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen,

Copenhagen, Denmark

Oligodendrocytes wrap myelin sheaths around central nervous system (CNS) axons to facilitate the transmission of neuronal signals and to maintain axonal integrity. They derive from oligodendrocyte precursor cells (OPCs) during development, which remain in the adult brain as a self-renewing and proliferating stem/precursor cell population responsible for the repair of demyelinated areas. Despite recent studies suggesting that mature oligodendrocytes play a fundamental role supporting axons via transfer of lactate, the metabolic properties of oligodendrocyte lineage cells remain poorly understood. It is also unclear whether or not metabolic changes occur during differentiation, as it has been reported for other stem cell lineages, and what might be their role in myelination. This talk will cover recent data on the metabolic phenotypes associated with specific oligodendrocyte lineage stages and their importance for cell differentiation. Our approach combined the use of isotope-labelled glucose and mass spectrometry detection of glucose-derived metabolites with oxygen consumption measurements using the Seahorse Flux Analyser. Furthermore, we performed analysis of mitochondrial cellular distribution using imaging techniques and of parameters related to mitochondria biogenesis during differentiation. Our data suggests that a significant metabolic remodelling occurs during OPC differentiation, with an increase in glycolytic and mitochondrial metabolism as well as mitochondrial biogenesis. We propose that mitochondria could play an important role regulating other mechanisms involved in OPC differentiation. Further studies will help to understand the role of mitochondria in oligodendrocyte maturation, myelinating capacity, axonal trophic support, and CNS remyelination - a natural repair mechanism in the adult brain.

4. Neonatal hypoxic-ischemic insult alters process of gliogenesis in rat brains

Justyna Janowska, Małgorzata Ziemka-Nałęcz, Łukasz Strojek, Joanna Sypecka

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The process of gliogenesis is known to proceed most intensely during the early postnatal period. Since oligodendrocyte progenitor cells (OPCs) are very sensitive to fluctuations in the homeostasis of the nervous tissue, neonatal hypoxia-ischemia (H-I) might influence cell differentiation and their myelinogenic capability. The aim of our study therefore was to evaluate the OPC survival and differentiation after temporal H-I. The study was performed using the hippocampal organotypic slices subjected to a short glucose and oxygen deprivation (OGD) and the 7-day-old rat pups exposed to H-I conditions. Cell survival and differentiation were assessed by immunohistochemical detection with a panel of specific trackers and antibodies in organotypic slices and on brain sections. Gelatinase activity was visualized by in situ zymography. The obtained results indicate that the number of OPCs is significantly reduced both in the hippocampal slices and in the neonatal rat brains after the H-I episode. The process of oligodendrocyte differentiation seems to have been altered as well, resulting in a decreased number of cells expressing GalC and active gelatinases. In conclusion, the hypoxic insult experienced in perinatal period is likely to alter oligodendrocyte differentiation. Supported by NCN (National Science Centre, Poland) grants 2014/15/B/NZ4/01875 and 2012/05/B/NZ3/00436.

Neuroeconomics 12.15 – 13.45 chaired by: : **Barbara Fryzeł** (Jagiellonian University, Krakow, Poland)

1. Behavioral and neural basis of inequity aversion in rats

Tobias Kalenscher

Comparative Psychology, Institute of Experimental Psychology, Heinrich-Heine University Düsseldorf, Germany

Inequity aversion is a behavioral, motivational and/or emotional response to an unfair reward distribution, given equal efforts to obtain rewards. Disadvantageous inequity aversion can be caused by a reward distribution that leaves the decision-maker worse off than a partner, advantageous inequity aversion can result from a reward distribution in which the decision-maker is better off than a partner. Both types of inequity aversion have been shown in humans and non-human primates, but it remains elusive if they evolved earlier in the phylogenetic history. In my talk, I will provide evidence that rats show disadvantageous and advantageous inequity aversion. I will argue that the rats' social preferences are most likely the consequence of social reinforcement learning in which social signals emitted by the conspecifics shape the rats' preferences for equal reward outcomes. I will furthermore present data suggesting that the integrity of basolateral amygdala is necessary for developing mutual reward preferences – the presumed motive underlying advantageous inequity aversion.

2. The effect of stress on thinking and decision making

Adam Schweda

Comparative Psychology, Institute of Experimental Psychology, Heinrich-Heine University Düsseldorf, Germany

Acute stress has been found to affect a variety of cognitive domains, such as learning, memory and even perception. Given its broad impact on a wide range of signaling pathways also related to social cognition, it is reasonable to assume systematic modulation of social decision making as well. Our work attempts to capture these stress effects applying neuroeconomic paradigms. This allows us to give a nuanced picture of the underlying multitude of processes in social decisions.

3. How the perspective-taking brain turns the future self into a stranger: role of the temporoparietal junction in delay gratification

Alexander Soutschek

Department of Economics, University of Zurich, Switzerland

The ability to delay gratification is an important cornerstone of individual and societal well-being. Prevalent neural models of intertemporal decision-making focus on the role of a frontal control network in guiding impulsive choices.

However, intertemporal choices correlate also with activation in the temporo-parietal junction (TPJ), which is often ascribed a role in social cognition. This raises questions regarding the functional role of the TPJ in temporal discounting, and whether it can be reconciled with social accounts of TPJ functioning. Here, we used transcranial magnetic stimulation (TMS) to assess the role of the TPJ in intertemporal and interpersonal decision-making. Disrupting the TPJ increased discounting of delayed and shared rewards by impairing the ability to overcome the egocentricity bias of the present self. We conclude that a common neural mechanism related to egocentrity bias contributes to temporal and social discounting and that the TPJ plays a crucial role in implementing this mechanism.

4. Why we stay with our partners: Psychological and neural mechanisms of stay/leave decisionmaking

Amber Heijne

Center of Neuroeconomics (MU-CEN), Maastricht University, the Netherlands

Despite a psychological need for social connections, people often decide to terminate their social relationships. I present a functional Magnetic Resonance Imaging (fMRI) study with which we investigated the underlying mechanisms of social stay/leave decision-making. We provided behavioural, computational and neural evidence that these decisions fit within a biological framework of value-based decision-making. Moreover, we demonstrated how our brains implement a neural bias towards staying with our social partners specifically.

Interactive Session of Medical Case Reports 12.15 – 13.45 chaired by **Marcin Wnuk** (Jagiellonian University Medical College, Krakow, Poland)

1. Traumatic basal subarachnoid hemorrhage or ruptured brain aneurysm in 16-year-old boy? - case report

Rafał Skowronek^{1,} Mariusz Kobek¹, Zbigniew Jankowski², Artur Pałasz³, Ewa Zielińska-Pająk⁴, Joanna Pilch-Kowalczyk⁵

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Traumatic basal subarachnoid hemorrhage (TBSAH), represents 1.8% of all of subarachnoid hemorrhage cases diagnosed during autopsy. This report presents such a case from the current practice of the authors. 16-year-old boy was beaten by the aggressors. Suddenly he lost his consciousness and fall after he received a single blow in the neck. He was resuscitated immediately, but died at the scene. In the cranial cavity we found extensive subarachnoid hemorrhage, located mainly on brain basis, in the posterior cranial fossa and covering the subtentorial structures. During the preparation of blood vessels we noticed a slight change of morphology suggesting damaged vessel/aneurysm/vascular malformation located in the basilar artery bifurcation, which was taken to detailed microscopic evaluation using the special stainings (Verhoeff-van Gieson, Masson). Histological examination showed vital interruption of the basilar artery wall with massive extravessel bleeding, without the presence of general microscopic pathology. From the medico-legal viewpoint, to determine its traumatic background it is necessary to find the coexistence of the following circumstances: a sustained trauma, post-mortem findings consistent with a time of injury, the presence of perior vascular malformations.

2. Misleading CT findings in patients with non-convulsive status epilepticus

Patrycja Mołek, Tomasz Klepinowski, Gabriela Rusin

Jagiellonian University Neurology Students' Club, Jagiellonian University Medical College

Non-convulsive status epilepticus (NCSE) is a prolonged seizure that manifests primarily as altered mental status with no generalized motor seizures. Its clinical presentations may include: confusion, abnormal behaviour or subtle motor manifestations. Case Report: A 46-year old female was admitted to the Department of Neurology due to confusion and sudden exacerbation of chronic headache on the previous day. Past Medical History included alcoholism, alcohol withdrawal seizures and epilepsy. On neurological examination patient was conscious, drowsy, had sluggish pupillary reaction, left-inferior quadrantanopia, left arm weakness. Brain CT on admission revealed an irregular, ring-shaped contrast enhancement in right parieto-occipital area that raised suspicion of tumor. EEG showed focal NCSE derived from the enhancement area. After treatment with carbamazepine and dexamethasone patient's condition improved and NCSE was not observed in control EEG. Control CT did not show any contrast enhancement. Patient was discharged and referred to control MRI after 1 month. MRI revealed several glial scars but no tumor. Conclusion: NCSE may have multiple possible etiologies and reversible neuroimaging changes can be also observed. This case highlights that diagnosing etiology of NCSE is challenging and requires a comprehensive approach, especially when several causes of seizures are possible.

3. Recurrent myelitis with fluctuating anti-aquaporin-4 autoimmunity in the course of neuromyelitis optica spectrum disorders (NMOsd)

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Background. Neuromyelitis optica (NMO) is an inflammatory, demyelinating disease affecting the optic nerve and spinal cord. Recently, "neuromyelitis optica spectrum disorders" are considered as anti-aquaporin-4 (AQP4-IgG) seropositive patients with NMO.

Methods. The diagnosis of NMOSD is based on 6 core clinical characteristics (e.g. optic neuritis, acute myelitis), AQP4-IgG, magnetic resonance imaging (MRI), cerebrospinal fluid examination and other laboratory tests. Acute myelitis with longitudinally extensive transverse myelitis (LETM) is one of core clinical features.

Results. We present 38-years-old women with recurrent LETM and fluctuating AQP4-IgG. The disease started with sudden-onset back pain in the morning. Gradually, she manifested weakness of the lower limbs and sphincer disturbances. Neurological examination at first relapse revealed lower limbs paresis, brisk knee jerks, sensation disturbances below Th6, positive Babiński's and Chaddock's signs. MRI of thoracic vertebral column showed T2-hiperintense lesion extending from Th6 to Th8. AQP4-IgG were positive. The patient was treated with standard doses of methylprednisolone with good clinical response. Nine and nineteen months later she experienced further relapses always with reappearence of spinal cord lesions on MRI and AQP-4 seropositivity. During clinical remissions neuroimaging and AQP-4 results were normal.

Conclusion. AQP-4 autoimmunity is a marker of disease activity in NMOsd patients manifesting LETM.

4. Neuromyelitis optica and Sjogren Syndrome - pathophysiological relationship or comorbidity?

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Background: Sjogren's Syndrome(SS) is an autoimmune disease which affects exocrine glands such as salivary or lacrimal glands, and other organs including genitourinary system, muscles and nerve tissue. In turn, neuromyelitis optica (NMO) is an autoimmune condition which involves optic nerve and spinal cord.

Methods: Laboratory diagnostics of SS is based on the evaluation of antinuclear antibodies in a typical patterns SS-A and SS-B. NMO is diagnosed basing on core clinical manifestations, magnetic resonance imaging (MRI), anti-aquaporin-4 (AQP4-IgG) antibodies testing and cerebrospinal fluid investigations.

Results: We present 48-year who experienced visual disturbances in the right eye initially diagnosed as optic neuritis. After one month she presented the same dysfunction in the left eye. Then after three recurrent optic neuritis episodes the Sjogren syndrome was diagnosed. After next 39 months she manifested lower limbs paresis and paresthesias in upper limbs. MRI revealed T2-hiperintensitis between C1 and C5. AQP4-IgG seropositivity was found as well.

Conclusions: NMO core symptoms can precede Sjogren's syndrome diagnosis even or few years suggesting common pathomechanisms.

5. Fiction or reality - the image of neurological disorders in feature films and TV series

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Background: Neurological disorders are present in considerable percentage of population, yet the common knowledge about them is still not widespread. Therefore, the way they are presented in feature films and TV series plays an important role in how they are perceived by people without medical education (as suggested by Ford i Larner, 2009).

Aim: Our presentation aims at analyzing at least ten examples of neurological disorders as presented in high-budget feature films and TV series produced between 2000-2015 – such as "The Iron Lady", or "The Theory of Everything". Materials & methods: We want to focus on correctness of presenting the signs and symptoms of each disorder, which we are going to support with appropriate scientific data. We hypothesize that in a part of the analyzed films and TV series the image of neurological disorders is far from appropriate according to medical knowledge.

Conclusions: Since people with medical education are just a small percentage of the population, the analysis of popculture works seems valuable. The correct presentation of signs and symptoms of the disorders, their therapy and associated problems has a great educational value for viewers who may suffer from the disease themselves or experience it among their relatives.

Sleep & Circadian Rhythms

16.45 – 18.15 chaired by: **Etienne Challet** (Regulation of circadian clocks Team, INCI, CNRS and University of Strasbourg, France)

1. Circadian clocks, feeding and metabolism

Etienne Challet

Regulation of circadian clocks Team, Institute of Cellular and Integrative Neurosciences, CNRS and University of Strasbourg, France

The feeding-fasting rhythm is controlled by a circadian multi-oscillatory system. The master clock localized in the suprachiasmatic nucleus of the hypothalamus which controls the phase of secondary clocks, is mainly reset by light. Several secondary circadian clocks in the brain, and numerous clocks in peripheral organs, such as liver, heart and adrenal glands, are sensitive to the synchronizing effects of meal timing. Furthermore, metabolic cues can affect the master clock. Calorie restriction (i.e, when only a hypocaloric diet is given every day) alters synchronization of the suprachiasmatic clock to light, via increased light-induced phase-shifts. By contrast, high-fat diet slows down the free-running period and reduces light-induced phase-shifts. The obese (ob/ob) mice and severely diabetic (db/db) mice show differential alterations of photic synchronization. Exogenous leptin can act as chronomodulator in ob/ob mice by normalizing the phase-shifts induced by light. Chronic jet-lag in diurnal Grass rats causes not only a circadian desynchronization, but also glucose intolerance, and shortening of telomeres, a biological marker of cellular aging. In conclusion; there are reciprocal interactions between metabolism and circadian clocks, metabolic disruptions being associated with circadian disturbances. Conversely, circadian desynchronization is a potential cause for the metabolic syndrome.

2. Dissecting the role of melanopsin retinal ganglion cells in generation and modulation of infra-slow oscillatory activity in the mouse visual system

Patrycja Orlowska-Feuer¹, Annette E. Allen², Timothy M. Brown², Riccardo Storchi², Hanna J. Szkudlarek¹, Marian H. Lewandowski¹, Robert J. Lucas²

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Besides light sensitivity, some neurons in the subcortical visual system exhibit infra-slow oscillatory activity characterized by alternating changes in firing rates lasting minutes. The activity was suggested to participate in classic and non-image forming vision, as it is strongly modulated by light. Rat studies revealed that oscillations in the olivary pretectal nucleus (OPN) depend on contralateral retinal output and are modulated by all class of photoreceptors. We set out to investigate whether a lack of melanopsin or rods and cones will affect the rhythm generation in genetically modified mice lacking particular types of photoreceptors. Two structures were analyzed: the OPN and the lateral geniculate nucleus (LGN) by means of multi-electrode in vivo recordings. Oscillatory neurons constituted 30% of all recorded cells and their period lasted 4 minutes. Importantly, the presence of functional photoreceptors was not required to observe infra-slow rhythm. Although the percentage and period length of oscillatory neurons were very similar between structures and genotypes, the major differences occurred in melanopsin knockout mice, were oscillations were the fastest and the least frequent. This is the first study to show the existence of infra-slow oscillatory activity in the mouse visual system and to characterize its retinal origin.

3. The dorsal lateral geniculate nucleus of the thalamus responses to light are modulated by sleep-like states – in vivo electrophysiological study on urethane-anesthetized rat

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The dorsal lateral geniculate nucleus (dLGN) of the thalamus is a gateway station for the visual information transmission between retinal photoreceptors: rods, cones, melanopsin retinal ganglion cells and the cerebral cortex. Activity of the dLGN neurons is strongly modulated by the brain state, visible as activation/deactivation changes in the EEG signal. Mice studies have shown three types of light-induced responses in the dLGN: sustained, transient ON and OFF, where only sustained (melanopsin-derived) neurons encoded increases in the irradiance. We set up to verify, weather sleep-like stages occurring in urethane-anaesthetized rats influence light responses in the LGN. We performed single-unit in vivo experiments combined with light stimulations and EEG recordings. As in mice, we also recorded sustained, transient ON and OFF cells and only sustained neurons tracked changes in the light intensity. The EEG modulation of light responses were observed in 48% of cells and the most frequently only the strength of light responses (n=6) were influenced. The remaining neurons either didn't respond to light stimulation during deactivated phase of urethane sleep (n=3) or had altered type of response (n=4). Our result suggest that light sensitive neurons within dLGN transmit visual information in a state-dependent manner, which depends on either cortical or brainstem activity. Supported by 2013/08/W/N23/00700.

4. Synchrony is the key: jet lag consequences in epileptic rats

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Negative consequences of jet lag such as sleep disturbances, decreased alertness and performance result from internal desynchronization between different circadian rhythms. In WAG/Rij rats, a validated animal model of childhood absence epilepsy, internal desynchronization facilitates epileptic activity manifested as an increased number and mean duration of spike-wave discharges (SWDs). Given a close relationship between SWDs and vigilance, we aimed to determine factors responsible for a seizure rise and to reveal potential coupling between sleep-wake rhythms and SWDs after a light phase delay imitating a westward flight across 8 time zones. Simultaneous EEG and EMG recordings in WAG/Rij rats performed during baseline, an 8 h phase shift and 10 consecutive post-shift days revealed significant differences in shift magnitude and subsequent re-synchronization of different sleep-wake rhythms and SWDs. Changes in the rhythms phase-relationship and different speed of re-synchronization point to internal desynchronization. Coupling between SWDs and light slow-wave sleep, and between active wakefulness and deep slow-wave sleep suggests a common circadian mechanisms governing these pairs of rhythms. The post-shift increase in the number of SWDs of absences, a result of increased passive wakefulness and reduced deep slow-wave sleep, may be of significant importance for people with epilepsy planning a long trans-meridian flight.

Rehabilitation After Acquired Brain-Injury

16.45 – 18.15 chaired by: **Luciano Fasotti** (Radboud University Nijmegen, the Netherlands)

1. Cognitive and Graded Activity Training for persistent fatigue after Stroke: A randomized controlled trial

Luciano Fasotti

Donders Institute for Brain, Cognition and Behaviour, Nijmegen, the Netherlands & Klimmendaal Rehabilitation Centre, Arnhem, the Netherlands

Fatigue is a common and persistent consequence of stroke and to date no evidence-based treatments were available to alleviate fatigue. We developed a new treatment combining cognitive therapy (CO) and graded activity training (GRAT) to reduce fatigue related symptoms in stroke patients. A randomized, controlled, assessor-blind clinical trial was conducted in 8 Dutch rehabilitation centers to compare the effectiveness of COGRAT with a CO intervention only. The results show that both treatments produce significant benefits on fatigue and other secondary outcomes. However, the number of individuals showing significant levels of clinical improvement in the COGRAT group exceeds those in the CO only group.

2. A randomized controlled trial of errorless Goal Management Training in persons with brain injury

Dirk Bertens

Donders Institute for Brain, Cognition and Behaviour, Nijmegen, the Netherlands & Pro Persona, Thalamus section, Wolfheze (Arnhem), the Netherlands

Both errorless learning (EL) and Goal Management Training (GMT) have been shown to be effective rehabilitation methods aimed at optimizing the execution of complex everyday tasks after brain injury. We examined whether a combination of EL and GMT is superior to traditional GMT for training such tasks in brain-injured patients with executive problems. This assessor-blinded randomized controlled trial was conducted in 67 chronic patients with executive impairments, referred for outpatient rehabilitation. Individually selected everyday tasks were trained using 8 sessions of an experimental combination of EL and GMT or via conventional GMT, which follows a trial-and-error approach. This study is the first to show that preventing the occurrence of errors during executive strategy training enhances the acquisition of complex everyday activities in brain-injured patients.

3. Monitoring the auditory textures processing in human cortex to distinguish states of consciousness

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Background: Reliable distinction between patients with disorders of consciousness (DOC) i.e. minimally conscious (MCS) and vegetative state (VS) requires measurements that directly assess their cortical state e.g. in reaction to stimuli. The principal objective here was to present complex acoustic textures and analyse how the neural integration of those complex sounds differs in conscious and unconscious subjects.

Methods: We performed EEG recordings from 15 healthy controls in two stages: wakefulness and deep NREM sleep and from 10 patients in various DOC states (CRS-R-based diagnosis) to assess their brain's response to a change in stimulus statistics. These stimuli reflect natural sounds and changed their statistics at a randomized time.

Results: Detection of the change in statistics requires an internal model of these statistics. We found that the integration of its evidence occurs in parietal and prefrontal areas, and only under awake conditions. EEG responses in MCS group could readily be distinguished from those in VS patients, although the response to the change in statistics was less indicative of parameters of the stimulus.

Conclusions: Our results suggest that the processing of statistical stimuli varies with the state of consciousness, thus allowing a discrimination of the consciousness level in noncommunicative patients.

4. Resting state EEG during recovery to consciousness

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Recovery after coma goes through different states of consciousness. First patients enter into the vegetative state/unresponsive wakefulness syndrome (VS/UWS): they wake up without any signs of awareness of self or of the environment. With recovery to the minimally conscious state (MCS), they demonstrate minimal but definite behavioural evidence of self and environmental awareness. Currently, resting state brain activity has been a topic of interest since it is not dependent of any reactivity to external stimuli, and could be indicative for 'stimulus independent thoughts' and 'mind-wandering'. Changes in resting state brain activity during recovery to consciousness were described every two weeks in 12 initially unconscious patients (aged 4-25), over a period of 3.5 months. Patients were also behaviourally scored on level of consciousness by using the Post-Acute Level Of Consciousness scale. Brain activity was compared to a healthy norm group. The EEG of UWS patients was characterized by a high amount of slow activity and specifically the ratio of Alpha/Delta power increased with recovery to consciousness and reaching MCS they started to resemble values of the norm group. It is currently investigated whether the resting state EEG and its changes over time might be usefull as predictor for recovery from UWS.

Psychophysiology of Higher Cognitive Functions

16.45 – 18.15 chaired by: **Tytus Sosnowski** (University of Warsaw, Poland)

1. Patterns of brain and cardiovascular activation

Tytus Sosnowski¹, Małgorzata Wordecha¹, Anna Kępkowicz¹, Adrianna Majewska¹, Aleksandra Pstrągowska², Andrzej Rynkiewicz¹, Tomasz Oleksy¹, Marek Wypych³, Artur Marchewka³

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Our previous research showed that mental tasks that involve rule application (RA tasks), e.g. performing arithmetic operations, cause grater tonic increase in cardiovascular activity than tasks requiring rule discovery (RD tasks), e.g. logical completion of a series of digits. However, it was not clear what brain mechanism was responsible for this difference. The aim of two studies was to compare patterns of brain and cardiovascular activity while solving the two kinds of tasks, matched for their duration, level of difficulty, and amount of incentive. The cardiovascular study (N=16) showed larger increase in HR, SBP, DBP, and MAP during solving the RA than the RD tasks. On the other side, the fMRI study (N=18) revealed larger brain activation during solving the RD than the RA tasks. Especially, the RD tasks caused larger increase in activity of superior, middle and inferior frontal gyrus, medial frontal gyrus, middle temporal gyrus, and cingulate cortex. The results support the hypothesis that the two tasks involve different modes of information processing. If we assume that cardiovascular changes during mental task solving are indices of motivational arousal, the obtained results suggest that RA tasks and RD tasks evoke qualitatively different motivational processes.

2. Heart-coded. Heart rate variability as a psychophysiological marker of cognitive performance and psychological functioning – an EEG-ECG study

Ewa Ratajczak^{1,2}, Jakub Wojciechowski^{2,3}, Julita Fojutowska^{2,3}, Piotr Szczęsny², Jan Szczypiński^{2,3}

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Heart rate variability (HRV) reflects the interplay between the sympathetic and parasympathetic branches of autonomic nervous system. High HRV parallels healthy psychophysiological states, while low HRV is usually associated with stress, negative emotions and poor health, reflected in both somatic and mental disorders. Moreover, HRV appears to be related to executive functioning and cognitive performance. In our study 28 young adults underwent psychometric testing of fluid intelligence, temperament, anxiety and affect. EEG and ECG signal was collected during resting-state, as well as during the following performance of cognitive tasks involving divergent thinking and attentional processes. Complexity of bioelectrical activity was calculated using Higuchi\'s Fractal Dimension (HFD). HRV indices were calculated including standard time- and frequency-domain methods, as well as the non-linear approach (entropy measures). The relationship between HRV indices and HFD values during resting-state and task conditions, measures of cognitive performance and results of psychometric questionnaires were investigated. As expected, lower HRV was related to higher state anxiety. More interestingly, resting HRV seems to be related to temperamental traits (eg. activity, persistence), as well as to brain function complexity in fronto-central regions both during resting-state and task condition. The general picture emerging from the study is discussed.

3. Crucial role of right frontopolar cortex in directed exploration

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Effective adaptation in a dynamic and ever-changing environment requires optimizing the balance between exploiting well known options and exploring new ones. Recent behavioral evidence suggests that people use at least two distinct strategies while exploring the environment: directed and random exploration (Wilson et al, 2014). Directed exploration is driven by uncertainty and the need of obtaining essential information about the less known option

while random exploration is driven by mechanisms related to behavioral variability. However, it has not yet been shown that these two types of behaviors have separate neural origins. In this study we present first causal evidence of the involvement of right frontopolar cortex (RFPC) in directed exploration. We designed a within-subject experiment using continuous theta bursts TMS protocol and a modified, sequential version of the Horizon Task (Wilson et al, 2014). We examined 16 participants in two conditions: vertex (control) and RFPC stimulation (experimental). Inhibiting the RFPC significantly reduced directed exploration while not affecting random exploratory behaviors nor ambiguity preference. This finding establishes the uniquely human role RPFC plays in exploration and inspires the creation of more detailed, mechanistic models of higher cognitive functions.

4. Brain activations related to saccadic reaction time and response conflict

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Establishing a role of the dorsal medial frontal cortex in the performance monitoring and cognitive control has been a challenge to neuroscientists for the past decade. In light of recent findings, the conflict monitoring hypothesis has been elaborated to an action-outcome predictor theory. One of the findings that led to this re-evaluation was the fMRI study in which conflict-related brain activity was investigated in terms of the so-called time on task effect, i.e., a linear increase of the BOLD signal with longer reaction times. The aim of this study was to investigate brain regions involved in the processing of saccadic response conflict and to account for the time on task effect. A modified spatial cueing task was implemented in the event-related fMRI study with oculomotor responses. The results revealed several brain regions which show higher activity for incongruent trials in comparison to the congruent ones, including presupplementary motor area together with the lateral frontal and parietal regions. Further analysis accounting for the effect of response time provided evidence that these brain activations were not sensitive to time on task but reflected purely the congruency effect.

5. Functional network reconfiguration related to increasing cognitive effort

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The vast majority of functional connectivity MRI (fcMRI) studies investigated brain network organization at rest. Changes of the functional network topology during cognitive tasks in relation to behavioral outcomes remain unclear. The aim of our study was to determine cognitive effort-dependent changes in complex network organization (global efficiency, local efficiency and modularity) using graph theoretical framework and its relation to behavioral performance. Participants (N=35) were scanned using 3 Tesla fMRI scanner while performing a letter n-back task. Pairwise connectivity values were calculated for structural (90 nodes) and functional (264 nodes) parcellation schemes. We found an increase of global efficiency and a decrease of both local efficiency and modularity with an increase of cognitive effort. Modules of default mode network, cingulo-opercular network and visual network contributed mostly to this change. Moreover, the difference in the whole-brain modularity was associated with the behavioral performance. Our findings provide strong evidence for global workspace theory by demonstrating a shift from locally segregated to distributed network organization related to increasing cognitive effort. These results also highlight the potential for explaining behavior by studying graph theoretical properties using the task-based data. This study was supported by a grant (2015/17/N/HS6/03549) from the National Science Center, Poland.

PLENARY LECTURE: 18.30 – 19.30

Re-imagining vision following the discovery of new photoreceptors

Robert Lucas

Faculty of Life Sciences, University of Manchester, UK

Although most text books still tell us that the mammalian retina only contains two sorts of photoreceptor (rods and cones), we have actually known for >10 years that this is not the case. Rather, a subset of the retina's output neurones, retinal ganglion cells, are capable of acting as autonomous photoreceptors thanks to their expression of a photopigment called melanopsin. I will provide an overview of how melanopsin photoreceptors work, what we use them for, and how their discovery has changed our understanding of how the retina encodes the visual scene. I will

also describe the practical applications of this knowledge, how it is already changing the world around us and what might happen in future.

April 24, 2016 (Sunday)

PLENARY LECTURE: 9.30 – 10.30

Stress and emotional arousal effects on memory

Benno Roozendaal

Dept. Cognitive Neuroscience, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, the Netherlands

Stressful or emotionally arousing experiences are typically well remembered. In my presentation, I will describe findings from animal experiments indicating that stress hormones (epinephrine and glucocorticoids) released from the adrenal glands are crucially involved in enhancing the consolidation of memory of emotionally arousing life experiences. In contrast, these stress hormones impair the retrieval of memory processing. Stress hormones do not uniformly modulate memory of all kinds of information but, rather, preferentially influence the consolidation and retrieval of memory of emotionally arousing information or during emotionally arousing test situations. These findings fit well with extensive evidence from our laboratory indicating that emotional arousal-induced noradrenergic activation within the basolateral complex of the amygdala (BLA) is critically involved in mediating such stress hormone effects on memory consolidation and memory retrieval. In turn, BLA activation regulates neural plasticity and information storage processes via its efferent projections to many other brain regions. Such arousal-induced BLA activation not only influences the strength of memory but also has important consequences for on how accurate we can remember past events.

Neuropsychiatry

11.00 – 12.30 chaired by: **Ingo Willuhn** (The Institute for Neuroscience, Institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, the Netherlands)

1. Striatal dopamine dynamics during flexible behavior and compulsive actions

Ingo Willuhn

Academic Medical Center, Department of Psychiatry

The Institute for Neuroscience, Institute of the Royal Netherlands Academy of Arts and Sciences, Amsterdam, the Netherlands

The basal ganglia provide brain structure for the selection of motivated actions. Dopamine neurotransmission in the striatum, the main input nucleus of the basal ganglia, is central to regulating such actions. The striatum has multiple functional units, where the limbic region is thought to mediate motivational aspects of actions and the sensorimotor region their automation. Recent findings of my group and others show that contrary to the assumption of a uniform dopamine signal throughout the brain, dopamine release is in fact region-specific. In this talk, I will present studies that utilized electrochemistry in freely-moving rats to investigate the role of regional differences in dopamine release in the regulation of behavior. Our findings identify signals that are governed by a striatal hierarchy and indicate that individual differences of such regional coordination can lead to inflexible and compulsive execution of motivated actions. The results will be discussed in light of relevant functional anatomy, the putative role of regional dopamine in behavioral flexibility and compulsivity, and potential clinical relevance.

2. Investigating affective biases in Sprague Dawley rats using hormonal manipulations

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Changes of circulating hormone levels are known to influence emotional processing. It also has been observed that pharmacological and social manipulations of the emotional states modulate affective biases in rats. In the present study, we have investigated t1he effects of hormonal manipulations on affective biases in rats using the Affective Bias Test. Male Sprague Dawley rats were trained in this bowl digging task, that involves repeated pairing of a rewarding outcome (obtaining a food reward) with a neutral stimulus (specific digging substrate) under control conditions or following a hormonal manipulation. The affective bias is quantified using a preference test where both previously rewarded substrates are presented together over 30 randomly reinforced trials. Animals were tested using acute treatment with gonadal hormones (oestradiol, progesterone, testosterone), androgen receptors antagonist (flutamide), aromatase inhibitor (formestane), and oxytocin and vasopressin analogues (carbetocin and desmopressin, respectively). Treatment with oestradiol, flutamide and carbetocin induced positive affective bias, while progesterone, testosterone and formestane resulted in negative affective bias in rats. Desmopressin treatment showed no significant effect in rats. For the first time we demonstrated that hormones alter formation of the affective biases. JKP was supported by UoB Studentship, and also MRC and BBSRC project grants awarded to ESJR.

3. Regulation of gene transcription in response to depressive-like behavior induced by morphine abstinence

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Major depression is one of the most frequent neuropsychiatric comorbidities associated with opioid addiction. The association between morphine withdrawal and depressive-like symptoms is well documented, however, the molecular mechanism underlying opiate withdrawal-induced depression remains unclear. We used a mouse model of repeated morphine administration to examine the molecular mechanisms that contribute to withdrawal induced depressive-like behaviors. C57BL/6J mice were injected twice a day for 3 weeks with morphine (increasing doses, 20-100 mg/kg), dexamethasone (4 mg/kg i.p.) or saline (10 ml/kg). To evaluate depressive-like behavior, three different tests were conducted: tail suspension test, light/dark box and social interaction test. We used real-time PCR and next-generation sequencing to comprehensively map transcription in the hippocampus and nucleus accumbens. Both morphine and dexamethasone- treated mice exhibited a variety of depression-like behaviors, which were accompanied by an increased expression of GR-dependent genes in the hippocampus and nucleus accumbens. The present study extends previous findings by showing that prolonged opioid withdrawal-induced depressive-like behaviors are regulated by stress related genes, and shed light on the few genes as potential therapeutic agents for the treatment of depressive-like behaviors induced by opiate withdrawal.

4. Imipramine treatment partially reverses the effects of maternal separation stress on synaptic modification range in the rat lateral amygdale

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Maternal separation (MS) of rat pups has been shown to induce persistent alterations in brain functions. We have previously shown that in the cortical input (CoI) to the lateral amygdala (LA) MS has shifted the potential for bidirectional synaptic modification towards LTD, but it shrank the synaptic modification range in the thalamic input (ThI) to the LA. Here we studied whether the effects of MS on the LA could be reversed by imipramine (IMI) treatment. Rats previously subjected to MS were administered IMI for 14 days. Control rats received saline. Saturating levels of LTP or LTD were induced by electrical stimulation in brain slices containing the LA. Both LTP and LTD were reduced in ThI in slices obtained from MS subjected rats receiving saline when compared to controls. In slices prepared from MS subjected rats receiving IMI the magnitude of LTP and LTD was similar to controls, but the magnitude of LTP in slices prepared from stressed rats administered IMI was still smaller, when compared to controls. Treatment with IMI fully reversed the effects of MS in ThI. In CoI the reversal was only partial. Support: National Science Center, Poland, grant no. 2011/03/N/NZ4/02176.

1. Are early ERP components the result of a phase reset of ongoing pre-stimulus oscillations?

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Many researchers derive event-related potentials (ERPs) from the electroencephalogram (EEG) as specific ERP components are thought to be related to specific cognitive processes. For example, the early visual N1 component has been related to stimulus discrimination. Nevertheless, several scientists have proposed that ERPs may actually be the result of a phase reset of various ongoing oscillations. As ongoing oscillations are mostly related to the state of an individual, one could therefore even argue that observed effects on early ERP components reflect state differences rather than processing differences. EEG data of 123 individuals that took part in a go/nogo face recognition task were analyzed to examine whether individual differences in pre-stimulus baseline oscillations largely explained individual differences in early ERP components was examined. Despite the fact that early ERP components may very well be described as the sum of various stimulus-evoked oscillations, individual differences in stimulus-evoked oscillations were only to a moderate extent related to pre-stimulus baseline oscillations. These findings question the idea that ERPs are solely due to a phase-reset of ongoing oscillations, and suggest that ERP components are processing-related rather than state-related electrophysiological markers.

2. Loss of inner awareness is related to hyper-correlated brain activity

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Introduction: Consciousness is identified with presence of both, overt responsiveness to external stimuli and covert inner awareness. Yet, during REM sleep or ketamine sedation a vivid "stream of consciousness" can be experienced despite lack of responsiveness. Here we aimed to identify neural correlates of subjective inner awareness by studying brain functional interactions in a range of anaesthesia and sleep states.

Methods: Data from two independent experiments were analysed: i) anaesthesia experiment where ECoG data were recorded from macaque monkeys sedated with different anaesthetic agents; ii) sleep experiment where depth-electrodes recordings were acquired from 10 epilepsy patients. Correlation coefficient between envelopes of five classic frequency-bands was calculated as a measure of functional interactions.

Results: The beta-band activity became hyper-correlated (more correlations and less anti-correlations) during propofol-induced loss of awareness, but not during ketamine sedation and wakefulness. In the sleep experiment hyper-correlated alpha-band activity was observed during slow-wave sleep, but not during REM sleep and wakefulness.

Conclusions: The subjective "stream of consciousness" is maintained when brain activations are relatively independent from each other, but when brain signals become hyper-correlated the inner awareness is lost. The present approach is potentially promising in the context of diagnosing consciousness in unresponsive patients.

3. Normalization of Abnormal Frontal Lateralization in ADHD via Deep TMS

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Attention deficit/hyperactivity disorder (ADHD) is associated with abnormal frontal hemispheric lateralization. ADHD patients show reduced ability to suppress default network (DMN) activity during task performance, leading to attentional deficits. Rest frontal theta-power is inversely related to DMN activity. The current study examined the effect of deep transcranial magnetic stimulation (dTMS) treatment on ADHD symptoms and on frontal lateralization. ADHD patients received 15 sessions of repetitive high-frequency dTMS (n=15), figure-8 (n=10) or sham (n=13) treatment to the right frontal cortex. A healthy control group (n=47) did not undergo treatment. Rest electroencephalogram was recorded before and after treatment. Lateralization was calculated for a frontal region of interest. Before treatment, total power was more right-lateralized for controls vs. ADHD patients. Treatment led to symptoms alleviation only in the dTMS group. In this group, abnormal theta-band left-lateralization was found only in patients who responded to treatment, and was abolished following treatment. Symptoms alleviation after treatment was correlated with theta left-lateralization before treatment, and with its reduction following treatment. Results indicate that: (1) ADHD is characterized by deficient right-lateralization during rest; and (2) ADHD dTMS treatment effectiveness is correlated with abolishment of abnormal frontal theta-band left-lateralization, which may stem from normalization of DMN activity.

4. Resting state brain networks predict the characteristics of visual evoked potentials

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In this study, we aimed to determine the effect of the resting state networks to visual event related potentials (ERPs). Several neurological disorders, mental diseases, or psychological abilities have characterized by both altered ERP components and resting state functional connectivity patterns, but the relationship between these two distinct predictors haven't been investigated yet. The EEG data of 22 subjects were recorded by 61 channels. ERPs latency and amplitude were determined. The functional connectivity values between all pairs of electrodes were calculated from a 5 minutes eyes open resting state section. Network-based statistics were applied to determine the resting state functional subnetwork correlations with the latency and amplitude of ERP components. Theta, alpha (fronto-central network) and beta band (left central network) phase synchronization indicated shorter latency for the ERP components. Higher synchronization at the theta band (occipito-parietal network) and beta band (left parietal network) corresponded to higher amplitude. Our results suggest that highly synchronized, distinct resting state subnetworks can facilitate both the processing speed and neuronal responsiveness for an incoming visual stimulus.

5. Electrophysiological correlates of visual search asymmetry; a visual mismatch negativity study

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We investigated the automatic part of the cognitive process underlying visual search (VS) with visual mismatch negativity (vMMN) component. VMMN is an electrophysiological index of automatic change detection. VMMN is elicited by infrequent (deviant) changes embedded in stimulus sequence of repetitive (standard) stimuli. The performance of the VS is primarily defined by the target-distracter differences. Search asymmetry is when the performance of VS tremendously changes by the reversion of the target-distracter relation. We investigated two robust VS asymmetry phenomenon: VS is faster when the target contains an additional feature by comparing with the lack of the same feature; similarly, VS is faster, when the distracters are familiar (in contrast with non-familiar) stimuli. In the first study, standards and deviants were either patterns of circle with or without an additional line. VMMN was elicited by both deviants; however, when the changes were the appearance of an additional feature, the vMMN was earlier (deviant-target analogy). In the second study, standards and deviants were either patterns of (familiar) N or (non-familiar) I stimuli. We registered earlier vMMN when the standards were the familiar N letters (standard-distracter analogy). The results support the existence of automatic sub-processes in the complex cognitive mechanism underlying VS.

1. The study of defense behaviors as alarm cues

Marta Moita

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Living in a group has an adaptive value for a number of reasons. In the lab we focus on social interactions in different contexts, namely when individuals perceive a threat or when they are foraging for food. The neural mechanisms by which animals use social information to detect impending danger are largely unknown. In this talk I will focus on our experiments aimed at understanding how animals use defense behaviors of con-specifics as alarm cues. In particular I will discuss our findings showing that rats use freezing as an alarm cue, which is sensed through a sudden cessation of movement-evoked sound. Using optogenectis we found that the lateral amygdala and the MGd, a subdivision of the auditory thalamus, are required for rats to freeze in response to silence onset. In addition, there is evidence that prior experiments under way in our lab that suggest that it is the association between freezing and shock that promotes observational fear suggesting that learning from self-experience with an aversive event is important for rats to respond to freezing displayed by others.

2. Neural circuits underlying emotional contagion

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Human empathy emerges over phylogeny from various behavioral precursors. One of the simplest is emotional contagion, i.e. sharing emotional states between individuals, which can be modelled in rodents. In our model of socially transferred fear we showed that a brief social interaction with a fearful cage mate (demonstrator) promotes aversive learning in an otherwise naïve rat (observer) and activates the amygdala of the observers, especially its central part (CeA). To elucidate the role of neuronal circuits in the central amygdala of the observers, we used two methods of functional mapping: transgenic rats expressing in behaviorally activated neurons a PSD-95:Venus fusion protein and injected with anterograde tracer and a combination of retrograde tracing with c-Fos ISH. We discovered strong activation especially in the periaqueductal gray (PAG) and dorsal raphe nuclei (DRN), structures receiving dense projections from the CeA and implicated in fear and anxiety disorders. Moreover, using optogenetics, we showed that specific activation of CeA neurons involved in socially transferred fear results in increased anxiety. These findings suggest that there exists a group of neurons in the CeA that is involved in integrating information about a threat, activated during socially transferred fear and subsequently recruited by learning of fear responses.

3. Closed-loop control of hippocampal memory processing in freely behaving rats

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The formation and retrieval of new memories is supported by a complex dialogue among different brain structures coordinated by the hippocampus. Hippocampal neurons have two characteristic features of a memory system: (1) they display experience-specific firing patterns (e.g. position-specific firing of 'place' cells) during active states, (2) they sequentially reactivate the same experience-specific firing patterns during sleep and restorative wakefulness. In the rodent brain, sequential recapitulations of experience (termed 'replays') occur in bouts of 80-400 ms of milliseconds. Hippocampal replays are thought to support formation and retrieval of salient memories but no direct evidence linking replay content (trajectories of an explored environment) and memory-guided behavior exists. In order to bridge this gap, we developed a hardware-software architecture that implements a brain-computer interface (BCI) for content-specific closed-loop manipulation of replay events in freely behaving rats. Here we show how neural activity from a large population of neurons is used by our BCI to identify replay of different contents within a short latency (40-60 ms) and how we interrupt such events with electrical stimulation in a closed-loop fashion.

4. Studying ultrastructure of stimulated synapses with 3D electron microscopy

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Investigating the structural changes in neurons allows to better understand the processes of neuronal plasticity. One of the models in which those changes can be studied is the chemically induced long-term potentiation (cLTP) model. Ultrastructural features such as the shapes of postsynaptic densities or the presence of spine apparatuses can only be studied with electron microscopy (EM). Serial block-face scanning EM (SBEM) is a novel technique that allows obtaining of 3D ultrastructural data of high quality. In this work have prepared the CA1 regions of organotypic slice cultures (OHCs) for visualization with SBEM according to a protocol modified by our group. Two weeks old OHCs were assigned to either control (n = 4, DMSO) or cLTP (n = 4, forscolin 50 μ M, picrotoxin 50 μ M, rolipram 100 nM in DMSO) group. 30 min after the stimulation slices were fixed and processed for SBEM visualisation. Ultrastructural analysis revealed, among others, significant increases of the number of dendritic spines containing spine apparatuses and of the number of perforated synapses in the cLTP group. Overall, we report a successful adaptation of SBEM method for organotypic hippocampal slice culture and show the ultrastructural changes of dendritic spines and related structures upon chemical stimulation.

Neural Correlates of Motor Activity

14.30 - 16.00

chaired by: Emilia Zabielska-Mendyk (John Paul II Catholic University of Lublin, Poland)

1. The temporal involvement of the left Supramarginal Gyrus in planning functional grasps

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The brain mechanisms underlying tool use are highly lateralized to the left cerebral hemisphere. The present study aimed to highlight the temporal contribution of one of the critical nodes of this left-lateralized network to planning functional grasps of tools. We focused on the left supramarginal gyrus (SMG), whose role - as evidenced by functional magnetic resonance imaging (fMRI) studies - is critical in tool use actions. Repetitive transcranial magnetic stimulation (rTMS) was used to transiently interfere with the function of left SMG in 3 different time points. This was done to impair participants' abilities to perform the task. The stimuli were high resolution pictures of tools and non-tools displayed on the screen. A control site (Vertex) was stimulated to rule out differential contribution of this area to planning functional grasps. rTMS over left SMG selectively affected task performance when the pulses were delivered at stimulus onset triggering the planning phase. This disruptive temporal specific effect was evident neither when the pulses were delivered at later time points, nor to the Vertex. These findings indicate that neuromodulation is a valuable tool to decipher the temporal nature and critical role played by the brain areas involved in tool use behaviors.

2. Diminished somatosensory perception of the affected hand in children with unilateral Cerebral Palsy – an Event-Related Potential study

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Apart from hemiplegia, children with unilateral Cerebral Palsy (uCP) might also suffer from a decreased sense of touch, an important sense with respect to motor control. Our main aim was to study if somatosensory perception was indeed diminished with respect to the affected hand (AH) compared to the less-affected hand (LAH). In addition, we determined if there was a relation between a decreased somatosensory response and a diminished hand capacity. Somatosensory Event Related Potentials (SSERPs) were recorded from the ongoing EEG in 27 children with uCP (aged 8-23). Stimuli consisted of short vibrations of 167 Hz with a 100 ms duration. SSERPs were captured after stimulation of both the AH and LAH. Each hand received 80 stimuli. SSERPs contained a clear P2 (100-120), N2 (190-220), P3 (280-320), and N4 (410-440) component. We found that the P2 component was diminished after stimulation of the

LAH over the contralateral hemisphere (F(1,26)=4.45; p=.045). However, regression analyses between the amount of P2 suppression and hand capacity did not show a relation between these two deficits. Possibly, children with uCP rely on different modalities for motor control (eg visual information) to compensate for the diminished somatosensory and/or proprioceptive perception of the affected hand.

3. Are mirror movements in children with unilateral cerebral palsy related to secondary degeneration of the posterior part of the corpus callosum?

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Some children with unilateral Cerebral Palsy (uCP) demonstrate a prolonged retention of mirror movements (MM) compared to typically developing children. Previous research has suggested that secondary degeneration of transcallosal axonal colaterales innervating the posterior body of the corpus callosum (CC) might cause these MMs due to reduced collateral inhibition between the motor cortices. This pilot study attempts to investigate this relationship. It is hypothesized that children with uCP and relative thinning of the posterior CC will show enhanced MMs. Twelve children with uCP were included. A repetitive unimanual squeezing task was used to determine the amount of MMs. This was done by cross-correlating the force pattern between hands while either the more affected hand (AH) or the less AH was actively squeezing. The ratio between the posterior and anterior CC was estimated from T1-weightedMRI-scans. Pearson's correlations revealed a trend between the CC-ratio and MM appearing in the more AH when the less AH was actively moving (R2=0.209, p=0.058). No relation was found for MM appearing in the less AH. MMs in the AH may partly be explained by hypogenesis of the posterior CC. A possible alternative underlying factor for MMs may be retention of ipsilateral corticospinal projections during development.

4. Connectivity of the primary motor cortex in bilateral upper limb congenitally amputated patients: a DTI study

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The aim of this study was to test the hypothesis if patients with bilateral upper limb congenital amputation have significant lower number of white matter fiber connections than healthy control subjects. Diffusion weighted images were obtained at 3T in 2 patients with bilateral upper limb congenital amputation and 8 healthy subjects. From the acquired diffusion data images, tract-based spatial statistics (TBSS) and probabilistic tractography (ProbTrackx) were done. ProbTrackx gave the approximate numbers of white matter fiber tracks in certain regions of interest (ROIs), between primary motor cortex (M1) and: supplementary motor area (SMA), premotor cortex (PM), primary sensory cortex (S1), independently for both hemispheres. Results of TBSS showed that patients had lower fractional anisothropy values than control group for: genu of corpus callosum, anterior corona radiata, cingulate gyrus, forceps minor and anterior thalamic radiation. Results of ProbTrackx showed less white matter fiber connections in patient group at ROIs, except for connections between M1-SMA, which were greater. This observation can be explained by adaptive changes of white matter fiber connections of the M1 and abnormalities in callosal connectivity due to congenital upper limb deficiency. This work was supported by grant National Science Centre, Republic of Poland DEC-2011/03/B/NZ7/00588.

5. Decrease of total power of the EEG after motor imagery training in patient with bilateral upper limb congenital transverse deficiency

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The aim of the study was to assess the electroencephalogram (EEG) power measurement related to motor imagery of reaching (MIR) before and after 12-weeks of the motor imagery training (MIT) in a congenitally amputated patient

and healthy, control subject. The 128-channels EEG data were collected during MIR of right hand before and after 12weeks of MIT. For frequency analysis, the Fast Fourier Transform was applied. A total power [μ V2] and a relative power (as a percentage of the total power) was calculated for standard bands. The relative power of the four bands was lower before training in patient vs control subject, except higher power of the delta band. After training we noted a subtle increase of the relative power of alpha, beta and gamma bands in patient and only in alpha band in control subject. The value of total power was twice higher in patient than control before MIT and decreased after training only in patient but still remained higher than in control subject, which may reflect the greater effort to perform the motor imagery task by patient vs control subject. This work was supported by the grant: National Science Centre, Republic of Poland DEC-2011/03/B/NZ7/00588.

CLOSING LECTURE: 16.15 – 17.15

Vision and eye movements

Karl Gegenfurtner

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The existence of a central fovea, the small retinal region with high analytical performance, is arguably the most prominent design feature of the primate visual system. This centralization comes along with the corresponding capability to move the eyes to reposition the fovea continuously. Past research on perception was mainly concerned with foveal vision while the eyes were stationary. Research on the role of eye movements in visual perception emphasized their negative aspects, for example the active suppression of vision before and during the execution of saccades. But is the only benefit of our precise eye movement system to provide high acuity of small regions at the cost of retinal blur during their execution? In my talk I will compare human visual perception with and without eye movements to emphasize different aspects and functions of eye movements. I will show that the interaction between eye movements and visual perception is optimized for the active sampling of information across the visual field, and for the calibration of different parts of the visual field.

POSTER SESSION I

NEUROPHYSIOLOGY

1. Effect of sulforaphane on the seizure threshold in mice

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Sulforaphane is a natural isothiocyanate found in cruciferous vegetables, especially broccoli. It works as an Nrf2 activator and has gained much attention as a chemopreventive agent. Sulforaphane was also shown to produce neuroprotective effects, which suggests that it may have anticonvulsant properties. Therefore, the aim of our study was to investigate the influence of sulforaphane on seizure thresholds in three acute seizure tests in mice: the intravenous (i.v.) pentylenetetrazole (PTZ) infusion, maximal electroshock seizure threshold (MEST) and 6 Hz-induced psychomotor seizure test. Sulforaphane was administered intraperitoneally at doses of 10, 50, 100 and 200 mg/kg, 60 min before the tests. Sulforaphane at the highest dose tested, i.e. 200 mg/kg, significantly decreased the thresholds for the onset of the first myoclonic twitch and generalized clonic seizure in the i.v. PTZ test as well as the threshold for the 6 Hz-induced psychomotor seizure. It did not affect the threshold for the i.v. PTZ-induced forelimb tonus or the threshold for the tonic hindlimb extension in the MEST test. The obtained results suggest that sulforaphane may increase the risk for seizures. Therefore, further studies are required to evaluate the toxicity of sulforaphane and to estimate the risk-to-benefit ratio for sulforaphane usage in patients with epilepsy.

2. Effects of different doses of morphine injection into the pedunculopontine tegmental nucleus on behaviour elicited by ipsilateral stimulation of the mesolimbic system

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The pedunculopontine tegmental nucleus (PPN) directly regulates burst firing in the ventral tegmental area (VTA) dopaminergic neurons, the initial structure of the mesolimbic system. The aim of the study was to investigate the influence of activating opioid receptors by morphine at various doses within the PPN on behaviour induced by electrical stimulation of the ipsilateral VTA. The behavioural model of the VTA stimulation-induced feeding or locomotor response in rats was used. Latency to behavioural response was measured as a function of stimulation frequency before and after unilateral intra-PPN injection of morphine (doses: 0.25, 0.5 and 1.0 μ g). This experimental method allowed us to distinguish between motivational vs. motor aspects of tested reactions. Morphine caused a dose-dependent improvement of behaviour evoked by stimulation of the ipsilateral VTA, which manifested as a decrease in the reaction threshold and a leftward shift of the latency/frequency curve. We observed that lowest dose (0.25 μ g) induced substantial behaviour-increasing effects compared to the highest dose (1.0 μ g). Modulation of the ipsilateral VTA through the PPN by opiates direct injection effect the motivational rather than motor aspect of induced behaviour. Research was financed by the Polish National Science Centre (NCN) allocated based on the decision no: DEC-2013/09/D/NZ4/02499.

3. Noradrenergic signaling in ventral tegmental area of the rat – an electrophysiological and microiontophoretic study

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¹ Department of Molecular Neuropharmacology, Institute of Pharmacology, PAS, Krakow, Poland ² Department of Neurophysiology and Chronobiology, Institute of Zoology, Jagiellonian University, Krakow, Poland The role of dopaminergic (DA) ventral tegmental area (VTA) neurons in motivation, reward-related learning and addiction has been well established. All these functions are also influenced by noradrenergic neurotransmission system. Some electrophysiological studies show that noradrenergic system modulates DA neuronal activity, however, no consistent image of interaction between these systems has emerged so far. In this study, in vivo electrophysiological recording combined with microiontophoretic drug application was used to determine the influence of specific adrenergic receptor activation on rat VTA neuronal activity. Application of clonidine (α 2-adrenergic agonist) had no effect on DA and non-DA (presumably GABAergic) neurons' activity. Similarly, isoprenaline (β -adrenergic agonist) had no effect on DA neurons and induced weak excitation only in a few cases of non-DA neurons. In contrast, phenylephrine (α 1-adrenergic agonist) while having only a small tendency to inhibit some of the studied DA neurons, was inducing clear excitatory effect on non-DA neurons. GABAergic VTA neurons are responsible for generating behaviorally relevant pauses in firing of DA neurons. We hypothesize that weak inhibitory effect of DA neurons' activity after phenylephrine application results from concomitant activation of GABAergic terminals. Moreover, α 1-mediated GABAergic VTA neuron excitation could be involved in aversive stimuli processing.

4. The Role of T- type Calcium Channels in Regulation of Absence Seizure in S1po area of WAG/ Rij Rats

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Introduction: Absence seizures in genetic rodent models are characterized by symmetric, bilateral, synchronous 11-7 Hz spike-wave discharges (SWD). Cells in the deep layers of the perioral region of the primary somatosensory cortex (S1po) are the initiation site of these activities. T-type calcium channels are involved in regulating neuronal excitability and production of SWD. In this investigation we studied the effect of L-ascorbate and PMA on SWDs (T-type channel antagonist and agonist).

Methods: Eighteen WAG/Rij rats were scrutinized. Two cannulas were implanted in S1po area. EEG recording electrodes were implanted in cortex. EEG was recorded for 20 min before and one hour after injection of PMA (500 nmol) and L-ascorbate (100μ mol).

Results: L-ascorbate reduced both the number and mean duration of SWDs while an increase in mean number of SWDs was found after administration of PMA, both in comparison with the injection of solvent. Neither drug affected the mean peak frequency of SWDs.

Conclusion: The results confirm that S1po is an excellent place for the modulation of SWDs, that T type calcium channels determine number and duration somewhat differently. It can be assumed that both drugs have an effect on the probability of calcium channels opening and alter local neural excitability and SWD number. Considering that the duration of SWDs is determined by a directional drive from cortex to rostral reticular thalamic nucleus, it is proposed that Ascorbate may inhibit this and as a consequence, SWDs will last longer.

5. Investigation of the effects of chronic 4-aminopyridine treatment in rat brain slices using different electrophysiological techniques

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Epilepsy is a very common brain disease therefore it is important to investigate its underlying mechanisms. In our experiments we used 4-aminopyridine, a potassium channel blocker, to induce epileptic discharges and we investigated the changes in electrophysiological features in entorhinal cortex on network and on cellular level. Rats were treated with the convulsant for twelve consecutive days. Brain slices were prepared either immediately after the treatments (acute test) or following a longer time interval (chronic test). With glass microelectrodes, features of field afterdischarges evoked by brief bursts of high frequency electrical stimulation were investigated with parallel detection of intrinsic optical activity. Whole-cell patch clamp recordings were performed on neurons of the CA1 pyramidal cell layer. We found it was easier to induce afterdischarges in the slices from treated rats and the burst length was longer than in control animals. The optical investigations showed correspondence with the electrophysiological studies. In the patch clamp experiments several physiological parameters were assessed. Some neurons from 4-AP treated rats displayed spontaneous spiking, even bursting, which was rarely observed in control neurons. Altogether we can say that long-term 4-AP treatment caused mild seizure susceptibility, which become slightly increased later in time.

6. Involvement of key binding site residues of GABA_A receptor in full and partial agonist binding

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The lack of crystal structure of a typical GABA_A receptor ($\alpha 1\beta 2\gamma 2$) and limited functional information regarding agonist-protein interaction prompt in silico investigations. Herein, we addressed interactions between key GABA_AR binding site residues with GABA and P4S (partial agonist). A homology model based on novel GlyR crystal structure and ligand docking were done. We found that both ligands are oriented perpendicular to the pore axis, pointing the amine groups towards the receptor center. Amine groups form strong contacts with Thr202 of principal subunit and Thr129 of complementary subunit. This binding site area is lined by aromatic rings of Tyr205 and Tyr157 of principal subunit and, similarly, its front is lined by Phe200 and Phe45 (principal and complementary subunit). Most significant difference in binding of GABA and P4S was found in loop D. Arg66 (complementary subunit) formed interaction with carboxylic group of GABA, but not of P4S. In addition, in the presence of GABA, Arg66 formed interaction with Ser201 on principal subunit, enhancing intersubunit coupling. We conclude that although GABA and P4S show similarities in their dockings, their interactions with specific complementary subunit residues may affect the intersubunit cross-talk affecting the GABA_AR activation. Supported by NCN grant DEC-2013/11/B/NZ3/00983.

7. The influence of the electrical stimulation of the raphe magnus in rats on selected lymphoid organs

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Serotonin (5-HT) is a neurotransmitter present either in the brain or body. It plays an important role outside of the central nervous system in immune signaling. In our study we checked whether the stimulation of the raphe magnus (RMg) has an influence on the main lymphoid organs. We performed the experiment on male Wistar rats. Animals were implanted with electrodes into the RMg under isoflurane anaesthesia. After 10-days convalescence 16-days electrical stimulation began. Rats were divided into stimulated (n=6) and non-stimulated (n=7) groups. Every day 25 stimulation trials were carried out for each stimulated rat. Blood samples were collected by heart puncture under anaesthesia one hour after the last stimulation. Next, rats were sacrificed and either spleens or thymuses as well as brains were removed. Electrical stimulation of the RMg decreased the 5-HT level in the plasma. The total leukocyte number was comparable. In turn, the thymus weight was elevated after RMg stimulation. On the other hand, macroscopic changes in the spleen were comparable. The obtained results suggest that the stimulation of 5-HT production in the brain affects the 5-HT level peripherally and has an influence on immunity. Funding: Young Researcher grant, 538-L124-B941-15.

8. The electrical stimulation of the raphe magnus affect rats behaviours but has no influence on immune cells

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In the brain serotonin (5-HT) is produced by the raphe nuclei and is involved in the regulation of different behaviours. 5-HT is also active peripherally where, for instance, affects immune signaling. The aim of our study was to checked how the stimulation of the raphe magnus (RMg) affects rats behaviours and has any influence on immunity. Male Wistar rats were implanted with electrodes into RMg. After convalescence animals were divided into stimulated (n=6) and non-stimulated (n=7) groups and 16-days electrical stimulation began. Every day 25 stimulation trials were carried out for each stimulated rat. We measured the mobility during each experiment, the anxiety level on third day and sociability on eighth day – both after last daily trial. One hour after the last stimulated rats. Furthermore, their sociability was reduced. In turn, stimulation had weak influence on the anxiety level. The numbers of lymphocytes populations: T (also Th and Tc), B, and NK cells measured via flow cytometry were comparable. The obtained results confirmed the role of 5-HT in behavioral control however do not indicate its effect on main immune cells. Funding: Young Researcher grant, 538-L124-B941-15.

9. Are we able to predict drug - CYP450 interaction by in silico method? Preliminary studies on selected anticonvulsant drugs using MetaSite

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Epilepsy is a central nervous system disease concerning above 1% of the population. It is estimated that around 30% seizures are drug-resistant, in most cases requiring polytherapy. It is associated with drug interactions, including hepatic enzyme induction and inhibition and protein-binding displacement. Most commonly used anticonvulsants are eliminated through hepatic metabolism catalysed by isoforms of CYP450 enzymes, with number of these drugs affecting the metabolism of other drugs. The aim of present study was to evaluate metabolite prediction and inhibitory potential of selected anticonvulsants using software MetaSite. A test set of 10 antiepileptic compounds with divergent chemical structures, differences in the extent of I-st phase metabolism and possible inhibition of CYP450 enzymes was chosen. MetaSite was tested for 9 isoforms of CYPs in two settings: docking with or without reactivity corrections. It provided data on metabolic soft spots of studied compounds, their possible metabolites and qualitive information on inhibitory potential. For every compound literature data on detected CYP450 interaction and formed metabolites were compared with our prediction. We conclude that MetaSite software has many advantageous features in prediction drug-CYP450 interactions, but needs refinement to obtain an accepted profile. Supported by NCN grant UMO-2013/11/B/NZ7/04834.

10. Effects of different frequency of electrical stimulation of dentate nuclues upon epileptic foci and role of thalamic nuclei

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The dynamic of penicillin – induced epileptogenic foci (20.000 IU/ml), created in the anterior suprasylvian gyrus of myorelaxed and artificially ventilated cats was investigated under conditions of n. dentatus electrical stimulation (ES). It was established that low frequency ES (6-12 Hz) which was delivered when contrlateral foci generated spike discharges with amplitude of 1,5-2,0 mV and frequency 30-40 discharges/min reliably provoked generation of ictal type of discharges. High-frequency (100 – 300 Hz) ES were followed by suppression of interictal discharges generation, along with the conversion of negative phase of spikes into positive ones in poststimulative period. Low-frequency facilitation was abolished by electrolytic (5,0 mA, 60 s) destruction of contrlateral ventral lateral and damage of reticular nuclei of thalamus, while suppressive effects of high frequency stimulation became less pronounced. Similar low-frequency ES of factigeal nucleus was not followed by ictal epileptogenesis provocation, while high frequency ES effectively suppressed focal epileptic activity. Gained data are in favor for the involvement of thalamic nuclei, namely ventral lateral and reticular ones in the development of effects of n. dentatus ES upon focal epileptogenesis. Such assumption was supported by the precipitation of recruitment response in suprasylvian gyrus in the course of low-frequency ES of n. dentatus.

11. The effect of MMP-3 activity on long-term plasticity of NMDAR-mediated synaptic transmission, postsynaptic Ca²⁺ and c-Fos expression in the CA1 hippocampal region

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Matrix metalloproteases are involved in remodeling of the extracellular matrix and play a critical role in synaptic plasticity, learning and memory. However, the underlying mechanisms remain elusive. Recently, MMP-3 was shown to cleave NR1 subunit of NMDARs. We previously reported that tetanic stimulation of Sch-CA1 projection led to long-term potentiation of isolated synaptic NMDAR-mediated transmission (LTPNMDA) that was absent when slices were treated with MMP-3 inhibitors NNGH (10μ M) or UK356618 (2μ M). Here, we analyzed whether MMP-3 activity affects NMDAR-dependent immediate early gene cfos product expression. Immediately following cessation of LTPNMDA

recording, acute brain slices of P40-P50 C57BL6 mice were fixed and stained against cFos and NEUN (a neuronal marker). We found that LTPNMDA magnitude correlated with cFos expression level and was significantly downregulated upon MMP-3 inhibition. Since cFos expression is induced largely by postsynaptic Ca2+ entry, we analyzed NMDA-mediated Ca2+ waves with a ratiometric indicator Fura2 in hippocampal primary neuronal cultures. We found that recombinant MMP-3 protein (1 μ g/ml) enhanced the fraction of neurons showing NMDAR-mediated Ca2+ waves following multiple NMDA applications. Altogether, our data show that MMP-3 activity may support NMDAR-mediated Ca2+ waves and cFOS expression which may participate in downstream gene expression accompanying formation and maintenance of memory traces. This work was supported by National Science Center grant SONATA/2014/13/D/NZ4/03045.

12. Chronic exposure to cannabinoid agonist R(+)WIN55,212-2 alters stop mechanism of absence seizures in rats

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Single exposure to cannabinoid agonist R(+)WIN55,212-2 is known to reduce absence seizures 3h after treatment. In this study the effects of chronic exposure to the drug on spike-and-wave discharges (SWDs) in adult WAG/Rij rats were investigated. 16 male rats were used, of whom 8 were injected with cannabinoid agonist (6 mg/kg in 3 ml/mg olive oil, s.c.), and 8 with vehicle (3 ml/mg olive oil, s.c.). Injections took place 3 times a week during 4 weeks. EEG was recorded for 24 hours before treatment, after treatment, and subsequently after 2 and 4 weeks. The WIN group showed an increase in total SWD duration in week 0 and 2. Interestingly, this is mainly due to an increased percentage of long (> mean + 2 SD) SWDs. This suggests that the stop mechanism of SWDs is influenced by the drug. These effects were no longer seen in week 4, which suggests down-regulation of the CB1-receptor, kinetic tolerance or a lower bioavailability.

13. Disinhibition of the rat intergeniculate leaflet neurons in the model of absence epilepsy

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The intergeniculate leaflet of the rat thalamus (IGL) is a retinorecipient, GABAergic brain structure implicated in the modulation of circadian rhythmicity. In urethane-anesthetised Wistar rats, a subpopulation of IGL neurons is known to express an infra slow oscillatory (ISO) pattern of activity during in vivo recordings, under photopic conditions only. WAG/Rij rats used in this study are the well-established model of absence epilepsy (AE) often connected with retinal pathologies and insufficiency of sleep-promoting system. The aim of presented research was to elucidate possible pathologies of IGL's neuronal network in WAG/Rij rats. The in vitro patch-clamp study on presymptomatic rats revealed the changes in GABAergic synaptic transmission - the amplitude of miniature inhibitory postsynaptic currents was lower in AE model. However, the amplitude of tonic current evoked by GABA (100 μ M) application did not differ between Wistar and WAG/Rij rats. The in vivo single-unit extracellular recordings on adult WAG/Rij rats indicated the presence of ISO activity in IGL even during the dark conditions. Our data show the disinhibition of IGL neurons in AE model caused by weakened synaptic transmission (presumably impaired synaptic GABA_A receptors) and serve as a novel insight into the probable involvement of IGL in the mechanism of absence epilepsy. Supported by MSHE grant: 0001/DIA/2014/43.

14. Orexin-A depolarize the rat intergeniculate leaflet neurons via two different mechanisms

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The intergeniculate leaflet (IGL) of the thalamus is a small but important structure of the mammalian biological clock. The well-known function of the IGL is integration of photic and non-photic stimuli and sending these informations to the master biological clock – suprachiasmatic nuclei. One of the nonspecific brain projections that transmit non-photic information is orexinergic system. Orexins are involved in many behavioral states such as arousal, sleep, stress, and

feeding. Our previous studies indicated depolarizing effect of orexins on the IGL neurons. The aim of this study was to examine which mechanisms are involved in this effect. Whole-cell patch clamp in vitro technique was used on the acute brain slices ($250\mu m$) containing IGL from 13–18 days old male Wistar rats. Our preliminary data shows that depolarizing effect of the orexins was attenuated by two main solution containing: NMDG-Cl / K+ ACSF mixture and blocker of nonspecific cationic channels. We hypothesize the involvement of two different mechanisms: potassium channels inhibition and activation of nonselective cationic channels. These two mechanisms were described earlier in other brain structures as the main targets of the orexinergic effect. This work is supported by NSC grant OPUS V: 2013/09/B/NZ4/00541

15. Repeated corticosterone treatment changes pyramidal neuron morphology in the rat motor cortex

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Exposition to stressors influences morphology and physiology of neurons, what may impair functioning of many brain regions. According to our recent work, repeated corticosterone treatment, a rat model of chronic stress, induces changes in excitatory postsynaptic currents, but does not affect dendritic spine density of the rat motor cortex (M1) layer II/III pyramidal neurons. The aim of the current study was to examine the influence of the corticosterone treatment (7 days) on other M1 neurons morphological parameters, as changes in cell morphology are often linked to physiological alterations. Effect of the treatment was studied on Wistar rats M1 pyramidal layer II/III neurons. Neurons were filled with biocytin, stained with Cy3-conjugated avidin and examined under a confocal microscope. Apical and basal dendritic trees were analyzed independently. Semi-automatic dendrite tracing was performed. Tracing data underwent Sholl analysis and were processed in L-Measure. Corticosterone treatment increased complexity of the neurons apical part, escalating the number of branches and bifurcations. Basal dendrites remained unaffected. We conclude that prolonged corticosterone administration induces changes in M1 pyramidal neurons morphology, what may contribute to stress caused motor functions deterioration. Previously revealed rise in synaptic strength might be evoked by new synapses formation on more complex apical dendrites.

16. Changes of ionic concentrations during seizures transitions - a modelling study

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Traditionally, it is considered that neuronal synchronization in epilepsy is caused by a chain reaction of synaptic excitation. However, it has been shown that synchronous epileptiform activity may also arise without synaptic transmission. We developed realistic computational model of hippocampal network to investigate the respective roles of synaptic interactions and non-synaptic mechanisms in seizure transitions. The computational model included pyramidal and interneuronal cells embedded in common extracellular space with realistic dynamics of Na+, K+ and Cl-ions, glial uptake and extracellular diffusion mechanism. The modelled network behavior with fixed ionic concentrations is quite different from the neurons' activities when more detailed modelling of ionic dynamics is included. In particular, in the extended model, strong discharge of inhibitory interneurons may result in long lasting accumulation of extracellular K+, which sustains depolarization of principal cells and causes their pathological discharges. This effect is not present in a reduced, purely synaptic network. These results point to the importance of non-synaptic mechanisms in initiation and progression of seizures in focal epilepsy.

17. Mutation at the binding site β 2E155 residue affects both binding and gating properties of α 1 β 2 γ 2 GABA_A receptors

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The GABA_A receptors play a crucial role as the primary mediator of inhibitory neurotransmission in the adult brain. Glutamate 155 of the GABA_A receptor β 2 subunit is located at the binding site and has been implicated in direct

interactions with the neurotransmitter (Cromer et al., 2002). Moreover, β 2E155 seems to be initial trigger for ion channel opening (Newell et al., 2004) as movements of amino acids in this GABA-binding site region are involved in coupling GABA binding to channel gating. We used the patch clamp technique with ultrafast perfusion to examine the impact of cysteine substitution of β 2E155 on macroscopic currents mediated by mutated α 1 β 2 γ 2 and α 1 β 2 receptors. Mutations of this residue right-shifted the dose-response curves for GABA-elicited currents. Moreover, it also reduced macroscopic desensitization, accelerated deactivation kinetics and induced spontaneous openings. Nonstationary variance analysis showed for α 1 β 2E155C γ 2 receptors a reduction of maximal open probability (compared to wild type receptors) without affecting single channel conductance. Summarizing, β 2E155 residue has strong impact on both biding and gating. Supported by NCN grant DEC-2013/11/B/NZ3/00983 and ministry grant Pbmn135.

18. CRISPR-Cas9 mediated Tcf7l2 knock-out in primary thalamic neuron cultures

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The thalamus is a central integrator of sensory information, which is then initially processed and further transmitted to the cerebral cortex. Molecular mechanisms involved in thalamus development are not well understood, but the evidence suggest that the process might somehow depend on a canonical Wnt signalling effector – Tcf7l2. This gene exhibits alternative promoter usage, multiple splice variants and protein isoform switching during embryogenesis, an event probably significant for proper thalamic development. The project involves the use of CRISPR-Cas9 system in order to obtain an isoform-specific Tcf7l2 knock-out in mouse embryo. The aim is to assess its effects on thalamus development in different embryonic and postnatal stages. To this end, we designed several single guide RNAs (sgRNAs), specific to crucial Tcf7l2 exons, whose efficency in knock-out induction were then tested in primary thalamic neuron cultures. We present the results of this initial in vitro study, showing strong downregulation of Tcf7l2 levels in neuron cells and proving the efficiency and potential of CRISPR technology, which sets the foundation for future project stages, involving the in vivo experiments.

19. Brain state dependent changes in pattern of electrical activity of midbrain dopaminergic neurons of urethane anaesthetised rats

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Dopaminergic neurons in the ventral tegmental area (VTA) and substantia nigra pars compacta (SNc) are able to generate two distinct patterns of electrical activity: tonic and bursting. The latter one is essential for phasic dopamine release in target structures. It was previously found that activity of DA neurons is correlated with brain state changes of naturally sleeping animals, displaying bursting during REM and tonic firing during nonREM phase. Since urethane anaesthesia is postulated to be a model of cyclic, sleep-like brain state alternations, we have performed experiments aimed to correlate firing pattern of midbrain DA neurons with changes of the brain state. Extracellular in vivo recordings of midbrain DA neurons' activity and simultaneous electrocorticographic monitoring of the brain state were conducted on urethane anesthetised Wistar rats. Our results show that the activity pattern of putative DA neurons in the VTA and SNc strongly depends on the cyclic changes in the brain state. Interestingly, observed relationship was opposite to the one reported during natural sleep. We have observed tonic firing mainly during cortical activation (REM-like) whereas bursting pattern was predominant during cortical deactivation (nonREM-like). Our results confirm that activity of midbrain DA neurons is correlated with alternating states of the brain and emphasize that it should be taken under consideration during the experiments on anesthetised animals.

20. Unravelling the mechanisms of appetite control: relaxin-3 signalling in hypothalamic paraventricular nucleus of the rat

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¹ Department of Neurophysiology and Chronobiology, Jagiellonian University in Krakow, Krakow, Poland ² The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Melbourne, Australia Relaxin-3 (RLN3) and its cognate receptor-RXFP3, have been extensively studied due to their role in stress and feeding interactions. The orexigenic action of RLN3 is considered to be associated with RXFP3-mediated inhibition of neurons in the paraventricular nucleus of the hypothalamus (PVN). Our previous studies have shown that a selective RXFP3 agonist (RXFP3-A2) is a potent inhibitor of PVN neurons in vitro. The aim of current study was to extend these observations by examining the effect of human relaxin-3 and relaxin-2 within the PVN, using patch-clamp recordings from rat hypothalamic slices in vitro. Human RLN3 (H3, 100 nM) strongly inhibited a majority of recorded magnocellular PVN neurons. Similar to RXFP3-A2, this effect was largely direct (i.e. persisted in presence of TTX and glutamate/GABA receptor blockers). Post-recording staining revealed both oxytocin- and vasopressin-positive cells amongst relaxin-3-sensitive neurons. Human relaxin-2 (H2, 600 nM) was used to determine any acute effects of RXFP1 activation, however in most cases, electrical activity of PVN neurons was not affected. Our data support the idea that the mechanism of RLN3-mediated orexigenic effects involves inhibition of oxytocin and vasopressin PVN neurons and this inhibition is produced by RXFP3 activation. Funding: NSC, Poland DEC-2012/05D/NZ4/02984, MSHE, Poland 0020/DIA/2014/43, and Institute of Zoology, Jagiellonian University in Krakow K/DSC/002978.

21. An open source toolkit for combining neurophysiology and rodent behavior

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Understanding how neurons represent specific information about external stimuli and internal variables requires registering neuronal action potential firing while animals are engaged in different behaviors. The millisecond timing of neuronal firing has strong implications on the scope of such behavioral tasks. One can only hope to extract specific information carried by spike timing if behaviorally relevant events of the task, like sensory stimuli or behavioral feedback, are under the same precision of temporal control. We present an affordable, modular, open source system capable of flexible behavioral task design and execution, submillisecond precision hardware control, combined recordings and optogenetic stimulation. Key components of this system are (i) custom designed, modifiable environments for mouse behavior; (ii) open source microcontroller-based behavior control equipment; (iii) open source data acquisition system (Siegle JH, Voigts J) (iv) open source computer vision based position tracking (Lopes G); (v) open source pulse generator; (vi) light source (laser or LED) and a light coupling system for optogenetic stimulation; (vii) freely available Matlab software package. How this setup operates will be demonstrated on a simple associative learning task. We believe this system will be a useful tool for a broad community of neurophysiologists.

BASIC NEUROSCIENCE

22. Effect of long-term treatment with escitalopram on spexin expression in the rat brain

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Spexin (SPX) is an intriguing novel neuropeptide, a product of NPQ gene which was identified with bioinformatic tools. The SPX immunoreactivity was detected in the hypothalamic paraventricular and supraoptic nuclei. Spexin seems to have multiple physiological functions in mammals. Recent reports showed that spexin may be a novel strongly anorexigenic factor involved in weight regulation, with potential for obesity therapy. Some findings also demonstrates the central control of SPX in cardiovascular/renal function and nociception. A potential direct action of novel antidepressants at the level of brain spexin expression is still unsolved. Present study has an aim to complete this knowledge by determining whether escitalopram affects the expression of spexin mRNA in the rat brain. We assessed the SPX mRNA levels in the selected rat brain structures after extended (28-days) treatment with escitalopram using quantitative Real-Time PCR method. We have shown that escitalopram administered chronically have ability to upregulate the spexin mRNA level in the hippocampus, striatum and cerebellum. In turn, drug treatment highly decreased the neuropeptide gene expression in the hypothalamus and amygdala. These data may support the hypothesis that spexin may be involved in the serotonin-dependent actions of escitalopram and possibly also in the pathophysiology of mental disorders.

23. The high fat diet reduced NPY positive cells but not PV in the rat motor cortex

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Introduction: Excessive caloric intake is a major problem leading to obesity. Energy balance in the CNS is mainly controlled by orexigenic and anorexigenic transmitters like Neuropeptide Y(NPY). NPY is expressed on different types of neurons. Release of this neurotransmitter enhance food intake and may influence cognitive functions. Here, we have examined changes in the number of neurons expressing NPY or parvalbumin (PV) in rats fed high-fat diet (HFD).

Methods: Male Wistar rats were fed either HFD or standard laboratory chow for 12 months. Immunohistochemistry for NPY and PV was performed. Single NPY- or PV-positive cells were counted from bilateral rectangular areas of interest spanning the M1 cortex and also in hippocampi.

Results: Surprisingly we have found a significantly reduced number of cortical NPY-positive neurons in HFD fed rats. The number of cortical and hippocampal PV neurons was unchanged.

Discussion: Beside of reduced number of NPY-positive neurons we have previously found reduced gliosis and mild ketonemia in rats fed a HFD. It has been established that ketonemia evoked by diet rich in fat might have potentially positive effect on the CNS.

NCN grant 2012/05/N/NZ2/00641.

24. Immunodetection of calbindin (CB), calretinin (CR) and parvalbumin (PV) in the septum of the newborn and young guinea pig (Cavia porcellus)

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Calcium binding proteins (CaBPs) are useful neuroanatomical markers to follow maturation of GABAergic inhibiting network in developing brain. CB and CR are known as slow or fast calcium ions buffers, which are present both in excitatory and inhibitory neurons - positive for CB(+) or CR(+); whereas PV works only as slow buffer and relates only to GABAergic inhibiting interneurons (PV+). Therefore, the purpose of this study was to examine alterations in distribution of these CaBPs in the septum (SE), a crucial component of the inhibiting network in limbic/memory system. Brains from P0, P10, P20 (newborns, 10, 20 days after birth) were processed to obtain frozen sections for immunohistochemistry labelling. Results indicate that distribution pattern of CB and CR was almost unchanged during examined stages; but perikarya containing CB and CR were slightly more abundant at P0 than at P10 and P20. PV also occurred throughout all stages, but PV+ perikarya were observed at P10 and P20 in higher amount than at P0 (only single perikarya). CB and CR show diverse pattern of maturation in comparison to PV. The increasing PV-immunoreactivity after birth suggests functional maturation of inhibiting neuronal network of the SE in the young guinea pig.

25. Differences in stimulated locomotor activity in eye color mutant strains of house cricket (Acheta domesticus)

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For many years eye color mutant strains were commonly used as a basic model in insect physiology and molecular biology. Published data show that eye screening pigments (ommochromes and pteridines) are important for eye functionality and visual stimulus reception. Moreover, screening pigments synthesis pathways are tightly connected with metabolism of key neurotransmitters (serotonin and dopamine). It affects insect behavior like phototaxis, locomotion or memory. In 2015 in the Department of Animal Phisiology and Ecotoxicology (Faculty of Biology and Environment Protection, University of Silesia) two strains of eye-colored mutants were isolated - yellow and white

strains of house crickets (Acheta domesticus). There is no data about similar mutation in house cricket, also there is lack of data about behavioral effect of this kind mutation in hemimetabolic insects. Using TLC and spectrophotometric measurements we demonstrated that the yellow-eyed crickets have no ommochromes, while the white strain crickets lack ommochromes and pteridines. In this report we present differences in stimulated locomotor activity between three strains of Acheta domesticus.

26. Muscimol-evoked currents are profoundly altered by agonist binding site mutation β 2E155C in α 1 β 2 γ 2L and α 1 β 2 GABA_A receptors

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GABA is the major inhibitory neurotransmitter in the adult mammalian brain and it activates ionotropic, pentameric GABA_A receptor (GABA_AR). So far 19 GABA_AR subunits have been identified and the most common arrangement is $2\alpha_{1:2}\beta_{2:\gamma}^2$ with two binding sites on the α/β subunits interface. Muscimol is the principal psychoactive component of Amanita muscaria and behaves as a potent GABA_ARs agonist. In the present study using patch-clamp technique with ultra-fast perfusion system we investigate the kinetic properties of responses to this compound mediated by wild-type ($\alpha_{1}\beta_{2}\gamma_{2}L$ and $\alpha_{1}\beta_{2}$) and by mutated ($\alpha_{1}\beta_{2}E_{155}C_{\gamma}2L$ and $\alpha_{1}\beta_{2}E_{155}C$) GABAARs. Glutamic acid (E) at position 155 of β_{2} subunit is located at the GABA-binding site and directly interacts with the agonist. Our data show that this mutation right-shifted the dose-response relationship for muscimol-evoked currents for both GABA_AR types, however, the EC50 value for $\alpha_{1}\beta_{2}E_{155}C$ was higher than for $\alpha_{1}\beta_{2}E_{155}C_{\gamma}2L$. For both mutants, muscimol-evoked currents were characterized by deeper macroscopic desensitization and by slower deactivation constants compared to GABA-evoked currents. These data, together with our previous results, suggest that E155C mutation affects both binding and gating transitions during receptor activation. Supported by NCN grant DEC-2013/11/B/NZ3/00983 and NCN grant DEC-2013/11/N/NZ3/00972.

27. Look into a rat's brain

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Understanding the functioning of the brain in its entirety poses the major challenge for neurobiology. It is of particular interest to decipher how separate brain structures and circuitry within them work together. Visualization of the whole brain and consequent 3D reconstruction of its connectivity would be of great help in reaching this goal. Unfortunately, light scattering within the thick tissues prevents their imaging. However, recently, several techniques that allow to make such tissues optically clear have been developed. Since fluorescent labels, such as green fluorescent protein (GFP) and its cognates have become a popular tool in neuroscience, the tissue (including brain) transparency techniques should not obstruct fluorescent signals. In my study I have used three approaches for clearing rat brain that preserve fluorescence, namely Clarity, CUBIC and FluoClearBABB. These methods were previously employed for mouse brain, however, because of larger size and greater abundance of myelin, rat brains are more challenging to make the transparent. I have found the FluoClearBABB method to be most effective, as it takes less time as well as provides better preservation of the fluorescence as visualized using light-sheet microscopy, for half-brain imaging.

28. Towards an antibody based protein atlas of the mouse brain

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Background: Completion of the human and mouse genome projects paved the way for large-scale analysis of gene expression in the nervous system. Public available data generated within these projects has had a tremendous impact on our understanding of the molecular organization of the brain. However, the majority of these efforts are based on gene-expression and detection of mRNA, providing little information on the cellular and subcellular distribution of gene products.

Objectives: In 2011 we initiated the Mouse Brain Protein Atlas project, aiming to visualize the regional, cellular and subcellular distribution of hundreds of proteins in the mouse brain. Utilizing the extended and unique library of antibodies generated in the Human Protein Atlas (HPA) project we aim to visualize the expression and distribution of the majority of non-housekeeping proteins involved in normal brain physiology, brain development or pathogenesis of neurological disorders.

Approach: Target specificity of antibodies raised against selected proteins is validated on mouse brain tissue using western blot. Antibodies that pass western blot validation are applied to a series of coronal cut brain sections with a 400 μ m interval. The use of fluorescence detection methods allows multiplex labeling of target proteins in combination with nuclear markers and fluorescence reporter proteins. Entire brain sections are scanned using a 10x objective, creating large images with microscopic resolutions.

Results: All image data and quantitative analyses of regional distribution of the first hundred proteins are publicly available on the HPA project website (www.proteinatlas.org/humanproteome/mouse+brain). The new release of the protein atlas of the mouse brain in December 2016 will present data for a total of 500 proteins.

29. Polypeptide complex yolkin from chicken egg Yolk protect PC12 cells from oxidative stress and toxic effect of amyloid β42

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Introduction: Amyloid β 42 plays a central role in the pathology of AD. It is toxic for neural cells both in vivo and in vitro. In the amyloid toxicity increased production of free oxygen radicals (ROS) could be involved. Aim: The protective effect of polypeptide complex - Yolkin isolated from chicken egg yolk was studied on neuronal cell line PC12.

Methods: Cell viability was evaluated using MTT assay. The intracellular level of free oxygen radicals was detected by DCFH test.

Results: In the presence of Yolkin viability of neuron-like PC12 cells treated with amyloid β 42 was significantly increased. It was accompanied by decreased level of intracellular ROS.

Conclusion: The results obtained indicate that Yolkin is able to reduce the amyloid β 42 cytotoxicity and show neuroprotective properties by the reduction ROS in PC 12 cells.

30. Manipulating Prion protein gene in vivo with CRISPR/Cas9

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The prion protein (PrP) is a membrane-anchored glycoprotein, abundantly expressed in the brain of a wide range of species. The cellular form of PrP – PrPC – participates in synaptic plasticity, cell signaling and neuroprotection. The pathological form – PrPsc – is an infectious agent in prion diseases (PrDs), a group of peculiar neurological disorders. In certain aspects PrDs resemble more prevalent neurodegenerative conditions, like Alzheimer's or Parkinson's diseases, both of multigenic etiology. However, in PrDs a single protein (PrP) causes profoundly different disease phenotypes, selectively affecting distinct brain regions. What makes these regions more vulnerable than others? Key insights into the mechanisms of this peculiar phenomenon might come from studying mice expressing PrP mutants. However, manipulating the gene encoding PrP (Prnp) in mice is challenging. Indeed, the first knockout required screening of ~10,000 embryonic stem cell clones to isolate a single correct recombinant. We systematically tested CRIPSR/Cas9 tools to genetically manipulate the Prnp locus. Through this process we generated three Prnp knock-in mouse lines expressing combinations of fluorescent PrP variants and reporter genes controlled by the Cre/LoxP system. These mice will enable studies of prion replication and cell type-specific trafficking in different disease paradigms. Furthermore, we identified efficient CRISPR/Cas9 transcriptional activators of Prnp. These, in combination with existing mouse models, will allow manipulating PrP expression levels, thereby complementing the toolkit to study PrP physiology and neurodegenerative mechanisms.

CIRCADIAN RHYTHMS AND SLEEP

31. DmMANF protects glial cells and regulates the circadian system in the brain of Drosophila melanogaster

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Mesencephalic astrocyte-derived neurotrophic factor (MANF) is evolutionarily conserved neurotrophic factor responsible for the protection of dopaminergic neurons in mammals. It has been recently described in *Drosophila melanogaster* where it is important in development and knock down of DmManf (D. melanogaster Manf) gene leads to death of embryo. The purpose of the presented study was to investigate functions of DmMANF in the brain of D. melanogaster. It has been observed that DmMANF is expressed in both, neurons and glial cells but the function of this protein in the brain is still not clear. Interestingly, the silencing of DmManf by RNAi technique in glia induced neurodegenerative changes in the first optic neuropil (lamina) while its silencing in neurons had no profound effects on the structure of lamina neuropil. On the other hand, the period of locomotor activity of flies with silenced expression of DmMANF in neurons was lengthened. This effect was not observed after the same manipulations in glial cells. The role of DmMANF in the circadian clock regulation and its involvement in the protection and function of glial cells will be investigated in the further study.

32. Unraveling the orexins distribution pattern in rat lateral geniculate nucleus of the thalamus

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The lateral geniculate nucleus (LGN) of the thalamus is an important relay center of the visual pathway from retina to occipital cortex. In rats LGN is composed of three nuclei: the dorsal and ventral geniculate nuclei (DLG and VLG, respectively) divided by the intergeniculate leaflet (IGL). The LGN functioning is under control of many modulatory mechanisms, including the orexinergic system of lateral hypothalamus. Orexins (OXA and OXB) are neuropeptides implicated in physiological processes like arousal, control of the sleep/wake cycle and feeding. The aim of this study was to evaluate the possible circadian pattern of OXA/OXB distribution in the geniculate complex in connection with electrophysiological effects of orexins in LGN. For this goal, adult male Wistar rats were submitted to a tissue fixation process by paraformaldehyde transcardial perfusion over 24h, at 4h intervals. Optical density measurements were performed at digital pictures of brain slices processed by immunostaining for OXA, OXB and neuropeptide Y (marker of IGL). We observed orexinergic fibers regardless of the time of a day in the whole LGN. The innervation was sparse for DLG, dense in case of IGL and moderate for VLG. We hypothesize, that orexins may affect the functioning of the LGN by means of both synaptic and volume transmission, acting upon long distances. Our study strengthens the importance of orexinergic innervation in the mammalian visual pathway on the level of thalamus and its implication in the neuronal mechanism of circadian system. Supported by NCN grant OPUS V: 2013/09/B/NZ4/00541 and K/DSC/002968 (Institute of Zoology, Jagiellonian University).

33. Slow-wave activity enhances evoked potentials in the piriform cortex

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Slow-wave sleep plays a critical role in memory consolidation in many systems, including the olfactory system, through strengthening connections between distant brain structures. Direct evidence of changes in synaptic connectivity during slow-wave activity in the olfactory system, however, is missing. In the current study we took advantage of the fact that rats under urethane anesthesia spontaneously shift between slow- and fast-wave activity, which allowed us to monitor synaptic changes typical for sleep. We used electrically evoked synaptic potentials to examine how sleep state modulates the functional connections between distant parts of the olfactory system. We performed acute recordings from the anterior piriform cortex of urethane anesthetized rats. Stimulation electrodes were placed either in orbitofrontal (n = 5) or posterior piriform cortex (n = 4). In both pathways we observed robust sleep state-dependent synaptic potential modulation. During slow-wave activity, stimulation elicited significantly stronger responses. This confirms the hypothesis that the slow-wave sleep promotes more efficient communication between distant parts of the olfactory cortex. Our experiment shows how recording evoked potentials under urethane

anesthesia can be used for studying properties of slow-wave sleep with very simple and well controlled methods. It also highlights some important methodological issues for in vivo LTP induction.

GLIA

34. Changes in level of GFAP and GS in the hippocampal formation and frontal cortex as a result of high-fat diet treatment

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Demonstrated that excessive consumption of high fat diet (HFD) can contribute to loss of cognitive function and speeding up aging process. Mechanism of the impact of diet on the functioning of astrocytes is definitely less studied than on the neurons. Glial fibrillary acidic protein (GFAP) and Glutamine Synthetase (GS) are the very common proteins located in astrocytes. Changes in expression of this proteins may reflect changes in astroglial function. Male Wistar rats were divided into two groups which were fed different diet for a 6 months. The diet an experimental group supplied 70% of energy from fat. Diet for the control group had 10% of energy from fat. After 6 months rats were decapitated. Isolation procedure appropriate brain structures (hippocampal formation, cortex) was performed. Level of GFAP and GS were measured by Western Blot method. Expression of GFAP both in the hippocampal formation and cortex was increased in the experimental group. Differences in level of GS we observed only in hippocampal formation of rats fed HFD and we were found that level of GS was lower in this group. These data show that HFD have influence on proteins connected with astrocytes, which are getting more reactive in animals on HFD.

35. Autophagy in glial cells is involved in sleep regulation in Drosophila melanogaster

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Autophagy is a catabolic process that is important in cellular response to stress and survival of cells during starvation. The pathways that regulate autophagy are evolutionarily conserved. The main negative regulator of autophagy is the protein kinase Target of Rapamycin (TOR). Among genes involved in autophagy important role play Atg5 and Atg7 which are necessary for the formation of autophagosome. Disruptions of autophagy by mutations of Atg5, Atg7 or Tor in nerve cells can lead to neurodegeneration. The purpose of the presented study was to investigate the role of autophagy in brain functions in Drosophila melanogaster. We used transgenic flies to silence Atg5, Atg7 or Tor genes in glial cells. Then we measured locomotor activity and sleep, which was automatically recorded as 5 minutes of fly immobility. Our results showed that Tor silencing in glial cells lengthen the period of locomotor activity rhythm and duration of total sleep. In contrast, Atg5 and Atg7 silencing did not change the period of locomotor activity rhythm, but increased the duration of total sleep. These results suggest that autophagy in glial cells plays an important role in the regulation of Drosophila sleep while Tor regulates both sleep and the circadian rhythm of activity.

36. The impact of prenatal stress on the viability and activation of astrocytes in primary cultures

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Although prevalence of depressive spectrum disorder is increasing worldwide, still we do not know much about their pathophysiology. Post-mortem histopathological studies reported changes in glial cell numbers in various brain areas of depressed patients. It suggests that abnormal functioning of glial cells could contribute to the pathophysiology of mood disorders. Moreover, a growing number of studies indicate that adverse early life experiences, due to effects on neurodevelopment, may also be an important factor involved in the pathogenesis of depression. Therefore, we hypothesize that prenatal stress procedure (well-characterized animal model of depression), influences astroglia function and activity, leading to further dysfunctions observed in affective diseases. To check this, we measured the metabolic activity and lactate dehydrogenase release in both prenatally stressed and control primary astroglia cultures by colorimetric assays using MTT and LDH tests respectively. Moreover, we assessed the release of nitric

oxide (NO), a neurotoxic mediator, in the cultures' medium by the Griess reaction. We found reduction in metabolic activity in primary astroglia cells evoked by prenatal stress procedure. Furthermore, the increase in LDH as well as in NO release were demonstrated. These data suggest that prenatal stress leads to malfunction of astroglia functioning, which imply a potential role of these cells in the development of depressive disorders. However, more investigations are needed. Supported by the grant no 2013/09/B/NZ7/04096, National Science Centre, Poland and partially by the statutory founds Institute of Pharmacology, PAS.

LANGUAGE PROCESSING

37. Structural reorganization of early sensory areas supports cross-modal plasticity

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Learning complex skills can induce cross-modal reorganization in the human cortex. It remains unclear, however, which long-distance anatomical pathways can support such cross-modal plasticity. Here we enrolled sighted adults on a nine-month tactile braille reading course while resulting changes in brain structure were investigated with voxelbased morphometry and diffusion tensor imaging. Following tactile training, we observed grey and white matter reorganization in the peripheral early visual cortex. Grey matter volume in this region was correlated with progress in tactile braille reading. In addition, resting-state fMRI functional connectivity demonstrated that this part of visual cortex was preferentially communicated with the primary somatosensory cortex even before the onset of training. Non-human anatomical data indicates that peripheral parts of early sensory cortices are monosynaptically connected. We show that this connectivity might constitute the anatomical underpinning of cross-modal reorganization in humans. Based on our results, we propose that prolonged tactile training can re-arrange the flow of complex tactile input through these connections. As a result, tactile input is transferred from somatosensory to early visual cortices, and then subsequently processed in high-level visual areas. Our study demonstrates that the human brain can adapt its structural properties to support such global change in cortical processing hierarchy.

38. Orthographic representation of tactile Braille words in congenitally blind. Preliminary results of an repetition suppression study

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In our previous work (Reich, Szwed et al., 2011) we examined congenitally blind Braille readers with fMRI and found left ventral Occipito-Temporal cortex (vOT) activations for tactile reading versus touching nonsense Braille. The location of these activations was consistent with the location of Visual Word Form Area (VWFA), an area known to be activated by orthographical analysis of written words in sighted subjects. Our hypothesis is that the vOT in the blind performs a function analogous to the VWFA in the sighted. Here, we plan to test this hypothesis with the aid of an repetition supression paradigm. The series of experiments conducted by Glezer et al. (2009) has shown that the VWFA contains neural populations selective to orthographical difference as small as one letter (e.g. between "BOAT" and "MOAT"). In our experiment we would like to verify whether the same is true in the tactile modality, in congenitally blind readers. So, we designed analogous experiment but with Braille stimuli. Pairs of four-letter braille pseudo-words in tree experimental conditions were presented to congenitally blind expert readers. The preliminary results thus support our hypothesis that the vOT in the blind performs a function analogous to the VWFA in the sighted.

39. Are universal visual features necessary for reading? Preliminary results of a longitudinal study of visual Braille and Cyryllic alphabets' learners

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The "cultural evolution" hypothesis proposes that efficient reading is possible because all reading scripts were matched to natural capabilities of the visual cortex i.e. they rely on set of line-junctions and their combinations. Here we test a critical prediction of the "cultural evolution" hypothesis: reading atypical scripts (i.e. visual Braille) should be much less efficient than reading "normal" alphabets. We used a lexical decision task as a test of reading performance. We tested the speed and efficiency of Braille reading by eyesight – a skill common in sighted Braille teachers (N=29). As control, we decided to test learners of a natural visual script, Cyrillic (N=27) three times: before they started to learn and after three and six months of Cyryllic learning. Our preliminary results show visual Braille teachers). This is in clear contrast to a natural alphabet, where only three months of Cyrillic learning are sufficient to achieve relative proficiency. This suggests that certain visual features of the reading script might be necessary for efficient reading.

40. Eyes in your fingertips: reading process in the congenitally blind

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The mechanisms of functional specialization of particular sensory areas in the human brain and the extent to which they are fixed remain unclear. Words can be seen, heard or read by touch which makes the reading process a perfect tool to examine the functional specialization after life-changing events such as blindness. In sighted individuals, orthographical analysis of written words is carried out in the Visual Word Form Area (VWFA) an area in the left ventral occipito-temporal cortex (vOT). Interestingly, Braille reading in congenitally blind also activates the same brain region. Our hypothesis is that the vOT in the blind performs a function analogous to the VWFA in the sighted. We plan to test congenitally blind adults using the fMRI paradigm probing the details of orthographic processing, to establish whether the activation gradient in the ventral visual stream, corresponding to the one seen in the sighted, is found. Pilot results show that potential candidates for a "reading area" in the blind appear to be located in different brain regions (vOT/ Superior Temporal Sulcus/ Middle Occipital Gyrus). Our aim is to gain crucial insights on how the uniquely human cognitive architecture for reading is structured by sensory input and preexisting neuronal constraints.

41. Atypical processing of letters and speech sounds in children with familial risk for dyslexia: a functional magnetic resonance imaging study

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Learning letter-speech sound association is the first and critical step for reading development. Previous studies showed reduced responses to letters and speech sounds as well as no congruency effects in dyslexic subjects. Little is known however if such deficits are already present in children with familial risk for dyslexia (FHD+). 55 FHD+ and 41 FHD- children (mean age = 7 years) underwent fMRI scanning during which four experimental conditions were presented (letters, speech sounds, congruent and incongruent letter-speech sound associations). FHD+ children showed weaker activity for processing speech sounds in the left superior and inferior temporal gyri and in the left fusiform gyrus, while they had higher activity than FHD- children in the right intraparietal lobe and interior frontal gyrus. FHD+ children had also reduced activity for letters in the anterior temporal lobes bilaterally. Interestingly, in multisensory conditions, incongruent vs. congruent letter-speech sound association produced higher activation, observed for less transparent orthographies. In this condition FHD+ compared to FHD- children had significantly reduced activity mainly in the left tempo-parietal cortex. Our results suggest that some brain activity differences observed in dyslexic children and adults are already visible in beginning readers at risk of dyslexia.

42. Neural predictors of reading outcomes in beginning readers of Polish – a longitudinal fMRI study

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The neural predictors of reading gains were examined in 77 children entering formal education. At time-point 1 (TP1) reading and reading-related skills were assessed, whereas an fMRI localizer served to identify the neural substrates of speech (speech>vocoded speech) and print (print>false font). After a year (TP2) behavioral tests were repeated. Reading scores at TP1 and TP2 were positively correlated with phonological and orthographic awareness as well as with each other. However correlations between reading at TP1 and TP2 and neural response to print and speech showed only partial overlap For print, an overlapping positive correlation was observed in bilateral IFG, STG/STS and left fusiform, with additional bilateral calcarine and left IPL for TP1 and right fusiform for TP2 scores. Overlapping negative correlation was present in bilateral superior medial gyrus, left precuneus and middle orbital gyrus with additional insulae activation for TP2. For speech, better readers at TP1 had higher activation in the right precentral gyrus and bilateral STG, at TP2 in the left MTG. Negative correlations for print and speech with reading at both time-points supporting its multisensory integration role.

43. Lexical and semantic processing of polish language - a multimodal fMRI study

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The current neurobiological model of language processing suggests that a distributed cortical system is involved encompassing regions along at least two processing streams (Hickok and Poeppel, 2007). However, this model doesn't take into account linguistic processing difficulty and input modality at the same time. In present study we compare brain activity in Polish speaking subjects on two levels of language processing – lower (lexical) and higher (semantic) in two different modalities. 61 right-handed healthy females participated in the fMRI study. The experimental design was based on two tasks: Lexical Decision Task (LDT) and Grammatical Judgment Task (GJT) in two modalities (auditory and visual). In the LDT subjects had two decide whether presented word was a real word or a pseudoword. The GJT required the analysis of semantically correct (e.g. "sun shines") or deviated ("sun speaks") two-word phrases. The fMRI analysis revealed brain areas affected by task demands in left posterior superior and middle temporal gyri and and left inferior and middle frontal gyri. The left IFG and lateral temporal cortex (STG and MTG) involvement in semantic processing is in line with the meta-analysis of 120 fMRI studies (Binder et al., 2009).

44. The FN400 familiarity effects for concrete and abstract words

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Recognition memory depends on two neurocognitive mechanisms: familiarity and recollection. In studies using eventrelated potentials (ERP) they are reflected by the ["frontal N400"] (FN400) and the late parietal component (LPC), respectively. Recently, it has been argued that the FN400 is functionally identical to the classic N400 reflecting conceptual-semantic processing. There are claims that the frontal distribution of the FN400 is due to concreteness effects, the fact that concrete words or pictures (which are usually used in recognition memory experiments and yield frontal distribution on the scalp) can facilitate semantic processing. In the present study we tested this claim using a recognition memory paradigm in which subjects memorized concrete and abstract nouns; half of these words have changed font color between study and test. Frontally distributed FN400 effects were observed for both concrete and abstract words, contrary to the idea that word concreteness effects can explain anterior/posterior differences previously reported between the FN400 and classic N400. Instead, topographic differences were found in the domain of laterality, such that the false/new effect for concrete words was more right-lateralized than the false/new effect for abstract words. Surprisingly, the LPC hit/new effect was more frontally distributed for concrete than for abstract words.

COGNITIVE NEUROSCIENCE

45. Age differences in automatic perceptual integration - a visual mismatch negativity study

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Studies of age differences in visual perception reported slower information processing therefore increased sensory persistence in elderly. This may result in advantages in perceptual integration e.g. the unit formation from temporarily distinct parts. We conducted behavioral and event-related potential (ERP) experiments to investigate the automatic counterpart of the phenomenon. Stimuli consisted of two successive line-patterns which either formed a letter or a non-letter. The behavioural task was a two-alternative forced choice test with varied inter-stimulus interval (ISI) between the two parts of the stimulus (0, 20, 40, 80 ms). The ERP study applied passive oddball paradigm, the task-irrelevant stimuli (20% deviant) appeared in the screen center. The ISI between the two parts varied across sequences (0, 20, 40 ms). We applied control conditions with stimuli presented in one part. We hypothesized that if integration occurs visual mismatch negativity (vMMN) will be elicited to the deviant stimuli. In the behavioral part we found no age-related difference in integration. In the EEG study vMMN was registered in the control sequences in both age groups. In case of the elderly vMMN was elicited in the sequences with 0 and 20 ms ISI showing perceptual integration occurred at the automatic level.

46. Variability and replicability of the visual mismatch negativity

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The aim of our study was to investigate the intraindividual variation and the test-retest stability of visual mismatch negativity (vMMN) in response to windmill patterns presented in passive oddball sequence (deviant p = 0.1). Seven young subjects were participated in two highly similar recording sessions separated by 5 months. The results showed a good test-retest variability of the vMMN amplitude, especially in the early, 110-176 ms (r=0.83, p<0.01) and middle ranges, 212-244 ms (r=0.93, p<0.01). Intraindividual differences were moderate and quite consistent in the 106-138 ms interval (mean r= 0.57, SEM = 0.13), but showed considerable variation in the 156-194 ms time window (mean r = 0.22, SEM = 0.17). The results shows, that the early range of vMMN is more suitable for follow-up studies, possibly at the individual level also.

47. Modulation of electrophysiological correlates of auditory Go and NoGo responses: effect of gender and female sex steroid hormones

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Electrophysiological responses in Go/NoGo tasks serve objective measures of executive functioning. Prior to the wider application of Go/NoGo tasks in clinics, factors causing modulation of responses, like gender and level of sex hormones in females should be evaluated. 80 healthy volunteers (38 females and 42 males, Sample 1) and 34 females (Sample 2) at known menstrual cycle phases were enrolled. Subjects performed equiprobable (50/50) auditory Go/NoGo task. Amplitudes and latencies of N2 and P3 peaks from Fz, Cz and Pz electrodes were evaluated. 17 β -estradiol and progesterone levels in saliva samples were measured for Sample 2. N2 and P3 amplitudes were higher and latencies tended to be longer in females. The interaction between gender and electrode was observed for N2 amplitudes (higher N2 amplitudes in males over Pz) and a trend for P3 amplitudes was identified. No gender and task interaction was observed. With higher levels of 17 β -estradiol, Go-P3 latencies were prolonged and with higher levels of progesterone - NoGo-P3 latencies were shorter in Sample 2. Electrophysiological signatures of Go/NoGo differed between genders and were related to individual hormonal levels in females, pointing to a broader range of variation in healthy subjects potentially masking or pronouncing between-group differences in clinical studies.

48. The Electrophysiology of Familiarity and Recollection

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Recognition memory can be thought of as consisting of two processes, familiarity and recollection. Familiarity is responsible for recognition without context, while recollection is responsible for recognition with context. Since little is known about the electrophysiology of these processes, the aim of this study was to isolate ERP components and EEG oscillations involved in familiarity and/or recollection. We recorded EEG during a verbal memory task. In the encoding phase of the memory task, participants had to make a pleasantness judgement regarding the presented word. In the retrieval phase participants had to make a recognition-based old/new judgement followed by a confidence judgement. Results showed that the parietal old/new effect and theta power was related to recollection, and the FN400 component was related to familiarity. A greater response-locked ERP during encoding was related to subsequent recollection. The results of this exploratory study contribute to the disentangling of neuronal processes related to familiarity and recollection.

49. Neural mechanisms of maladaptive decision-making in state oriented people

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Action control is a theoretical construct describing individual differences in choice commitment and action implementation. It distinguishes people who flexibly and efficiently implement their decisions (action oriented) and people who have difficulty initiating action (state oriented). High levels of state orientation have a detrimental effect on overall well-being. State oriented people consider too many alternatives and have trouble terminating the decision process which leads to maladaptive hesitation and indecisiveness. We believe this effect can be conceptualized by dysfunctionally high and rigid threshold for choice commitment. Neural correlates mediating threshold flexibility involve fronto-parietal network and functional connections between key structures involved in cognitive control and action initiation. We present the outline of the study and preliminary results (N=20). In the first part of the project we aim to characterize the behavioral differences in perceptual and strategic decision making between the two groups. We will use three decision paradigms that quantify flexibility of decision threshold and speed of evidence accumulation, given varying probabilities and values of rewards in perceptual and strategic choices. These parameters can be extracted and quantified using sequential sampling models.

50. The relationship between cortical thickness and resting-state functional network properties

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Despite a growing number of studies concerning properties of the human brain structural and functional networks and development of new computational models, relationship between these two modalities remains unclear. The aim of this study was to examine correlation between various resting-state network's functional connectivity attributes (such as Global Efficiency, Local Efficiency and Modularity) with brain structure measured as cortical thickness. We demonstrate results of a preliminary analysis on a group of 10 participants. The data was analyzed using General Linear Model (GLM). Results show a positive correlation between mean cortical thickness values and modularity. We hope that further research on this field will provide us better understanding of the relation between brain's structural organization and functional network properties. This study was supported by a grant (2015/17/N/HS6/03549) from the National Science Center, Poland.

51. Different phenotypes of resting-state cognition: functional connectivity study

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Resting-state fMRI can be used to study functional connectivity of the brain not engaged in any explicit task. Our aim in this study was to quantify different dimensions of thought during rest and find their correlates with functional networks. Scans were collected from 35 participants during 6 min resting-state sessions, after which we asked them to fill out the Amsterdam Resting-State Questionnaire, a retrospective self-report concerning their subjective experience. The questionnaire was used to assess 10 dimensions of thought: Discontinuity of Mind, Theory of Mind, Self, Planning, Sleepiness, Comfort, Somatic Awareness, Visual and Verbal Thought and Health Concern. Functional networks were identified using Independent Component Analysis. Our findings include decrease of activity in the salience network for Somatic Awareness, decrease in the fronto-parietal network for Sleepiness and others. Reports on the subjective state of mind helped to explain variance in measured time courses. Correlating dimensions of thought to measures of functional connectivity can lead us to better understand the significance of different networks in the brain. This study was supported by a grant (2015/17/N/HS6/03549) from the National Science Center, Poland.

52. Frontal complexity: higher variability correlates with lower creativity and lower HRV

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Heart rate variability (HRV) reflects the change of time intervals between adjacent heartbeats. HRV is considered to be a good indicator of control over our health or psychological challenges. High HRV is associated with good health and well-being, while low HRV is related to pathological states. In order to investigate the relationship between HRV and creativity, a group of 28 young adults was tested with a computerized version of the Guilford's Alternative Uses Task (AUT): the idea AUT (iAUT), developed basing on previous work of Fink and colleagues (Fink 2009). Upon the task the participants were instructed to announce their idea by pressing an 'idea button' and reported it. Creativity levels were assessed with respect to their fluency (number of ideas) and originality. The EEG signal was recorded duringresting-state and the following iAUT task performance. The latter was analysed in epochs corresponding to the time period of idea generation. Complexity of bioelectrical activity was calculated using Higuchi's Fractal Dimension (HFD).Statistical analysis showed negative correlation between resting-state frontal HFD index and HRV. Moreover, complexity of the EEG signal recorded from the frontal and central regions of the scalpboth upon resting-state and task condition (idea generation) correlates negatively with creativity (originality).

53. Reconfiguration of brain subnetworks related to increasing cognitive effort

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Large-scale functional connectivity enables to investigate dynamical changes of brain networks during changing external demands. These networks can be divided into multiple distinct modules (subnetworks), which allow efficient information processing. Despite growing number of studies investigating functional networks, temporal changes of particular modules remains unclear. The aim of our study was to determine which modules play crucial role in whole brain network reconfiguration during changing difficulty level in standard n-back letter task. In order to address this question we used novel network based statistic (NBS) approach and graph theory measures applied to predefined network division. For increasing working memory load, we found disconnection of brain subnetwork consisting

mainly of regions belonging to default mode network (DMN). Furthermore, we found significant decrease of overall network modularity. This effect was a result of topological changes in DMN, cingulo-opercular and visual networks. Our findings suggest that whole network topological changes observed in other studies may arise as a result of connectivity decrease between DMN regions. Moreover, we provide evidence that changes of specific brain subnetworks can contribute to overall network modularity differences. This study was supported by a grant (2015/17/N/HS6/03549) from the National Science Center, Poland.

54. A matter of connectivity: Action video game training affected functional dependencies between cortical regions during resting state activity

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Study. Playing action video games, especially first person shooters is highly demanding for cognitive system. Recent studies suggest that there is a causal relationship between action game training and improvement across wide range of cognitive tasks. However, it is still unclear how this improvement might be reflected in connectivity pattern of resting state brain activity (RS). In this context, the aim of our study was to investigate whether action video game training affected functional dependencies (in particular synchrony) between cortical regions during RS.

Methods. We consider resting EEG data recorded from 19 women before and after training using video game. The control group (N =10) were women playing simple non-action game ("Neverball 3-D Puzzle Game"), while experimental group (N = 9) were women playing action game ("Unreal Tournament 3"). Phase locking between selected electrode pairs was calculated. Our approach is based on the Phase Locking Value as an average phase difference in time (Burgess, 2013).

Results. The study is expected to show the different synchrony maps across the groups. This will lead to knowledge about changes in dynamics of the synchrony between different regions of the brain caused by training using action games.

55. The cognitive training with the game "Kalkulilo" and mathematical abilities in children – the preliminary results of a pilot study

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The cognitive benefits of playing video games are widely proved and the use of computer technology to support learning has become popular. Several studies on the effect of this type of intervention on mathematical abilities provided promising results showing the positive outcomes, including counting skills, numbers recognizing and the spatial-numerical relationship. The aim of our study was to examine the effect of training with the use of computer mathematical game "Kalkulilo" on mathematical abilities in pupils aged 5-10. "Kalkulilo" is an educational tool that could be very useful for development and strengthening the processing of spatial-numerical association. The obtained results showed that training with the use of "Kalkulilo" did not improve an accuracy in any condition of number magnitude comparison task. However, after training we observed a reduction of response times in case of numbers presented in different formats (i.e. when dots vs. digits were compared). There were no significant differences found for numbers displayed in the same formats (digits vs. digits, dots vs. dots). This result may suggest that cognitive training using "Kalkulilo" supports the processing of mental representations of numerical magnitudes and switching between different notation of numbers, what may strengthen the number sense and mathematical skills.

56. Mental representations of the number magnitudes of simple and decimal fractions

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The SNARC (Spatial Numerical Association of Response Codes) effect is an example of the spatial-numerical relationship based on the Mental Number Line. It refers to faster left hand responses to low magnitude numbers and vice versa to high magnitudes and right-sided reactions. We investigated this relationship in case of fractions, both

simple and decimal. The participants were required to respond to the color of displayed fractions (the number magnitude of presented fractions was task-irrelevant). The trials were defined as congruent (in case of right/left response to high/low number magnitude of fraction) or incongruent (in a contrary case). The results revealed the SNARC effect for decimal fractions, however we found that this effect could be obtained only for fractions with one-digit numerator (e.g. 0,2 or 0,8). In the case of simple fractions the SNARC effect was obtained only for high magnitudes (e.g. ½ or ¼) as compared to low (e.g. 1/8). Additionally, we found that this effect is dependent on the proficiency in magnitude comparison skills. This results suggest the impact of experience in the spatial-numerical association development and that the spatial-numerical association is more pronounced in case of the fractions that we use more frequently in everyday practice.

57. No relation between leftward bias in gymnastic exercise and lateralized cognitive task performance

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We have measured performance asymmetry in a gymnastic exercise in male freshmen of the University of Physical Education in Krakow. The students performed series of jumps off the box. The distance from the target and lateral deviation were measured. We found a consistent group level leftward bias, inversely related to targeting precision. Attentional (pseudo-neglect) brain asymmetries have been hypothesized to be at play in similar behavioral asymmetries in sports. In an attempt at establishing the source of the leftward bias observed in our study we correlated the bias values with Nicholls' greyscales performance asymmetry and language asymmetry estimated with lateralized rhyme detection, as well as with a number of laterality measures. No meaningful correlations with measures of central asymmetry were found, which suggests that the side bias in jumping may be more of a peripheral than central character.

58. Battery Tests For Examination Cognitive Function - attempt to create a screening tool compared with the reference tool – preliminary reports

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The prevalence of cognitive impairment is increasing very fast all over the world. It is connect with the phenomenon of an aging society and the risk of dementia increases with age. According to Global Burden of Disease researches (2010) scientists have demonstrated that neurological diseases included dementia are the third cause of increasing amount of years when we are living with disabilities (YLD). Objective of the study was creating a shorter version of the tool using to screening cognitive disorders at people over 65 years old. This tool was create to finding alternative of paper tests with a view to significantly reduce the time the study and interpretation of the results. The study was attended by 73 people, with 46 people constitute a test group and a control group of 27 people. The inclusion criteria for the study group was the diagnosis of cognitive impairment made by the physician based on clinical diagnosis. Preliminary statistical analysis showed a correlation in the group of subjects between the results obtained in the computer-based test and the results obtained in the tests, which are tests of paper reference. In summary, preliminary results demonstrate the usefulness of the battery of tests for screening cognitive disorders. Using this tool may increase the detection of cognitive disorders including mild cognitive impairment at an early stage, and therefore affect the proceedings in the therapeutic process and improving the quality of life of people with dementia.

59. What does Baddeley's Grammatical Reasoning Test measure?

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The main aim of the study was to test validity of Baddeley's Grammatical Reasoning Test (BGRT) presented in the literature as a short general mental abilities test (GMA). In BGRT two letters and a sentence describing order of this letters are displayed on the screen, the participants' task is to read a sentence and decide whether it is true or not, e.g. A does not precede B - BA. TRUE/FALSE. BGRT consists of 64 combinations of sentences created according to 6 conditions: positive or negative, active or passive, true or false, precede or follow, A or B as a first letter in a sentence, a pair of AB or BA. There are 3 minutes to complete as many sentences as possible. To test BGRT validity we conducted

it with battery of cognitive abilities tests on a group of 42 students (M age=20). The tests that significantly correlate with BGRT were mean time of correct answers in WAIS-Digit Substitution Task (r=0,31) and accuracy in N3-back task (r=0,34). There was no significant correlation between BGRT and working memory capacity measures AutoOspan (r=0,03); SymmetrySpan (r=0,08), N2-back task (r=0,23), as well as fluid intelligence - 10min Raven Progressive Matrices (r=0,19). These results may suggest that BGRT is rather information speed processing measure than GMA test.

60. Accuracy of methods for measuring spatial memory in elderly

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Spatial memory is an ability which allows to remember object location, to navigate or to orientate in the environment. Apart from its great role in everyday life, spatial memory is considered to be a marker of dementia. Previous research prove that Paired Associates Learning from Cantab battery and Benton Visual Retention Test are accurate tests for measuring the pathological senile changes. We examined 22 healthy women aged over 64 in three conditions: (1) Standard Benton Visual Retention Test (2) Standard neuropsychological tests from Cantab battery (3) Non-standard, ecological navigation test (Koening et al., 2010). Age of subjects were used to assign them to younger or elder group (M=69). Results show that women who belonged to younger group had significantly less errors and higher correctness in Cantab tests (p<0,05). Furthermore correlation between age and scores in BVRT (r=0,49) and navigation tasks (r=0,50) were found. Our results indicate that all of the tests are sensitive in detecting differences between groups. However the accuracy of ecological tool in testing navigation is particularly important, because this aspect of spatial memory is considered as one of the first sign of early stages in Alzheimer's disease.

61. Differences in spatial memory in women

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Spatial memory is considered to be a strong marker of dementia. Despite of its role in diagnosing Alzheimer's disease, still there is no standard method for measuring all its aspects, including navigation which requires movement in the environment. In our research we tested two groups of participants: young (under 30 years old) and elder (over 65 years old) healthy woman (n=24). For better understanding the complexity of spatial memory, we chose standard (computer tests from CANTAB battery, Benton Visual Retention Test) and non-standard (virtual maze and ecological tasks in the building) methods. In both non-standard tasks memory were tested with and without postponement. Analysis showed that younger women have significantly less mistakes in both standard tests (p<0,05). The lower scores at elderly have been noticed after half an hour interval in ecological test (p<0,01), and similarly in the virtual labyrinth. Additionally strong correlation between scores from BVRT, virtual maze and ecological task were found. The different results of standard and non-standard tests can indicate that younger and elder women cannot vary in tasks which include everyday items and movement. The implementation of new devices and maintaining task in a memory for a longer time can be more difficult for elderly.

POSTER SESSION II

NEUROPSYCHIATRY

1. Alterations in BDNF level in the frontal cortex of suicide victims are associated with NMDA and AMPA receptors changes

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There is evidence for an association between suicidal behavior and depressive disorders. Numerous studies indicate that the pathogenesis of depression is related with disturbed glutamatergic neurotransmission in the brain, and that the number and activity of NMDA and AMPA receptors may be crucial for the dynamics of neuroplasticity processes in the brain. The aim of study was to investigate the level of NMDA (GluN1, GluN2, GluN2B) and AMPA (GluA1, p-S831-GluA1, p-S845-GluA1) subunits, cAMP-response element-binding (CREB, phospho-Ser133-CREB), BDNF and postsynaptic density protein 95 (PSD-95) in the frontal cortex of suicide victims (n=17) and sudden death controls (n=6) using Western blotting. Our analysis revealed that there was a statistically significant decrease in the protein level of GluN2B (by 35%) and p-S831-GluA1 (by 21%) in the frontal cortex of suicide victims relative to the controls. These alterations were associated with decreases in both the BDNF (by 42%) and PSD-95 (by 38%) levels. Obtained results indicate that the changes in the NMDA subunits levels and AMPA modifications (recorded as a decrease of GluN2B and p-S831-GluA1, respectively) are potentially involved in the pathophysiology of suicide-related disorders (including depression), which may lead to synaptic plasticity and neurogenesis disturbances. This study was partially supported by grant UMO-2013/09/D/NZ7/02520

2. Enhancement of the anti-immobility action of antidepressants by ADN-2013 in mice

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Schizophrenia is a severe debilitating mental disorder affecting about 1% of global population. About 30% of schizophrenic patients meet the criteria of concomitant mood disorders what is considered to be a great clinical problem in terms of optimalization of pharmacotherapy. The study was aimed at assessing the potential ability of a novel mulireceptor acting compound ADN-2013, an aripiprazole analogue, with antipsychotic- and antidepressant-like activity to facilitate the antidepressant effect of reference drugs in the forced swim test in mice. As a comparator aripiprazole was used. ADN-2013 administered at a subeffective dose of 0.625 mg/kg enhanced the anti-immobility action of reference antidepressants, i.e. imipramine, reboxetine, S-citalopram and moclobemide, given at their ineffective doses (reduction of the immobility time from 24% to 86%). In comparison, aripiprazole at inactive doses of 0.03 and 0.06 mg/kg, significantly enhanced the antidepressant-like effect of subeffective dose of inipramine (34% and 45%, respectively), S-citalopram (32 and 39%, respectively) and reboxetine (29% only at a dose of 0.03 mg/kg), without an influence on moclobemide action. ADN-2013 may facilitate anti-immobility activity of antidepressants, presenting different mechanism of action. The observed activity of ADN-2013 is more extensive than that of aripiprazole, suggesting its potential application in adjuvant treatment of depressive states.

3. Short alcohol sensitization induce increased alcohol seeking and leads to functional changes in the central amygdala

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Alcohol is a psychoactive substance which regularly abused leads to alcoholism. Animal models provide the opportunity to study alcohol abuse and indicate new pathways of addiction therapy. In our study we investigated the behavioral and physiological consequences of the short-term alcohol treatment. C57BL6/cmdb mice were treated with saline or ethanol for 7 days and their locomotor activity was measured after withdrawal. Such short alcohol exposure induced long-term sensitization of locomotor response observed after 7-day withdrawal and persisting for 30 days. Molecularly alcohol sensitization decreased the expression of glutamatergic markers in the central and basolateral amygdala, indicating remodeling of the glutamatergic synapses. Furthermore, the whole cell patch-clamp experiment showed that alcohol sensitization led to decreased AMPA/NMDA currents ratio in BLA-CeM pathway indicating reduced glutamatergic transmission. In order to investigate the long-term behavioral consequences of alcohol short pretreatment we used the IntelliCages which allow for monitoring alcohol self-administration and alcohol-related behaviors in freely behaving mice. Mice pre-conditioned with alcohol did not differ in alcohol consumption, however they showed higher motivation for alcohol and alcohol seeking during withdrawal and cue relapse. Overall, our study indicates that short alcohol exposure leads to functional changes in the central amygdala and long-term increase in alcohol seeking.

4. Emerging role of chronic fluoxetine administration on the fractalkine signaling in the brain of adult prenatally stressed animals

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Recently, a lot of attention is focused on fractalkine (CX3CL1)/fractalkine receptor (CX3CR1) system in brain. Data suggested that disturbances in this axis during neurodevelopment may cause long-term behavioral changes in adult animals. In the present study we investigated the impact of prenatal stress procedure on behavioral parameters and on CX3CL1/CX3CR1 gene expression in the brain areas of adult offspring rats. Moreover the impact of chronic treatment of fluoxetine on the above-mentioned parameters was evaluated. Pregnant rats were subjected to restraint stress. At 3 months of age, after behavioral verification, rats were chronically treated with fluoxetine. After 2 weeks the animals' behavior were tested again and the gene expression of CX3CL1/CX3CR1 was measured by qRT-PCR assay in hippocampi and frontal cortices. The study confirmed that adult offspring rats after prenatal stress procedure exhibit behavioral disturbances. Biochemical study showed significantly lower expression of CX3CL1 and CX3CR1 in both brain areas in prenatally stressed offspring. Chronic treatment of fluoxetine normalized behavioral disturbances and gene expression of both analyzed proteins. Our study showed that beneficial property of fluoxetine on the behavioral disturbance may be related to its impact on the brain fractalkine signaling. Acknowledgements: Supported by the grant no. 2013/09/B/NZ7/04096, National Science Center, Poland.

5. Behavioral aspects of chronic administration of caffeine

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Caffeine, a non-selective adenosine receptor antagonist, is the most widely used behavioral active drug in the world. Research data indicate that caffeine can reverse the monoaminergic system changes observed in depression. The main goal of the present study was to evaluate the influence of caffeine chronic administration (5 and 10 mg/kg) on animals' behavior in the forced swim test (FST) and tail suspension test (TST). Locomotor activity was estimated to verify and exclude false positive/negative results. The results showed that caffeine at doses of 5 and 10 mg/kg administered twice daily for 14 days did not affect the mice behavior in FST and TST. Caffeine at a dose of 10 mg/kg given 40 min before the test after chronic administration of caffeine also at a dose of 10 mg/kg resulted in a significant shortening of the immobility time in both FST and TST. Such changes were not observed in the case of the use of caffeine at a dose of 5 mg/kg in the same treatment schedule. Chronic treatment with caffeine at the tested doses had no significant effect on mice locomotor activity. The obtained results suggest that caffeine might be useful in the treatment of depression.

6. Effects of glucocorticoid receptor stimulation on morphine intake in high and low responsive mice

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Behavioral responsiveness to the novel environment, used as a model of novelty-seeking, was found to be a predictor of drug addiction. Glucocorticoid (GR) responsiveness seem to underlie behavioral differences between high and low responders to novelty (HR/LR). The aim of the present study was to evaluate effects of GR stimulation on morphine intake in mice classified as a HR or LR. C57BL/6J mice were defined as a HR or LR according to their responsiveness in a various behavioral tests. After phenotyping procedure, behavior of the mice was monitored by the IntelliCage system. We behaviorally challenged animals to test for symptoms of compulsive morphine drinking. What is more, we observed the effects of GR agonists treatment (dexamethasone 4mg/kg; corticosterone 10mg/kg) on morphine intake. HR compared to LR mice self-administered more morphine and exhibited symptoms of increased craving measured in intermittent access paradigm. Dexamethasone treatment resulted in significant increase of morphine intake in HR mice, when compared to LR. Corticosterone treatment caused similar effects in both groups. The results indicate that our model of novelty-seeking may be effective way to understand individual differences in vulnerability to addiction. Moreover GR receptor seems to be involved in modulating morphine intake according to phenotypic differences.

7. Glucocorticoid receptor signaling in astrocytes mediates the acquisition and extinction of contextual aversive memory

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Alterations in glucocorticoid receptors (GRs)- dependent function are thought to be the key factor of development of various stress-related disorders. Increasing evidence points to the important role of astrocytes in mediating GR-dependent effect in the brain, however the exact mechanism of their contribution remains unclear. Here, we investigate a transgenic mouse model where GR is selectively ablated from astrocytes expressing connexin 30 (Cx30). The expression of GR-dependent genes after GR stimulation in mutant mice was weakened in hippocampus, hypothalamus and spinal cord. Mutant mice presented similar locomotor activity to controls in open field test, responded similarly in memory tasks: novel object recognition test and Y maze test. Moreover, no changes were found in depressive-like symptoms measured by saccharin preference test and tail suspension test, indicating that basal behavior of the animals remained unchanged. However, mutants were less immobile than control animals when subjected to stressful context in fear conditioning paradigm (foot shock, 4 retrieval sessions) indicating accelerated extinction of contextual fear memory. What is more, mutants did not acquire conditioned place aversion (naloxone). In conclusion, our data bring the first evidence for the causative role of GR-dependent signaling in astrocytes in central effect of stress. Support: Polish National Science Centre Grants 2013/08/A/NZ3/00848, 2011/03/B/NZ3/01683, 2011/03/B/NZZ/02479.

8. Alterations in phospholipid-protein profile in the serum of rats subjected to the chronic mild stress procedure

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The neurobiological bases of depression are poorly understood, but abnormalities in the neural proteins function and peptides activity seem to be crucial for its development. Lipids (especially phospholipids) define the placement and function of membrane proteins and regulate synaptic throughput in neurons. In this study we examined the alterations in the phospholipid-proteins balance induced by chronic mild stress (CMS; animal model of depression) and antidepressant (AD) treatment in the blood serum of rats using Raman, Fourier Transform Infra Red, and UV-Vis spectroscopy. Moreover, the level of lipid peroxidation (measured as TBARS) was evaluated. Results showed that CMS decreases both the phospholipids and proteins levels in the serum, which was accompanied by an increase in TBARS level. 5-weeks imipramine (10 mg/kg) administration did not influence (compared to control stressed rats) the phospholipid profile and TBARS level, but increasing slightly the one of proteins. UV-Vis spectroscopy combined with the second derivative calculated from the FTIR spectra provided information that the proteins (but not phospholipids) in blood serum of stressed rats were normalized after AD. Our findings suggest that CMS (main cause of depression), may induce permanent (irreversible) damages of the phospholipid structure, which may be a consequence of intensification of oxidative processes. The study partially supported by grant DEC-2013/09/D/NZ7/02520.

9. Suppression of cocaine-induced conditioned place by ceftriaxone

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According to European Drug Report from 2015 13% of all reported patients entering specialised drug treatment cited cocaine as the main drug taken. Nevertheless, it lacks FDA approved drug that would be effective for cocaine addiction treatment. Moreover, recent literature data indicate that decreased expression of glutamate transporter EAAT2 in the addict's brain due to cocaine administration may underlie drug abuse and addiction. Based on these reports we aimed to investigate if ceftriaxone, an antibiotic with power to increase EAAT2 expression in brain, would be effective in reversion of cocaine-induced conditioned place preference in rats. To achieve this goal we used male Wistar rats (n=40) which underwent 12-day unbiased conditioned place preference procedure (CPP) with cocaine (15

mg/kg;i.p.). After the completion of conditioned place preference animals received injections of ceftriaxone (200 mg/kg, i.p., once a day) for 7-days and 24 h after last injection they were re-exposed to conditioned place preference test. Our results showed that ceftriaxone suppressed cocaine-induced conditioned place preference in 80% of treated animals in the re-exposure to CPP. In the future, we plan to investigate how the level of EAAT2 changed both in animals that respond to treatment and in those that were resistant to it. The study was supported by research grant from the National Science Centre Poland No.UMO-2013/11/N/NZ7/01617.

10. The influence of glucagon-like peptide-1 receptor agonists on corticotropin-releasing hormone promoter gene in a hypothalamic cell line

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Reports indicate a distinct role of glucagon-like peptide (GLP-1) as a brain modulator of neuroendocrine processes, emphasizing its implication in hypothalamic-pituitary-adrenal (HPA) axis activation. Considering that chronic HPA axis activation is an important factor in the pathogenesis of depression which can also stimulate type 2 diabetes development in some depressed patients, the aim of the present study was to determine the effect of glucagon-like peptide-1 receptor (GLP-1R) agonists, on the regulation of corticotropin releasing hormone (CRH) gene expression. Experiments were conducted on hypothalamic cell line: mHypoA-2/12 which was stably transfected with a plasmid DNA containing the sequence (from -663 to +124 bp) of human CRH promoter gene conjugated with luciferase reporter gene. The cells were treated with GLP-1 and its stable analogue: exendin-4 (10 nM) for 6 and 24 hours. Reporter gene activity was determined by measuring chemiluminescence based on the reaction of luciferin oxidation, accompanied by light emission. Both exendin-4 and GLP-1 significantly influenced the activity of the reporter gene, thereby showing their influence on CRH gene promoter sequence. Obtained results strongly suggest that GLP-1 receptor agonists may have the ability to modulate the activity of HPA axis on the hypothalamic level. This work was supported by grant 2012/07/N/NZ7/04394; National Science Centre, Poland.

11. Effects of acute and repeated administration of escitalopram on binding of [3H]CP55,940 to cannabinoid (CB)1 receptors in rat brain structures

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Depression is one of the most frequent causes of disability in the 21st century. The potential participation of the endocannabinoid system in the pathogenesis of depression and in the mechanism of action of antidepressants has been highlighted in recent years. The aim of this study was to investigate the effect of the clinically effective antidepressant - escitalopram (ESC, 10 mg/kg) on the cannabinoid (CB)1 receptor labelling pattern in selected rat brain structures. Male Wistar rats received ESC intraperitoneally acutely and chronically for 14 days. Twenty four hours after the last drug administration the animals were decapitated and their brain CB1 receptors were analyzed by quantitative autoradiography using [3H]CP55,940. Acute and repeated administration of ESC decreased the levels of [3H]CP55,940 binding in the laterodorsal striatum. Significant increases in [3H]CP55,940 binding were seen in the cortical brain areas, including motor cortex (I-III layers), prelimbic cortex (I-III layers), infralimbic cortex and cingulate cortex, after chronic ESC administration. Our data confirm the potential engagement of CB1 receptors in the effects of ESC, but a more detailed explanation for the underlying mechanism of such an association requires further investigation. The study was supported by the research grant UMO-2012/05/B/NZ7/02589 from the National Science Centre, Kraków, Poland.

12. Pro-cognitive effects of arylsulfonamide derivatives of (aryloxy)ethylpiperidines, the 5-HT7 receptor antagonists, in novel object recognition test

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Impaired cognitive process constitute an integral part of central nervous system (CNS) disorders including depression and schizophrenia. Several preclinical studies revealed that 5-HT7 receptor antagonists may produce beneficial procognitive effects in animal models of cognitive decline. The selective blockade of 5-HT7 receptors may be a potential

target for cognitive improvement in CNS disorders. The novel object recognition (NOR) test for rodents has been increasingly used as an ethologically relevant paradigm for studying visual episodic memory. This task is based on spontaneous exploration of novel and familiar objects. Successful object recognition is demonstrated by a longer time spent interacting with the novel object at the retention trial. NMDA receptor-based models are commonly used to mimic some symptoms of schizophrenia in laboratory animals. Acute administration of phencyclidine (PCP) evokes a broad range of schizophrenia-like symptoms, including cognitive impairment. The aim of present study was to evaluate the effects of the 5-HT7 receptor antagonists, the compounds PZ1404, PZ1140 and PZ1371 (arylsulfonamide derivatives of (aryloxy)ethylpiperidines) on a phencyclidine-induced deficits in novel object recognition test in rats. The acute administration of PCP attenuate a learning and this was reversed by co-administration of compounds PZ1404, PZ1140 and PZ1371. This effect was similar to SB-2699670, whose efficacy was demonstrated before in PCPinduced learning impairment in rats. These findings warrant further studies to explore the therapeutic potential of a new class of 5-HT7 receptor antagonists for the treatment of cognitive deficits in CNS disorders. This study was supported by the National Science Center Grant No DEC-2012/05/B/NZ7/03076 and by the Statutory Funds of the Institute of Pharmacology, Polish Academy of Sciences.

13. Opioids and glucocorticoids regulation of conditioned fear response in mice

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Both glucocorticoids and opioids play a crucial role in the stress response. However, their interactions in fear memory processing are incompletely understood. Here, we aimed to investigate the contribution of opioid and glucocorticoid receptor ligands to fear responses in a mouse model of contextual fear conditioning (5 mild footshocks: 0.3 mA, 1 s each). Mice were injected with drugs on conditioning day and during three consecutive tests - retrievals. As a fear memory expression, freezing behavior was measured. Pretreatment with opioid antagonist naltrexone (NTX, 2 mg/kg) led to an increase in freezing, indicating an involvement of endogenous opioids in adaptation to stress conditions. In order to assess interactions between opioid and glucocorticoid systems, we investigated whether the level of freezing after NTX injection can be modulated by glucocorticoid receptors (GR) stimulation. GR agonist dexamethasone (DEX, 4 mg/kg) administered after tests had no effect on freezing reaction induced by mild footshocks. However, DEX attenuated naltrexone-induced high conditioned fear. Thus, it appears that effect of opioid blockade on conditioned fear response can be partly inhibited by GR stimulation. The obtained results indicate an interplay between glucocorticoid and opioid systems. It seems that glucocorticoids may modulate effect of opioid blockade under stress conditions.

14. Influence of chronic administration of caffeine on the effect of atypical antidepressant drugs

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Due to the widespread presence of caffeine in non-alcoholic beverages, stimulating dietary supplements, as well as analgesic drugs, it seems to be important to look into the problem of simultaneous consumption of caffeine products and treatment with antidepressants. Therefore, the main objective of our study was to investigate the influence of chronic administration of caffeine (5 mg/kg twice a day for 14 days) on the activity of an acute, and per se inactive, dose of agomelatine (20 mg/kg) or mianserine (10 mg/kg), i.e. the atypical antidepressant drugs. The forced swim test (FST) and the tail suspension test (TST) were used in order to assess the antidepressant-like effect in mice. 14day treatment with caffeine at a dose of 5 mg/kg did not change mice behavior either in the FST or TST. However, the same dose of caffeine given chronically considerably potentiated an effect of a single injection of agomelatine in both applied tests. The significant interaction between prolonged administration of caffeine and acute administration of mianserine was demonstrated in the FST, whereas it was not detected by the TST. Our findings suggest that the clinical outcome in patients receiving an antidepressant therapy may be influenced by daily caffeine intake.

15. Optimistic rats are willing to risk; a role for dopamine

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Although cognitive theories have implicated cognitive judgment bias (optimism/pessimism) in psychopathology of different mental disorders, the role of optimism in risk-based decision making remains relatively unexplored. The

present study investigated the effects of traits optimism/pessimism on risky choice using two recently developed behavioural paradigms in rats. Initially the animals have been trained and tested in the rat version of the probabilistic discounting task, where over discrete trials, rats chose between two levers; 'small/certain' lever always delivers one reward pellet while 'large/risky' lever delivers four pellets, but with various probabilities. Subsequently, the rats were re-trained and evaluated in a series of ambiguous-cue interpretation tests, what allowed classification of animals displaying 'optimistic' and 'pessimistic' traits. As dopamine has been implicated in both investigated processes, in the last experiment we compared reactivity of dopaminergic systems of 'optimistic' and 'pessimistic' animals using apomorphine sensitivity test. The results of our study demonstrated that together with increased risk, the proportion of risky lever choices decreases significantly slower in the animals classified as 'optimistic' compared to 'pessimists' and that these differences are associated with different reactivity of dopaminergic system to apomorphine challenge. Our findings highlight a link between cognitive judgment bias, risky decision-making and dopamine. This work was supported by the National Science Centre (Research grant: OPUS-2014/13/B/NZ4/00214) and the statutory funds of the Institute of Pharmacology Polish Academy of Sciences.

16. Cognitive and motivational implications of cognitive judgment bias measured in attentional set shifting test in rats

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We have demonstrated recently that cognitive judgment bias (CJB, optimism/pessimism) may determine different cognitive and motivational processes in animals. Present study has been designed to investigate of whether CJB could determine cognitive flexibility of rats measured in the attentional set shifting test (ASST). For this, initially we subjected group of rats to a number of ambiguous-cue interpretation tests what allowed classification of single animals as 'optimistic' and 'pessimistic'. Subsequently the animals were trained in ASST procedure. Additionally, half of the rats was subjected to chronic restraint stress lasting 2 weeks. The effects of traits optimism/pessimism and chronic stress on cognitive flexibility were measured in the ASST in one week intervals along the entire experiment. Although we did not observe statistically significant effects of the investigated traits and stress on cognitive flexibility (probably due to the relatively small group numbers), the optimistic and pessimistic animals differed significantly in their motivation to approach experimental rewards (significantly shorter latencies). Results of the present study along with our previous reports, indicated clearly that traits 'optimism' and 'pessimism' could determine animals' motivation. Further studies on the effects of CJB on cognitive flexibility are in progress. This work was supported by NCN grant: OPUS-2014/13/B/NZ4/00214.

17. Modeling co-existence of depression and cocaine addiction in rats: the effects of N-acetylcysteine on cocaine extinction and seeking behavior in bulbectomized rats

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Several clinical reports indicate a high comorbidity between depression and substance abuse disorders. One of the leading hypotheses explaining this correlation called 'self-medication'. Depressed patients may use addictive substances to feel better and reverse anhedonia and/or unhappiness. The present study investigated the effects of N-acetylcysteine in rats underwent olfactory bulbectomy (an animal model of depression) and cocaine self-administration procedures. Male Wistar rats with implanted catheters intravenously and with olfactory bulbs removal (OBX) or SHAM-operated controls were trained to self-administer cocaine (0.5 mg/kg/infusion). Later on, extinction procedures (10 days) were instituted in witch animals were exposed on the chambers without cocaine delivery or drug associated cue. In this phase the animals were given N-acetylcysteine (100 mg/kg, ip) before each daily session. Reinstatement of cocaine seeking was induced by cocaine (10 mg/kg, ip) or contextual cues (tone + light) previously paired with cocaine self-administration. Our findings indicate that repeated treatment with N-acetylcysteine attenuated the cocaine seeking behavior evoked by either cocaine priming dose or the drug-associated conditioned cue in SHAM animals. In conclusion, we suggest that N-acetylcysteine may be effective in patients suffering from cocaine use disorder, but not in patients with comorbit depression and cocaine addiction.

18. Paroxetine and risperidone influence the level of heterodimers of dopamine D2 and serotonin 5-HT1A receptors in brain cortex neuronal cells

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Background of the study: The aim of the study is to investigate heterodimerization of dopamine D2 and serotonin 5-HT1A receptors after paroxetine and risperidone treatment, which are often combined in therapy of obsessive-compulsive disorder.

Methods: Mouse brain cortex primary neural cells was cultivated for 14 days. Heterodimerization of D2 and 5-HT1A after paroxetine and risperidone was evaluated by Proximity Ligation Assay (PLA), which enables to detect, visualize and quantify the heterodimers. As a negative control, D2 expression was silenced with Accell siRNA (Dharmacon). Additionally, immunocytochemistry with markers for astrocytes and neurons (i.e. GFAP and NeuN) was performed. Results: After 1 day of combined paroxetine and risperidone treatment, the decrease in the level of D2 and 5-HT1A heterodimerization was observed.

Conclusions: D2 and 5-HT1A receptors can form heterodimers on neural cells. Paroxetine and risperidone seem to act synergistically on the level of D2/5-HT1A heterodimers.

The study was financially supported by National Science Center Grant PRELUDIUM UMO-2012/05/N/NZ7/00664.

19. GABA transporters as targets for the antidepressant-like action

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Background: Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the mammalian central nervous system. In contrast to its thoroughly investigated physiological functions comprising sedative, hypnotic, anxiolytic-like and anticonvulsant effects, little is known about the role of GABA in the regulation of mood disorders, in particular depression.

Methods: To establish a potential role of impaired GABAergic neurotransmission in depression, we used tiagabine, a selective GABA transporter subtype-1 (GAT1) inhibitor, and four novel, non-selective GAT1-4 inhibitors (GAT affinities ranging between 4,57-21,88 μ M). CD-1 and C57BL/6 mouse strains and two behavioral assays were used: forced swim test (FST) and tail suspension test (TST).

Results: In FST tiagabine was the most efficacious drug of all. In contrast to FST, in TST tiagabine was not active, while other compounds significantly reduced immobility.

Conclusions: Our results indicate that GABAergic neurotransmission is implicated in the regulation of mood. Noteworthy, both mouse models of depression are variously sensitive to selective or nonselective GAT inhibitors. Taking into consideration that all four GAT isoforms are differentially expressed in the brain, our results may suggest that distinct GABAergic neural circuits are involved in the antidepressant-like effects observed in FST and TST models. Supported by National Science Centre grant (DEC-2012/05/B/NZ7/02705).

LEARNING AND MEMORY

20. The role of alpha 7 nicotinic acetylcholine receptors in the modulation of attention in rats

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Attentional impairments are related to several psychiatric conditions, including schizophrenia and Alzheimer's disease. Nicotine can improve attentive behaviour in animals and humans, but the role of α 7 nicotinic ACh receptor (α 7nAChR) in attention is contentious. It has been suggested that proattentive action of nicotinic compound may be revealed preclinically only under specific task conditions. The aim of the present study was to investigate the effects of α 7nAChRs positive allosteric modulator (PAM), PNU120596 in comparison to nicotine on attention in rats in the 5 choice serial reaction time test (5CSRTT). Rats were trained in modified 5CSRTT protocol (lack of punishment for premature responses), until they had achieved stable performance. Animals were then injected with 1 and 3 mg/kg of PNU120596 or 0.2 mg/kg of nicotine 30 or 10 min before testing, respectively. To increase the attentional demands of the task, a variable inter-trial interval (vITI: 10, 7.5, 5 and 2.5 s) was introduced on a drug testing day. Treatment with PNU120596 (3 mg/kg) and nicotine selectively increased accuracy and did not affect any other task parameters. Our previous data obtained with standard protocol have shown no effect of α 7nAChR ligands on attentional performance. However, employment of a modified procedure revealed the proattentive action of this class of compounds. This findings suggest a possible role for α 7nAChR in attentional processing. This study was supported by the Polish

National Science Centre grant NCN 2012/07/B/NZ/01150 and grant NCN 2014/15/N/NZ7/02978. Agnieszka Potasiewicz is a holder of scholarship from the KNOW sponsored by Ministry of Science and Higher Education, Republic of Poland

21. Molecular changes of the area CA1 of the dorsal hippocampus during fear memory extinction

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Context fear conditioning is a form of associative learning in which the aversive stimulus is associated with the new context. Extinction training, in which a previously trained animal is exposed to the context without presentation of the aversive stimulus, results in reduction of conditioned fear responses. To investigate what regions and molecular processes contribute to the context fear memory extinction, we studied the involvement of the dorsal hippocampus CA1 area in this process. We found that in mice after fear memory extinction the levels of PSD95 decreased in most layers of the CA1. Furthermore, fear extinction resulted in decreased dendritic spines density in the stratum oriens and their shrinkage in the stratum lacunosum moleculare of CA1 neurons. Since decreased expression of PSD95 suggests its degradation and region inhibition we applied pharmacological and chemogenetic manipulations to test the role of functional inhibition of CA1 in memory extinction. Firstly, we found that injection of lactacystin (proteasome inhibitor) into dorsal hippocampus after fear extinction training promoted memory extinction. Next, we stimulated dorsal hippocampus with DREADD-CNO system during extinction session which prevented memory extinction. Overall, our data suggests that context fear memory extinction involves inhibition of the dorsal hippocampus and require controlled protein degradation.

22. Exogenous IL-1β mimics the effects of repeated restraint stress on the excitatory synaptic transmission and long-term potentiation in the rat frontal cortex

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Introduction: Previous studies indicate that stress induces an increase in the proinflammatory cytokine interleukin-1 β (IL-1 β) level in the brain. Some of the effects of stress could be blocked by intrahippocampal or intracerebroventricular infusions of interleukin-1 receptor antagonist. Moreover, behavioral effects resembling those of stress, could be mimicked by the administration of exogenous IL-1 β .

Aim: The aim of this study was to investigate if the effects of repeated restraint stress on the excitatory synaptic transmission and long-term potentiation (LTP) in the rat frontal cortex could be mimicked by exogenous IL-1 β .

Methods: Rats of the restraint stress (RS) group were restrained for 10 min, 2 times daily for 3 consecutive days. A separate group of animals received intraperitoneal injections of IL-1 β also 2 times daily for 3 consecutive days. The effects were studied ex vivo. Extracellular field potentials (FPs) were recorded from frontal cortical slices and LTP induction was attempted using standard protocols.

Results: Both, restraint stress and intraperitoneal injections of IL-1 β result in an increase in the amplitude of FPs and in a reduced potential for LTP in the frontal cortex.

Conclusions: These results suggest that exogenous IL-1 β exerts the effects which closely resembled those of the stress.

23. Amphetamine increases the impulsivity, but does not change the gambling strategy in the rat Iowa Gambling Task

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Pathological gambling (PG) is a form of behavioral addiction. Both substance and behavioural addictions are characterized by the impairment in decision-making processes and impulsive responding. These components of PG can be investigated in a rat Iowa Gambling Task (rIGT). It has been shown that dopaminergic systems are critically involved in the development and maintenance of addictions, including PG. Therefore, we investigated whether amphetamine, a compound that impacts on the DA systems, could alter gambling behaviour in rats. We employed a novel model of PG in rodents, called the rat Iowa Gambling Task. In this task, the rats are trained in the skinner boxes.

The animals choose among four nose-poke holes which differ in the amount of reward they provide, and in the probability and duration of punishing time-out periods, during which the reward cannot be earned. Subjects were trained to earn as many sugar pellets as possible within 30 min. After reaching a stable baseline, the test was performed. Amphetamine was administered at 1mg/kg, I.P., 10 minutes before the test. We report that amphetamine at a dose of 1mg/kg statistically increased the number of premature responses. The compound, however, did not change the pattern of aperture choices. This suggests that amphetamine do not impact on the choice of optimal strategy in this gambling task. [1. Dominik Rafa is a holder of scholarship from the KNOW sponsored by the Ministry of Science and Higher Education, Republic of Poland. 2. Supported by the statutory funds of the Institute of Pharmacology].

24. Effect of clozapine on ketamine-induced cognitive impairments in mice

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Important feature of schizophrenia is cognitive impairment. Atentional set-shifting task (ASST) is often used to model cognitive deficits in rodents. In that test, mouse has to learn to pay attention and respond to the relevant cue (i.e., digging medium) and ignore an irrelevant cue (i.e., odor), and pairing a food reward with the medium. In the crucial phase (Extra Dimension Shift, EDS) leading dimension (i.e. digging medium) is changed and then the odor becomes a new leading dimension. Ketamine evokes cognitive impairments, observed in the ASST as selective deficits of mice EDS performance. Therefore, modulation of the behavioral effects induced by ketamine in ASST provides good animal model to study the mechanism of action of antipsychotic agents. Our goal was to investigate if clozapine, as atypical antipsychotic, could reverse ketamine–induced impairments and improve cognitive function. Ketamine in a dose of 20 mg/kg was administered i.p. for 7 consecutive days, then exchanged for clozapine (0.3 and 1 mg/kg i.p.) for next 7 days. ASST was performed following 14 days of drug administration. Additionally, locomotor activity was also assessed. Supported by grant NCN UMO-2014/15/B/NZ7/01019.

25. Morris water maze as a tool for studies on spatial memory in rats on high fat diet

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Obesity recognized as civilization disease is a one of the major health problems XXI century. The most common obesity cause is gain fat induced by adipocyte hypertrophy. High-fat diet affects not only the metabolism or spatial memory, but it can also be associated with cognitive processes. Male Wistar rats (n=21) were fed high fat diet for six months. Experimental (HFD) and control group (normal food, n=19) were tested for spatial memory during consecutive three days using the Water Morris Maze. The distance which they covered to find a platform, travel time and immobility time were recorded by Videomex one. The results obtained in the Morris Water Maze suggest that during the three day testing time all the recorded parameters were shortened in both examined groups however, the results did not provide statistically significant differences between rats on different diets. Previous studies shown positive effects of high fat diet on learning, but they were performed using a 8-arm radial maze. The results allow to conclude that the Morris Water Maze used in studies on rat models of Alzheimer's disease and of other cognitive disorders does not appear to be a good tool for testing the spatial memory in this experimental design.

26. Pre-exposure to rewards reduces impairments in the reward discrimination task in Fmr1 knockout mice

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Lack of FMR1 protein is the most common monogenetic cause of autism and mental retardation and results in Fragile X Syndrome (FXS). Fmr1 knockout mice are used to better understand neuronal processes underlying social and cognitive impairments. Detailed characteristics of FMR1 knock-outs behavioral deficits and new therapeutic approaches that could fix cognitive malfunctions caused by the lack of Fmr1 expression are needed. In the present study we aimed at investigating Fmr1 knockout mice ability to discriminate rewards from neutral stimuli, which is impaired in FXS patients. We used IntelliCage - automated testing system which closely follows natural murine behavior offering well-standardized conditions and high data reproducibility. We found that Fmr1 knockouts are

severely impaired in the reward discrimination task. However, we also discovered that their performance may be improved by exposure to highly rewarding stimuli during the pre-learning procedure. This finding suggests that changes in rewards availability and/or the level of familiarity with the particular reward may affect learning abilities of impaired subjects, even resulting in rescue of the cognitive functioning.

27. Ultrastructure of central amygdala neurons in mouse model of Fragile X Syndrome

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Lack of expression of Fragile X Mental Retardation Protein (FMRP) – a key molecule in processes of synaptic plasticity – is the most common monogenetic cause of autism. It results in Fragile X Syndrome (FXS). Clinical studies and experiments in Fmr1 knockout mice - the best documented animal model of autism - show abnormalities in morphology and count of dendritic spines that are the main site for FMRP activity. However, there is hardly any data on structural abnormalities of dendritic spines in amygdala – a brain structure essential for emotional processing. It is noteworthy that - apart from dendritic spines - FMRP is also present in mitochondria and nucleus. Disclosing how its lack is influencing ultrastructure of organelles would be an important step towards understanding neural causes underlying FXS. Using transmission electron microscopy we described disrupted morphology of central amygdala neurons in Fmr1 knockouts. We found elevated number of synapses and substantial changes in organization of nucleolus. Moreover, the structure of mitochondria's cristae were similar to those of cells under oxidative stress. Our results show that lack of FMRP causes ample ultrastructure changes in central amygdala neurons. Described alterations could be used as a new diagnostic marker in mouse model of FXS.

28. Neuronal circuits involved in fear memory extinction

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Alpha calcium/calmodulin-dependent kinase II (alphaCaMKII) is one of the most abundant protein in the brain located in the glutamatergic synapses of the forebrain. Previously, it has been shown that α CaMKII autophosphorylation plays a pivotal role in long-term plasticity, learning and memory processing in the brain. Here we show that alphaCaMKII autophosphorylation-deficient heterozygous mice (T286A +/-) present an impaired remote (30 days after training) but not recent (1 day after training) fear memory extinction. To verify if this behavioural change is based on differences in the activation of brain regions involved in the fear memory extinction we performed c-Fos immunomapping on hippocampus, retrosplenial, anterior cingulate, prelimbic, infralimbic, entorhinal cortices, thalamus, amygdala and septal nuclei. Our results shows that T286A +/- mice have strong c-Fos expression upregulation in the retrosplenial, enthorinal, prelimbic cortices, thalamic nuclei (central medial, mediodorsal), septal nuclei (lateral, medial) and amygdala (lateral, basolateral) when remote fear memory extinction is impaired. These results suggests that alphaCaMKII autophosphorylation regulates remote fear memory extinction by activity adjustment of the circuit which include multiple brain structures, in particular mentioned above. In order to investigate the role of thalamo-retrosplenial connections in our model we plan to perform experiments using two-photon microscopy on awaken mice.

29. The role of Arc/Arg3.1 protein in the regulation of alcohol addiction-related behaviors

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Alcohol addiction is a health problem, characterized by compulsion to seek and take the alcohol. The glutamatergic system plays an important role due to its involvement in the brain reward system. Arc protein is involved in learning and plasticity and it is engaged in the regulation of AMPA receptor endocytosis. In order to analyze the role of Arc protein in the regulation of addiction-related behavior we conducted longitudinal study in the IntelliCages according to the previously published protocol. Arc KO mice were trained in a training composed of an initiation phase, free alcohol access periods, periods of withdrawal and alcohol cue-induced relapses followed by alcohol relapses. Our data indicates that Arc KO mice drink as much alcohol as WT, but they make more nosepokes to alcohol corner during

withdrawal and alcohol cue-induced relapse. Since the tested Arc KO mice have global Arc deletion, it is unclear in which brain regions Arc protein contributes to the extinction of this behavior. Thus in the following study we employed immunofluorescence to investigate the expression of Arc protein within brain reward system. In conclusions, our data support the role of Arc protein in the regulation of brain reward system activity during alcohol relapse.

30. Analysis of matrix metalloproteinase 9 activity in the brains of Fmr1 KO mice – a model of fragile X syndrome

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Fragile X syndrome (FXS) is the most common form of inherited intellectual impairment and the known single gene cause of autism. Mutation in fmr1 gene results in the absence of fragile X mental retardation protein (FMRP). In physiological conditions FMRP, as an RNA binding protein, regulates the local translation of transcripts that play an important role in synaptic plasticity. One of them, extracellular matrix metalloproteinase 9 (MMP-9) is involved in activity-dependent reorganization of neuronal dendritic spines architecture. Fmr1 KO mice exhibit immature, long and thin dendritic spines in contrast to mushroom-shaped and shorter ones observed in wild type mice. This phenotype has been linked to the elevated activity of MMP-9 in the brains of Fmr1 KO mice. Using the gel zymography method I measured the level of enzymatic MMP-9 activity in cerebral cortex, hippocampus, olfactory bulb and cerebellum of juvenile versus older Fmr1 KO mice decreases with their age what is important in the context of the minocycline administration – the drug that lowers the MMP-9 activity and that had been tested in clinical trials with children and adults.

31. The role of actin polymerization and posttranslational modifications in ethanol-induced amnesia

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Ethanol in high doses blocks new memory formation. Several studies suggest the crucial role of actin cytoskeleton in memory processes. Here we tested the hypothesis that alcohol-induced actin depolimerization is a mechanism of alcohol amnesic effects. We performed the contextual fear conditioning on alcohol injected mice and observed dose-dependent impairment in long-term memory formation. Using confocal microscopy and phalloidin staining we measured actin polymerization levels in the hippocampal area CA1. The levels of actin polymerization decreased after ethanol. Since alcohol leads to generation of free radicals in the cell, we tested the role of free radicals in the regulation of memory using a free radicals scavenger, ascorbic acid (AA). We observed a dose-dependent rescue of memory and actin depolymerization in mice injected with ethanol and AA. One of the possible mechanisms of actin depolimerization by free radicals is oxidation of Methionine 44 and 47. To investigate if actin is directly affected by ethanol-induced free radicals we performed an experiment using mass spectrometry analysis and observed increased levels of oxidated methionins in ethanol treated mouse in all identified actin peptides. Taken together these results suggest the free radicals-driven actin oxidation as a mechanism of ethanol-induced actin depolimerization and memory impairment.

32. Rescue of impaired reward learning in mouse model of Fragile X Syndrome

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Loss-of-function mutations in Fragile X Mental Retardation Protein (FMRP) result in fragile X syndrome (FXS), and is the most wide-spread single-gene cause of autism. In case of the complete silencing of FMR1 gene male patients have

an average IQ of 40 and cope with severe cognitive impairments. In our studies we exploited a mouse model of FXS mimicking above-described phenotype in humans. As FMRP is a local-translation suppressor, its lack leads to overexpression of many synaptic plasticity proteins. Among those matrix metalloproteinase-9 (MMP-9) is a crucial player in reward-motivated learning, specifically its proper level in central amygdala is required for mice' ability to discriminate between rewards and neutral stimuli. Using fully automated behavioral testing, to investigate characteristics that can be observed only in a long-lasting study, we showed that Fmr1 knockouts are unable to efficiently perform such discrimination tasks. However, down-regulation of heightened MMP-9 level in central amygdala was sufficient to fully rescue this impairment. This effect was obtained by a local injection of nanoparticles gradually releasing selective MMP-9 inhibitor. It is noteworthy, that nanoparticles are able to cross brain-blood barrier and thus the implemented paradigm holds promise of obtaining clinically relevant solutions for the most severely disabled FSX patients.

33. Enhancing memory consolidation: effects of manipulating sensory stimulation after learning

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Decreasing sensory stimulation after learning can promote long-term memory (LTM) formation. This effect assumedly reflects attenuated interference during memory consolidation. In contrast, the synaptic-tagging and capture hypothesis (STC) posits that lack of stimulation should cause forgetting, while increased sensory stimulation after learning will formed LTM. In this study we used object and object-location recognition memory tests. We exposed rats to objects placed into an open-field, procedure that promotes short-term memory but not LTM. We then tested whether modifying sensory stimulation would promote LTM formation. First, we used a highly familiar dark container immediately after object exposure in the open-field. We found that this promoted long-term retention of object-identity and object-location recognition memory. Next, we tested whether increased sensory stimulation would promote or impair long-term memory retention. After exposing rats to objects in the open-field, we placed them into a novel, highly stimulating environment, causing formation of object-location LTM. These results suggest that altered sensory stimulation can facilitate LTM formation. Interference accounts cannot explain the latter, while the STC model cannot fully explain the former outcome. We conclude that reducing interference will promote memory formation, but that novelty exposure can overcome the otherwise detrimental effects of sensory stimulation on LTM formation.

34. Behavioural and pharmacological validation of probabilistic reversal learning task in rats

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Changes in feedback sensitivity (FS), reinforcement learning (RL) and cognitive flexibility (CF) have been reported in several clinical conditions including depression, schizophrenia, Parkinson's disease and orbitofrontal cortex damage. Since perturbations of these functions weigh upon patients well being and recovery, it is important to understand the underlying neurobiology and develop pharmacological interventions. Recently, a test that engages FS, RL and CF in humans – the probabilistic reversal learning (PRL) task – has been successfully utilized in both rodents and primates, but necessary research is still scarce and a standardized animal version of PRL is yet to be developed. In the present study, we compared 3 versions of the PRL in a group of Sprague-Dawley rats. We report the effects of L-DOPA and somatosensory stimulation ("tickling") on FS, RL and CF at 3 different probability levels (90:10, 80:20 and 70:30). The results are discussed in light of their ecological validity and the potential of PRL to become a pre-clinical test aimed at evaluation of psychological functions that engage both affect and cognition. This work was supported by the National Science Centre (Research grant: OPUS-2014/13/B/NZ4/00214) and the statutory funds of the Institute of Pharmacology Polish Academy of Sciences.

35. Influence of metformin on the maternal diabetes-induced changes in the hippocampus of rat offspring

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Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland Maternal diabetes may increase the risk of neurodevelopmental disorders in the offspring. Previous data demostrated that chronic maternal hyperglycemia alters normal hippocampal development but there was no data about the impact of anti-diabetic drugs on the brain viability/death parameters and neurotoxic factors release.We investigated the influence of maternal diabetes on the viability/death parameters in basal and LPS-stimulated conditions in the hippocampal organotypic cultures. Furthermore, we evaluated the effect of metformin on the above mentioned parameters. Cultures were prepared from hippocampi of 7-day-old rats-offspring of control and diabetic dams. On the 7th day in vitro hippocampal slices were pre-treated with different concentration of metformin and stimulated for 24h with LPS. The death/viability parameters and NO realase using flow cytometry,LDH,MTT and Griess method were estimated. We observed that metformin (0,1-3 μ M) did not evoke any changes in hippocampal cultures, while 10 μ M concentration resulted in a significant decrease in viability, enhanced LDH and NO release-more susceptible to damage were slices of pups born to diabetic dams.Interestingly, we demonstrated beneficial impact of metformin, which attenuated the LPS-evoked changes by reducing the number of dying cells. Supported:grant 2014/13/N/NZ7/00279 National Science Centre Poland.

MEDICAL CASE REPORTS AND NEUROLOGY

36. Primary Central Nervous System Lymphoma (PCNSL) manifesting as visual disturbances

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Background: PCNSL is a very rare intracranial neoplasm which typically develops in patients with immunodeficiency or above 60 years old. The percentage of PCNSL in all brain tumours is barely 4%. Most frequently localized in the frontal lobe, hippocampus, corpus callosum, or periventricular area. In 34% of cases tumours are bilateral.

Methods: Computerized Tomography (CT) is a standard radiological procedure applied in patients with suspicion of an intracranial neoplasm. Magnetic Resonance Imaging reveals more accurate images of lesions. In order to determine the histological type of tumour the stereotactic biopsy is carried out.

Results: A seventy-six year-old man was admitted to the emergency department after causing two car accidents. During the examination he manifested visual disturbances. Contact with the afflicted was difficult, impaired counsciousness was reported. CT revealed multiple intracranial lesions. After further investigation, it turned out to be PCNSL.

Conclusion: Intracranial neoplasm is rare and dangerous for health and life. In our case of PCNSL on the ground of toughness in treatment and rarity of visual disturbances as a first manifestation without localization in the eye. Histological and immunohistochemical investigations are determinative.

37. Multiple radiation induced meningiomas following high dose cranial irradiation

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Radiation-induced meningiomas (RIM) are very rare complications in patients who underwent high dose irradiation for brain tumors. The mean latency period for induction of RIM in most of the series is 18.7±10.2 years. We report a clinical case of 42yo. woman diagnosed with multiple (seven) RIM with latency period of 39 years. She underwent whole brain radiotherapy with total dose of 25Gy as treatment of acute lymphoblastic leukemia in childhood. There were no symptoms of NF2. In 2015 she underwent neurological diagnostis because of incidents of new-onset focal seizures. Gadolinium-enhanced MRI showed seven tumors located: parasagitally on the left, 4 on convexity, olfactory groove and left anterior clinoid process. Patient underwent 2 different neurosurgical operations - three largest tumors were totally resected (Simpson grade I). Histopathological examination showed that tumors were benign (WHO I) variants: transitional and angioblastic meningiomas. Moreover patient has growth deficie ncy (1,42m) and endocrine problems due to radiation-induced hypopituitarism (confirmed secondary empty sella syndrome). Secondary intracranial meningiomas following highdose cranial irradiation represent a rare but distinct clinical entity. RIM is characterized by a younger age at presentation, increased rate of multiplicity and recurrence after treatment and by an increased percentage of atypical or anaplastic histology, as compared to spontaneous meningiomas.

38. The statistical analysis of patients hospitalised for multiple sclerosis between 2010 and 2014 in the Department of Neurology at the Bialystok Clinical Hospital

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BACKGROUND: In Poland there are only estimated epidemiological data about multiple sclerosis. The nationwide registry of MS patients is currently being compiled. Our aim was to determine correlations in MS patients from Bialystok Clinical Hospital.

METHODS: The database of MS patients hospitalised from 2010 to 2014 was created using the hospital registry. The following parameters have been included for the analysis: sex, age, season and length of hospitalisation, month of birth and place of residence.

RESULTS: Among 698 hospitalised patients there were 464 women and 234 men (2.05:1.00). The highest number of patients was observed in the age group 30-45 years (41.8%). The average duration of hospitalisation was 6 days. The analysis revealed that the most common month of birth was April (13.0%) however patients born in October required the longest hospitalisation (7 days +/-0.56). According to the database from 2010 to 2013 the urban-rural ratio was 2.78:1.00. The results of the analysis are statistically significant with the exception of the relationship between age and length of hospitalisation.

CONCLUSIONS: The outcome of the analysis confirms data from literature. This is an attempt to characterise MS patients based on the registry from the Department of Neurology at the Bialystok Clinical Hospital.

39. Sleep disturbances as a risk factor for post-stroke cognitive impairment

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Background: Sleep disorders are common in elderly population. They may disturb memory formation and contribute to cognitive impairment. Post-stroke dementia prevalence ranges from 6 to 32%. The aim of this study was to evaluate sleep disorders as a risk factor for cognitive dysfunction in acute phase of stroke.

Methods: We examined 250 consecutive patients admitted to the Stroke Unit, Department of Neurology. Cognitive functions were assessed with Montreal Cognitive Assessment (MoCA) twice, on day 1-2 (MoCA1) and 7-10 (MoCA2). Sleep disturbances were assessed using Neuropsychiatric Inventory (NPI). We defined sleep disorders as NPI>0 and normal sleep as NPI=0. 160 patients were excluded from the study due to: pre-stroke dementia, inability to undergo cognitive tests, death or discharge before second assessment, lack of NPI.

Results: Patients with sleep disorders had lower MoCA score on the first and second assessment. Group with sleep disturbances had worse results in the following MoCA1 domains: visuo-spatial, naming, attention, abstraction and MoCA2 domains: attention, fluency, memory and abstraction.

Conclusions: Pre –stroke sleep disturbances may be a risk factor for acute post-stroke cognitive impairment. Cognitive domain analyses suggest that sleep disturbances may impair alertness and logical thinking.

40. Emotion processing in Parkinson's disease – possible link between inability to decode complex emotional stimuli and impairment of executive functions

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Background: Emotion decoding abilities are important part of social interactions. Some studies have shown emotional decoding impairment in PD but others have not documented any deficit. Most of previous studies were based only on facial expression recognition and did not compare abilities to decode emotions in more complex tasks, which are more similar to scenarios present in patients' natural environment.

Methods: We assessed emotional processing using 4 sets of cartoon-like drawings of gradually increasing complexity. Each set showed basic emotions and more complex stimuli contained additional information about emotional content of drawings such as human facial expression, gestural poses or situational context. The assessment of executive functioning included: Trial Making Test Part 1 and 2 (TMT1, TMT2), digit backward, Rey–Osterrieth Complex Figure Test (ROCFT), Verbal Fluency Test, Stroop test-part 3, Tower of London test (TOL) and Clock Test. Controls were matched according to age and education. All patients underwent evaluation for depressive symptoms.

Results: We included 31 PD patients without signs of dementia and 34 healthy controls. PD performed worse (p<0.05) in recognizing emotions from more complex features of stimuli. Controls improved (p<0.05) in emotion recognition from stimuli of higher complexity, whereas PD did not improve. In addition to impairment of working memory and processing speed patients with PD performed worse than controls on: ROCFT, TMT2 and Stroop test indicating worse executive functioning among this patients.

Conclusions: Our study suggests that processing of complex emotional stimuli is impaired in patients with Parkinsons disease and might be associated with executive dysfunction.

41. What causes this all confusion? – Predisposing factors for delirium in stroke

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Introduction: Delirium occurs in 10-48% of patient in the acute phase of stroke. Some risk factors for delirium are regarded as universal eg. age or infection, while others are more specific for particular disorders eg. stroke type or severity. We aimed to investigate occurrence and predisposing factors for delirium after stroke or TIA in Polish population.

Methods: Consecutive patients admitted to the Stroke Unit, University Hospital, Krakow, with TIA, ischemic or haemorrhagic stroke were included in the study. They were assessed for delirium using DSM-V criteria during the first week. Information on predisposing factors were collected.

Results: 431 consecutive patients were included in the study: 360 with ischemic, 35 with haemorrhagic stroke and 36 with TIA. Delirium was observed in 24% of patients (n=105). We identified several predisposing factors for post-stroke delirium: older age, female gender, pre-stroke cognitive impairment, infection, higher stroke severity, use of anticholinergic drugs and presence of aphasia, visual disturbances and neglect.

Conclusion: The association of delirium in stroke with some, but not all predisposing factors reported so far was confirmed by our study. This highlights the need for investigation of population specific differences in predisposing factors as it may improve delirium-screening strategy across stroke-units.

42. To see or not to see = To be or not to be? Visual information processing during recovery from disorders of consciousness

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We examined Visual Evoked Potentials (VEPs) and visual behavioural responses during recovery to consciousness. Flash VEPs were examined longitudinally in 12 DOC patients (M=16.6 years; SD=5.3) every two weeks for an average period of 2.6 months, and were compared to a healthy norm group VEPs. Visual behavioural responses included visual tracking, comprehension of written commands, and object manipulation. Long-term outcome was assessed 2-3 years later. VEP responses were present always, and did not change along with recovery to consciousness. VEP amplitudes were significantly smaller, and latencies were longer in the patient group when related to the controls. VEPs characteristics at first measurement were able to predict long-term outcome up to three years after injury. Visual responding significantly increased during recovery to consciousness for all stimulation items: visual tracking, comprehension of written commands, and object manipulation. Rudimentary visual processing is present, yet according to VEP responses, poorer in DOC patients than in healthy controls, and remains poorer when DOC patients recovered to consciousness. A delay in visual information processing must be taking into account when working with DOC patients. Our findings offer new opportunities for future research on visual information processing at higher levels during the recovery of DOC patients.

43. 12 years after coma: A research and a documentary of patients with disorders of consciousness

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We investigated long-term outcome of patients with disorders of consciousness that received intensive neurorehabilitation ten to twelve years earlier. Survival rate, level of consciousness, functional independence, mobility, communication, and living situation were determined by using structured questionnaire. The cohort consisted of 44 children and young adults in Vegetative State(VS)/Unresponsive Wakefulness Syndrome(UWS) or Minimally Conscious State 1-6 months post-injury. At follow up, 11 patients were deceased, 10 of who were in VS/UWS or MCS at discharge from the program. Of the remaining 23 patients, 19 were conscious, of which 7 had recovered to functional independence. Twelve lived independently, of whom 6 required household support. Two of three MCS patients had recovered into full consciousness, albeit without any functional recovery, and two of three VS/UWS patients had recovered into MCS. Only one conscious patient lived permanently in a long-term care facility. All other patients lived either independently, or with their parents. Two main long-term outcome scenarios can be recognized: Two-thirds of the participating patients who were conscious at program discharge were able to live independently, whereas almost two-thirds of the participating patients who were in VS/UWS or MCS at discharge subsequently died. Additionally to these results, a short documentary will be presented.

44. Cocaine abusers default mode network - group ICA of fMRI data

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The default mode network (DMN) is a set of brain regions, which activate when people are not focused on any particular task. Previous studies have shown that changes in this network are associated with some neurological disorders, e.g. Alzheimer's disease. Thus, we investigated if there are abnormalities in DMN of people who are addicted to cocaine. We used fMRI data from 1000 Functional Connectomes Project INDI Retrospective Data. We analyzed resting state fMRI data using independent component analysis (ICA). Results from our study show that there are no significant changes in the DMN in the sample from cocaine-dependent population, in comparison to healthy subjects. However, there is a trend suggesting that there are some differences between cocaine-dependent and healthy subjects' components. The most interesting finding is slightly lower signal amplifications in frontal lobe, specifically in middle frontal gyrus in cocaine-dependent participants. Moreover, for cocaine-dependent group, we haven't found activations in right amygdala, probably due to insufficient number of participants or resting state sessions. According to the results of the ICA, DMN is not affected by the use of the cocaine. Our study has also shown that the DMN is probably not related to affective aspects of cocaine use.

45. Sensory integration therapy improves daily functioning and learning Science by children with autism

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Autism is a neurobiological disorder that impairs social interaction, verbal and non-verbal communication, and restricted and repetitive behaviour. Children with autism, even highly functioning kids, can find it difficult to process language with surrounding noise or smells. They may have a dysfunctional sensory system. Autism's symptoms often include difficulty processing sensory information such as textures, sounds, smells, tastes, brightness and movement. These difficulties can make social problems and interfere with daily functioning, even isolate individuals. Sensory integration therapy uses play activities designed to change the way the brain reacts to touch, sound, sight and movement. It takes place in a specially designed setting where kids are encouraged to play with balls of different sizes, textures and weights. Therapy sessions often involve playing with clay and other materials. Children may also be asked to bounce, swing or spin on special equipment. Sensory integration is an innate neurobiological process and refers to the integration and interpretation of sensory stimulation from the environment by the brain. In this study I analysed the behaviour, physical and social characteristics of autistic children and students during sensory

integration therapy and Science lessons. Sensory integration therapy has been fun for them because it resembles playtime and causes better educational effects.

46. Dual-task executive functions and balance control training in 40-60 years old adults

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The present study highlights the effect of a dual-task cognitive-motor training on cognitive functions in comparison to a single-task cognitive training in older adults. 32 healthy adults (40-60 years old) were recruited and randomly stratified into three groups: dual-task 'cognitive-motor group' (n=11), single-task 'cognitive group' (n=10) and control group - single-task 'motor group' (n=11). Each group received a training based on a specially designed computer game - "find a way in the maze". 'Cognitive group' used a keyboard to navigate mazes (executive functions training only). 'Cognitive-motor group' navigated mazes by postural sway using static posturography technology (executive functions and balance training). 'Motor group' navigated mazes exactly like 'cognitive-motor group', however an optimal path was exposed to the user in every maze (balance training only). The intervention was provided for 30 minutes per session, average 5 sessions per person, completed in no more than 2 weeks. Executive functions measures included: Mazes test, Tower of London, Trial Making Test, Stroop task. The results demonstrate that, dual-task cognitive-motor training and single-task cognitive training are both beneficial of improving executive functions, in adults between 40 and 60 years, providing an argument for developing more multimodal tools improving both motor and cognitive domains.

AFFECTIVE NEUROSCIENCE

47. Imagination feeds memory. On the influence of disgust and fear on long-term memory – fMRI study with the use of Nencki Affective Word List (NAWL)

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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 in the storage of emotionally-charged verbal stimuli after long delay. 50 subjects (25 F; aged 20-35) took part in two stages of fMRI study, with stimuli selected from the Nencki Affective Word List. During encoding session, they were presented with pairs of words (disgusting, fearful and neutral), instructed to imagine them as single mental representations and asked to rate how successful they were. After 16-18 days the subjects were invited for recognition session, presented with old pairs from encoding list and new pairs as lures, and asked to determine whether a word was old or new (O/N) and if they were sure or unsure (S/U) of their response. Behavioral analyses showed a higher rate of correct recognition of old pairs than false recognition. Disgusting and fearful stimuli were better remembered than neutral stimuli. At the neuronal level, analyses of the retrieval session showed increased activation for correctly recognized old vs. new pairs in ACC and PCC, bilateral IFG and thalami. These preliminary results provided evidence that neural substrates of verbal long-term memory performance depend on emotion.

48. Memory as an intentional process – an fMRI study on remembering and forgetting within the discrete emotion framework

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¹Laboratory of Brain Imaging, Neurobiology Centre, Nencki Institute of Experimental Biology, PAS, Warsaw, Poland ²Laboratory of Psychophysiology, Department of Neurophysiology, Nencki Institute of Experimental Biology, PAS, Warsaw, Poland Recent research disputes the extent to which people can exert control over their memory and the underlying processes enabling this control (Zwissler et al., 2015). Both remembering and forgetting has been shown to be in part intentional (Anderson & Hanslmayr, 2014). Although emotions modulate these processes (Nowicka et al., 2011), the precise impact of particular emotion has not been thoroughly examined. We conducted a pilot behavioral experiment (25 F) and a follow-up fMRI experiment (18 F), in which we adopted the item-method directed forgetting paradigm (Wylie et al., 2008). Neutral, fear, and sadness eliciting words (Wierzba et al., 2015) were used for emotion manipulation. Intentional mechanisms of memory processes were observed with better memory performance for tobe-remembered (TBR) than for to-be-forgotten (TBF) items, irrespective of emotion. Two different brain patterns corresponding to specific instruction types were observed. Middle (MFG) and superior frontal gyri (SFG) revealed more activity during the encoding attempts (TBR>TBF). Inferior parietal lobule (IPL) was more implicated in the suppression attempts (TBF>TBR). Activation in parahippocampal gyrus (PHG) was found for memory outcome inconsistent with the instruction. The emerging brain patterns were observed for fear, but not for sadness.

49. Aesthetic judgements of paintings in experts and laypersons and different saccadic context: An EFRP study

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Previous studies have shown that experts and laypersons differ not only in terms of understanding the concept of aesthetics but also with regard to the way they are looking at works of art. The question then arises: whether eye fixations of both groups on the fragments of beautiful and non-beautiful paintings trigger off different electrophysiological brain responses? The present study investigated aesthetic judgements-related brain activity with cortical eye fixation-related potentials (EFRPs). The study involved 62 people, including 30 experts. Their task was to evaluate 150 paintings as beautiful or non-beautiful. We analyzed EFRPs taking into account the length (short vs. long) of the eye fixations and preceding saccades. There were significant differences between EFRPs averaged for different eye movement context. It was found also that 'beautiful' 'non-beautiful' answers differed with respect to the EFRPs amplitude in early time windows (80-120 ms and 160-230 ms) at occipital electrodes, but only for laypersons. Many affect-related ERP modulations for picture stimuli have been reported in the 100-200 ms range. We may therefore assume that at the early stages of looking at paintings emotional factors may be of primary importance to aesthetic judgements of laypersons rather than experts.

50. Brain response to emotional images is independent of focusing overt attention on emotional objects

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Eye tracking studies have shown that emotional objects within images are found faster and hold attention longer than neutral objects, even if images have been severely degraded by introducing visual noise. We wanted to find structures responsible for this effect. Twenty healthy participants were scanned using Siemens Trio 3T magnet. Visual stimuli were binocularly shown with googles equipped with an eye-tracking camera. A set of negative and neutral natural scenes was selected from IAPS and NAPS. Semantic regions of interest for each picture were obtained in a separate evaluative study. To each original image pink noise was added in several proportions. Images were presented in a free viewing task in sequences from pure noise to complete lack of noise. Eye tracking data was converted to a measure reflecting the chance to look at the semantic region of interest. Image onset both in case of neutral and negative valence explained large activations in primary visual cortex, precentral gyri, middle frontal gyri as well as insula and amygdala. Noise level irrespective of valence explained robust activations in lateral occipital cortex, inferior temporal gyri, temporal fusiform cortex, middle and inferior frontal gyri and frontal orbital gyri. Additionally, in negative valence the noise level correlated with activations in precuneous, superior frontal gyri, and frontal medial cortex. Both in case of negative and neutral images chance of looking at the object explained activation in right lateral occipital cortex, which has been implicated in object recognition. We show that structures involved in guiding overt visual attention to the key semantic information are not valence specific. On the other hand, activity in structures typically involved in processing of emotional information is mostly linked to image clarity and onset. That implies that emotional response is not directly dependent on focusing overt attention on the key semantic object, but is rather related to overall image presence and clarity.

51. Does cognitive control may work as emotional control?

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Conflict-inducing tasks require to rapidly change previously well-established response or inhibit a prepotent one. As a result, they intensify cognitive control processes (e.g. incongruent trials in Flanker task). On the neural level, conflict-related activation in anterior cingulate cortex intensifies cognitive control by activating the dorsolateral or the ventrolateral prefrontal cortex. As the same regions are involved in emotional control, this event-related potentials study verifies if increased cognitive control decreases subsequent processing of negative emotional stimuli. 33 participants responded to either congruent (non-conflict) or incongruent (conflict) trials in modified Flanker task. After response, negative or neutral picture was presented. We used the N200 component as an index of the cognitive control, and the LPP (late positive potential) as an index of the depth of processing emotional stimuli. Incongruent trials (compared with congruent trials) triggered greater N200 component, indicating intensified cognitive control. Negative pictures (compared with neutral pictures) elicited significantly higher LPP, indicating greater depth of processing. Importantly, there was a significant interaction between congruence and valence factors. Negative pictures presented after incongruent trials elicited lower LPP compared with negative pictures presented after congruent trials. This suggests that cognitive control may modulate emotional responses and work as a form emotion control.

52. Subjective significance of words modulates arousal impact on Emotional Stroop Test - Eventrelated potential correlates of behavioral phenomenon

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Behavioral studies showed that interference control, measured in the Stroop Task, is sensitive to the affective meaning of verbal stimuli. Slowdown in response latencies is related to the arousal level of the stimuli, rather than their valence. Based on the duality of mind approach, we argue that there are two aspects to activation. The first is arousal, which is crucial for experiential mind and effortless processing. The second is subjective significance, which is specific to a rational mind and effortful processing (Imbir, 2016). We predicted that arousal would enhance interference in a modified Stroop Task as attention would be allocated to the meaning of the inhibited word. High subjective significance should have the opposite effect, enhancing the controlled and explicit color naming part of Stroop Task processing. We have tested these hypotheses using lists of words with 3 levels of arousal and 3 levels of subjective significance and controlled for other potentially important factors. We found that response latencies were modulated by the interaction between the arousing properties and subjective significance effects were found for 50-150, 150-290 and 375-530 ms time ranges.

53. Does happiness make us patient? Linking mood and impulsivity

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Impulsivity is considered an important factor in substance misuse and certain neuropsychiatric conditions, therefore, it is important to understand modulators of impulsive behaviour. This study investigated how mood affects impulsive behaviour in standard laboratory tests. Participants were randomly allocated to a mood induction procedure, during which they were experiencing either a failure (negative mood, N=10) or success (positive mood, N=10) on an intelligence test. A control group performed a low demand cognitive task (N=10). Participants' mood was assessed before and after manipulation using the Positive Affect Negative Affect Schedule. Following the mood induction, participants completed three behavioural tasks: the Stop Signal Task (SST), Two Choice Impulsivity Paradigm (TCIP), and Information Sampling Task (IST). Correlation analysis revealed that increased negative mood was associated with less information sampling in the IST (R=-0.4, N=30, p=0.029, increased reflection impulsivity). Increased positive mood was related to decreased response inhibition in the SST (R=-0.38, N=28, p=0.046, increased motor impulsivity), but decreased temporal impulsivity in the TCIP (Rs=-0.47, N=25, p=0.017). These results provide evidence for mood

as a modulator of impulsive behaviour and suggest that facets of impulsivity (reflection, motor and temporal) are differently affected by mood states.

54. The influence of reward on fear expression and extinction

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Conditioning paradigms are often used to understand how emotion influences behavior. To enable flexible behavioral adaptation, regulation of fear is key. Patient studies investigating anxiety disorders have shown that these patients often lack fear regulation strategies. A recent study has shown that rewards can be used to intervene with fear learning processes. There is some evidence for the interaction between the fear and reward systems, but this evidence is limited. The aim of the current study is to provide further evidence for the interaction between the two systems by investigating the influence of reward on fear conditioning, specifically on fear expression and fear extinction. 22 subjects participated in a fear-potentiated startle conditioning paradigm and during this experiment fear was measured on a subjective and on a physiological level. The influence of reward on fear expression and fear extinction was measured by differences between in subjective fear ratings and startle magnitudes in a threat plus reward contexts and threat context without rewards. On a physiological level, results demonstrated that fear levels were not statistically different in threat plus reward contexts versus threat contexts. Reward did thus not have an effect on fear expression and fear extinction. However, subjective fear results did indicate that fear extinction rates were higher for the threat plus reward condition. The incongruence between startle and subjective data could suggest that the intercalated cells, which mediate fear extinction, are differently activated. Further research should expand this research and should include brain-measuring techniques to delineate the role of the intercalated cells in fear extinction.

55. What can affect a face perception process? An ERP study

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Human faces provide wide range of social and emotional information. Not surprisingly, the mechanisms of face perception have been broadly studied in the area of brain research – with special attention to emotional expressions or facial distortions (e.g. Thatcher effect) - but the results remain inconsistent. In our study we adapted the research paradigm from Schacht & Sommer (2009) to investigate whether manipulating the type of facial expression and the face correctness affects EEG brain activity. 87 participants (34 M, mean age=35,9) performed an EEG task. They were asked to decide whether the presented face is correct or not. Correct faces were divided into 3 categories: happy, angry or neutral ones, while incorrect faces consisted of neutral faces with removed facial features (e.g. nose or eye). We investigated the ERP components associated with face perception and emotion processing (VPP, N170, LPC) in search of differences caused by experimental manipulation. The results showed significant difference (p < .05) in the amplitude of VPP, N170 and LPC for both, type of emotion and face correctness, and they stay in line with the results reported by Schacht & Sommer (2009).

56. Burnout and its impact on information processing - analysis of VPP component in a face categorization task.

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Background: Previous psychological research on burnout syndrome points at differences in emotional and cognitive processing between burned-out individuals and general population (Lorist et al., 2005; Boksem et al., 2006). There are also some neuroscience research that describe specific patterns of brain activity in burnout group (Durning et al.

2013; Tei et al., 2014; Golkar et al., 2014). The aim of presented study is to investigate if burned- and not burned-out individuals differ in cognitive and emotional functioning, analyzing EEG brain activity.

Methods: Participants: 87 active workers (mean age=35,92; 34 males) were divided into two groups based on Maslach Burnout Inventory-General Survey scores. Subjects performed an EEG task in which they were presented with different types of faces: neutral, negative, positive and faces with distorted features.

Results: The results show significant difference in the amplitude of vertex positive potential (VPP) between groups (F(1,85)=5,27; p < .05) - the amplitude is smaller for burned-out individuals. Significant difference between the burnt out subjects and the control group in VPP depending on the type of presented faces was revealed.

Conclusion: The obtained results may be a further evidence for impaired stimuli processing in the individuals presenting burnout symptoms.

57. Prior socio-affective experiences modulate the perception of otherwise neutral faces

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Recent years have brought an increased scientific consideration of the influence of prior experience on early stages of visual perception. A growing a number of electrophysiological studies provide evidence that emotional memory traces shape immediate perception of neutral facial expressions. The aim of the present study was to determine whether prior socio-affective experience can influence brain responses to neutral faces. 27 students, aged between 18 and 33 years, participated in the study. Participants performed an exchange game task, designed to elicit positive, negative or neutral attitude towards displayed faces of co-players with neutral expression. Event-related brain potentials were measured in response to subsequent exposures of the same faces used as cues in a gaze-cuing task. Our results revealed early (90-140 ms, 160-210 ms) and late (280-330 ms) modulations of brain responses to previously negatively associated faces of neutral expressions compared to non-affectively associated faces. These results provide evidence for the claim that human perception is modulated by prior socio-emotional experience in a top-down manner. Thus, the study supports recent models of neural pathways, linking prior experience with current sensory inputs.

THE EFFECTS OF EXPOSURE TO THE BLUE LIGHT

58. Daytime blue light exposure decreases EEG activity in alpha, beta and theta bands

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Background. There is a growing evidence on reduction in higher frequency range EEG activity by exposure to monochromatic blue light (MBL) at nighttime. The aim of the study was to find out the effect of MBL administered at different times of day on alpha1, alpha2, beta, theta, gamma, and delta EEG frequency bands.

Methods. Repeated-measures counterbalanced design was applied with two dim light conditions (LC) comparable with luminance level; experimental (MBL, 460 nm) and control polychromatic white light (PWL), and three times of day (S) of light exposure (sessions: 07.00-12.20; 12.20-17.40; 17.40-23.00 hours) with measurement times (MT) of EEG at their beginnings and ends. Participants (30 male students; aged M=22,87years, SD=3,34) took part in all sessions, one session/day.

Results. Three factorial analysis of variance with repeated measures on EEG activity with eyes closed data showed significant interactions of: LC and S in alpha 2 range and LC, S, and MT in alpha 1, theta, and beta bands.

Conclusions. Exposure to MBL during daytime decreased frequency of alpha 2 in the evening in central-parietal left and in morning hours in occipital cortical sites, and frequency of alpha 1, beta, and theta bands at midday in temporal-parietal left and occipital cortical sites.

59. The blue light effect on subjective arousal states and their relation to EEG activity

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Background. According to current findings, blue light may increase alertness, mood and cognitive functions. The aim of the study is to analyze if the positive blue light effect is observed in subjective arousal state at different times of day, and if it is correlated with EEG activity.

Methods. Repeated-measures counterbalanced constant-routine design was applied in two light conditions (LC): experimental- monochromatic blue light (MBL; 460 nm) and control- polychromatic white light. The measurements of EEG activity and subjective arousal (The Activation Deactivation Adjective Check List) were taken twice at each sessions: 07.00-12.20, 12.20-17.40, and 17.40-23.00. Participants: 30 male students; aged M=22,87years, SD=3,34.

Results. Three factorial analysis of variance with repeated measures on subjective arousal showed significant effect of LC (F=7,08 (1,29), p<0.02). Independently of the time of the day, in MBL sessions subjects had higher level of tension. No effects of MBL on energy, tiredness and calmness were found. Tension correlated positively with alpha2 frequency range in occipital area (r=0,41; p<0.05), and with delta range in frontal (r=0,40; p<0.05) and central areas (r=0,39; p<0.05).

Conclusions. Higher tension described as high preparatory-emergency activation may be an evidence of the stimulating effect of blue light, irrespectively to the time of the day.

60. Blue light effect on EEG activity and alertness in circadian type at different times of day

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Background. There is a growing evidence of monochromatic blue light (MBL) effect on alertness. However, its effect at different times of day in circadian types was not studied yet.

Methods. Within subject counterbalanced design was applied with two dim light conditions (LC) equal in luminance level and different in wavelength (monochromatic blue and polychromatic white). There were three sessions(S) (07.00-12.20; 12.20-17.40; 17.40-23.00 hours) with measurement times (MT) at their beginnings and ends. Thirty students (age: M=22,87years, SD=3,34) participated in one session per day. They completed mood questionnaires, and underwent EEG activity measurement. Circadian type (CT) was assessed by Circadian Type Inventory and alertness by Thayer's scale. Multiple factor analyses of variance with repeated measures with inter-object factor (CT) were applied. Results. Significant interaction of CT, LC, and S were found in alpha1 and alpha2 bands in temporal-parietal- right, central-parietal and occipital cortical sites. Decrease of EEG alpha1 and 2 bands were observed in flexible types in MBL when compared to PWL at midday. Significant interaction of CT and LC was found on calmness. Flexible types were calmer in MBL conditions than in PWL.

Conclusions. Circadian type may moderate the effect of blue light on EEG alpha activity and subjective alertness.

61. Temperament and the effect of daytime blue light on mood and EEG alpha band

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Background. There is a growing evidence of monochromatic blue light (MBL) effects on mood. However, moderating role of individual differences in this effect was not studied yet.

Methods. Within-subject counterbalanced, repeated measures design with two dim light conditions (LC); MBL and PWL (polychromatic white light), equal in luminance was applied. There were three sessions per day (07.00-12.20; 12.20-17.40; 17.40-23.00 hours) with measurement times at their beginnings and ends. Thirty students (age: M=22,87yeras; SD=3,34) participated all sessions (one per day), underwent EEG measurement and completed mood

(UMACL) and temperament questionnaires (FCB-TI). Three factorial analyses of variance with repeated measures were performed with inter-object factors (temperament dimensions).

Results. Significant interactions between LC, S, and reactivity in alpha1 and alpha2 EEG bands, and tension arousal, and also between LC, S and endurance in alpha2 and hedonic tone (HT) occurred. Alpha1 and alpha2 decreased in high reactive individuals in MBL in morning and evening hours in temporal-parietal left and occipital areas and tense arousal decreased. In MBL alpha 2 decreased in morning and evening hours in occipital area and hedonic tone increased in high endurance individuals.

Conclusions. Temperament (reactivity, endurance) moderate the effect of blue light on mood and EEG alpha1 and alpha2 bands.

62. The effect of prolonged blue light blocking on human performance and neural activity - a preliminary study

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The indirect 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 becomes more yellow reducing the transmission of short wavelengths. In this study we investigated longitudinal changes in behavior and neural activity while blocking BL exposure by using contact lenses that reduce transmittance of BL by approximately 90%. We examined 8 subjects (4 wearing blue-blocking and 4 controls wearing normal contact lenses) at baseline session and after 4 weeks of wearing the lenses. Participants performed 2-back auditory task during each session while being scanned in 3T MR scanner. The results show increased reaction time after 4 weeks in contrast to the baseline session only in BL-blocking group (p<0.01). An fMRI data analysis for 2-back task indicate an increased prefrontal activation in second session for BL-blocking group (p<0.001) when comparing to the control group. The findings of this preliminary study show that continuous exposure to reduced BL affect the behavior and neural activation of brain regions involved in attention and executive functions.

POSTER SESSION III

NEUROPATHOLOGY

1. Impact of peroxisome proliferator-activated receptor gamma agonist and antagonist on neuron viability and apoptosis in mouse neurons in vitro

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Peroxisome proliferator-activated receptor gamma (PPAR- γ) is a ligand-activated transcription factor that belongs to the nuclear receptor superfamily. Importantly, PPAR- γ receptor is widely expressed in the brain, where it has a crucial role in the regulation of nervous cell proliferation, differentiation and apoptosis. Although PPAR- γ activation reduces brain tissue damage in distinct models of brain diseases, how its activity is regulated in neurons is unclear. The aim of this research was to investigated the impact of new PPAR- γ agonist (GW1929) and antagonist (GW9662) on cell viability and caspase-3 activity in mouse neocortical neurons in vitro. The cultures of cells were prepared from Swiss mouse embryos and cultured in Neurobasal medium supplemented with B27 and glutamine and exposed to rising concentration of GW1929 or GW9662 for 6 and 24 h. Afterwards, LDH and caspase-3 activity were measured. The results showed that after 6 and 24 hours of exposure to GW1929 or GW9662 cell viability and caspase-3 were not affected. To conclude, in tested concentration GW1929 and GW9662 can did not induce apoptotic or necrotic cell death. Studied concentrations can be used in culture of normal neurons as a potent and safe agonist and antagonist of PPAR- γ receptor. Support by NCN grant 2014/13/N/NZ4/04809.

2. The role of PERK kinase inhibitors in treatment of Alzheimer's disease

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Alzheimer's disease is an individual clinical and pathological disease entities and the most common progressive cause of dementia, which is associated with memory loss and aggravation of cognitive function. It is characterized by deposition of amyloid beta plaques among the neurons and synaptic degeneration as a result of stress conditions, which leads to phosphorylation PERK kinase and activation the Unfolded Protein Response branches. We selected set of potential PERK inhibitors utilizing docking software. Next, we tested its biological activity by Time Resolved Fluorescence test. We selected 209 compounds for further analysis. Its specific ability to inhibition only PERK kinase was measured by evaluating PERK and eIF2 α phosphorylation at a concentration of 250 nM to 5000 nM of each inhibitor using the Radioactive Kinase Assay. We selected 4 compounds marked by numbers 1, 3, 12, 41. As a results inhibitor marked 1 was the most active and significant inhibition of PERK kinase was obtained at 500 nM and higher concentrations. In conclusion it is highly possible that discovery and characterization of a small molecule inhibitors of PERK may contribute to preventing the excessive accumulation of amyloid beta among the neurons, neuronal loss and memory impairment in Alzheimer's disease. This work was supported by grant HARMONIA no. 2013/10/M/NZ1/00280 from the Polish National Science Centre and by grant of Medical University of Lodz, Poland no. 502-03/5-108-05/502-54-170.

3. The neurotoxic effects of lead nanoparticles

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Problems of technogenic pollution by heavy metals salts, their toxic effects on living organisms, not lost relevance. Heavy metals, such as lead, violate the function of many organs and systems. Nanoparticles of lead exert the special influence. Therefore, the study of neurotoxicity, behavioral changes and morphological one in the brain tissue after 30 injections of 10 nm and 30 nm lead sulfide compounds nanoparticles at a dose of 1.08 mg / kg. m.b. on 45 white rats was the purpose of our research. We have identified of behavioral reactions changes: use of smaller dimensions nanoparticles, caused an increase of anxiety activity in rats, a bigger one - decrease of locomotors activity in animals. Expressed structural changes were observed in brain tissue after injection of lead sulfide nanoparticles of smaller sizes. In histological sections pronounced brain tissue swelling was in a perivascular space with single bleeding in the brain tissue. Blood vessels were narrowed, the vascular wall - thinned. The level of unsaturated fatty acids decreased significantly, the level of polyunsaturated fatty acids - increased. Lipid metabolism disorders were more pronounced with the injection of small size lead sulfide nanoparticles. According to behavioral reactions, morphological changes of the cerebral hemispheres cortex and its lipid composition, compounds of lead sulfide nanoparticles of 10 nm have a more toxic effect.

4. Apoptotic and neurotoxic actions of chemical UV filter benzophenone-3

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Benzophenone-3 (BP-3) is a chemical sunscreen agent, absorbing UVB and UVA radiations. The industrial use of BP-3 has been increasing over the past decade and nowadays 10000 tons of UV filters are produced annually for the global marked. In addition to its photostability, lipophilicity and persistence in the environment, BP-3 has been demonstrated as an endocrine disrupting chemical (EDCs). The most disturbing seems to be the fact that breastfeed babies are continuously exposed to BP-3, since its high concentrations have been found in human milk samples. In addition, increasing exposures to EDCs have recently been linked to etiology of neurodevelopmental disorders. Our study demonstrated that BP-3 (25-100 μ M) induced apoptosis in the mouse neuronal cell cultures as evidenced by activation of caspase-3 and formation of apoptotic bodies that was accompanied by significant increase of lactate dehydrogenase-release (LDH). Interestingly, neocortical neurons were more vulnerable to the actions of BP-3 both at early (2 DIV) and late (7, 12 DIV) developmental in vitro stages. Given that neurodevelopmental and neurodegenerative disorders are accompanied by apoptotic processes, knowledge about deleterious effects of BP-3 gives prospects for better understanding the pathomechanisms of action of EDCs. Acknowledgements: This study was

supported by the Polish National Center of Science grant No. 2014/13/N/NZ4/04845 and the statutory fund of the Institute of Pharmacology Polish Academy of Sciences, Krakow, Poland. Agnieszka Wnuk and Joanna Rzemieniec are holders of scholarship from the KNOW sponsored by Ministry of Science and Higher Education, Republic of Poland.

5. Human glucocerebrosidase expressed in the retina photoreceptors of Drosophila melanogaster causes changes in glial cells

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Gaucher's disease (GD) is a lysosomal storage disorder caused by defects in the GBA gene encoding glucocerebrosidase. We used the retina photoreceptors of Drosophila melanogaster as a model to study neuronal changes caused by Gaucher's disease. In our research we used flies with the expression of non-mutated human GBA gene and with two types of GBA mutations: R120W (mild neurodegeneration in human) or RecNcil (acute abnormalities). As a control we used wild type flies. We used transmission electron microscopy to investigate the effect of GBA expression on ultrastructure of the retina and the first optic neuropil (lamina). Our results showed that both mutations RecNcil and R120W cause degenerations in the retina photoreceptors. We also observed changes in pigment cells surrounding the photoreceptors. Their number was reduced either in strains carrying the mutations or non-mutated human GBA gene. Additionally, the number of invaginations in the photoreceptors terminals of epitheli al glia (called capitate projections) in the lamina of flies with mutation R120W was decreased when compared with control. Our results revealed that despite GBA is expressed in the retina photoreceptors, changes are also observed in neighboring glial cells. It suggests that human gene GBA has impact on both types of nerve cells.

6. The protective property of vitamin D3 in the hippocampal organotypic cultures stimulated by lipopolysaccharide

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Several data postulated that active form of vitamin D3 may have neuroprotective effects in experimental models of neuronal damage. In the present study we examined the effect of vitamine D3 on the LPS-induced changes in hippocampal organotypic cultures. Cultures were prepared from the hippocampi of 7-8-day-old rats. On the 7th DIV slices were pre-treated for 30 min with different concentrations of vitamin D3 and then stimulated for 24h with lipopolysaccharide (LPS, 100ng/ml). Next, the cell death/viability parameters (iodium propide, LDH and MTT tests) as well as NO production were measured. We found that vitamin D3 (5-25 μ M) did not evoke any significant changes in cell viability as measured by MTT assay and in cell death as evidenced by LDH and flow cytometry analyses. Addition of LPS increased cell death and enhanced NO release. In LPS-stimulated slices, we observed the beneficial effect of vit.D3 (5-10 μ M) which diminished the number of dying cells and suppressed LPS-evoked overproduction of NO. Concluding, vit.D3 shows the protective properties in hippocampal organotypic cultures stimulated by LPS. Therefore, our results suggest the need for further research to elucidate the intracellular mechanisms of vitamin D3 action. This work was supported by grant Nanoneucar number 199523.

7. Post-treatment of hippocampal cells with raloxifene and 3,3'-diindolylmethane protects neurons against hypoxia-induced damage

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Stroke is a 3rd leading cause of death worldwide. However, the only approved therapy against ischemic stroke is recombinant tissue plasminogen activator. This therapeutic strategy has certain limitations related to narrow therapeutic window and risk of hemorrhage. Therefore, scientists are still searching for more effective compounds to cure neuronal degenerations induced by hypoxic/ischemic events. Amongst them are selective estrogen receptor modulators (SERMs) such as raloxifene and selective aryl hydrocarbon receptor modulators (SAhRMs) whose representative is 3,3'-diindolylmethane (DIM). Recently we have shown that the treatment of neurons with raloxifene or DIM and simultaneous exposure to hypoxia leads to protection against hypoxia-induced neurodegeneration. However, there are no data on neuroprotective capacity of SERM and SAhRM used after episode of hypoxia which is

clinically more relevant. This study aimed to assess neuroprotective potential of raloxifene and DIM during 1 h posttreatment following hypoxia. We showed that hypoxia caused approximately 200% and 130% increase in lactate dehydrogenase release (LDH) and caspase-3 activities, respectively. Raloxifene or DIM applied after hypoxia inhibited caspase-3 activity and LDH release in a concentration dependent manner. Our data suggest that neuroprotective potential of raloxifene and DIM is retained after hypoxic insults which may contribute to development of new therapeutic strategies. Joanna Rzemieniec and Agnieszka Wnuk are holders of scholarship from the KNOW sponsored by Ministry of Science and Higher Education, Republic of Poland. The study was supported by statutory funds of the Institute of Pharmacology, Polish Academy of Sciences.

8. The influence of hyperhomocysteinemia, ischemia-reperfusion injury and ischemic preconditioning on antioxidant defense parameters in rat brain hippocampus

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Introduction: The hyperhomocysteinemia (hHcy) is a co-morbid risk factor of human stroke, which is a third leading cause of mortality worldwide. Plasma hHcy aggravates the ischemia-reperfusion (IR) injury by increased thiolation and homocysteinylation to proteins and enzymes. As a consequence, these post-translational modifications affect the function and activity of enzymes involved in the free radical protection. However, the induction of ischemic preconditioning (IPC) is a potential marker which can improve neuronal outcome after ischemia.

Material and methods: The male Wistar rats divided into control group, hyperhomocysteinemic group, IR and IPC group and IR and IPC group with hHcy were used in our experiments. Homogenized hippocampi were used for biochemical analysis.

Results and conclusion: Our results showed the increased of catalase activity, glutathione and total antioxidant capacity (TAC) in the hHcy group compared to the control group as well as the increase of these parameters in IR and IPC groups with hHcy compared to the corresponding IR and IPC groups. We showed that hHcy contributes to the deterioration of IR injury in rat brain hippocampus.

Acknowledgement: This work was supported by the project "Biomedical Center Martin" ITMS code: 26220220187 cofinanced from EU sources, and by VEGA 1/0128/16.

9. Effect of the pro- and anti-inflammatory factors on maintenance of blood-brain barrier integrity

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Preservation of the physical and biochemical barrier between brain and blood vessels is necessary for the proper functioning of the central nervous system. The endothelial cells in the brain vary from the cells of the same type in the other organs. Different expression profile of proteins forming cell-cell connections and zonulae occludentes (i.e. occludins, claudins, JAM proteins) has been observed in the case of endothelial cells in the brain compared to the same type of cells in other tissues. Alterations in the expression level, localization and post-translational modifications of these proteins may be responsible for leakage of blood-brain barrier in pathological states. These changes can be caused by increased levels of pro-inflammatory cytokines in both peripheral blood and in the cerebrospinal fluid. On the other hand, anti-inflammatory molecules could play protective role in maintenance the integrity of endothelial barrier. In our study, HBEC cells were treated with pro-inflammatory (TNF-a) and anti-inflammatory (TGF-b) factors for 24 hours. The application of mass spectrometry-based techniques allowed us to have deep insight into proteome of examined cells. We will present the obtained results concerning proteome alterations which may reveal the relevance of TNF-a and TGF-b in the etiology of neurodegenerative diseases.

10. The detrimental effect of apoptotic inhibitor ABT-737 on neuroblastoma cells

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Neuroblastoma is an agressive childhood extracranial solid tumour. Despite intensive therapeutical approaches, the prognosis is poor. Resistance to apoptosis is a common feature of tumour cells, which leads to the resistance to therapy. Selective targeting of the Bcl-2 family proteins can activate apoptotic cell death and thus overcome drug resistance to chemotherapy. In our study we tested apoptotic inhibitor ABT-737, which selectivelly targets anti-apoptotic proteins Bcl-2, Bcl-w and Bcl-xl, with the aim to determinate the influence on neuroblastoma cell line (SH-SY5Y) survival. We used colorimetric tetrazolium reduction (MTT) assay to measure cytotoxic effect and TaqMan® Human Apoptosis Array to detect apoptotic expression levels in neuroblastoma cell line after ABT-737 treatment. Our results showed inhibition influence of ABT-737 on neuroblastoma cell viability. We observed significant changes in expression levels of genes coding proteins from several apoptotic signaling pathways. The current available treatment of neuroblastomas is still not effective, therefore the new potencial apoptotic Bcl-2 inhibitor offers a novel approach to overcome drug resistance in this highly resistant tumour type. This study was supported by the Slovak Research and Development Agency under the contract No. APVV-0224-12 and project "Biomedical Center Martin", ITMS code: 26220220187, the project is co-financed from EU sources.

11. Comparative proteomic study of central nervous system tissue in hyperhomocysteinemic and healthy animals

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Elevated level of homocysteine, a side product of metabolism of amino acid methionine, is believed to be one of the independent risk factors for a development of ischemic stroke by accelerating atherosclerotic changes. Homocysteine increases production of reactive oxygen species by various mechanisms and thus contributes to oxidation of proteins, lipids and nucleic acids. The aim of this ongoing study is to create a proteomic profile from samples of cortex tissue from laboratory rats with induced hyperhomocysteinemia and its comparison to proteomic profile of healthy controls. Subsequently, proteins with different levels of expressions in these two groups will be selected and identified. Such proteins might play important role in homocysteine pathogenesis. Each group (with induced hyperhomocysteinemia and healthy control) includes 5 laboratory animals. Methods used in this study include protein profiling by two dimensional electrophoresis, statistic evaluation of acquired data and mass spectrometry analysis of proteins with statistically significant changes in levels of expression in hyperhomocysteinemic animals compared to healthy animals. This work was supported by grant VEGA 1/0128/16 Epigenetic and Molecular Markers of Neuroprotection and Ischemic Tolerance.

12. Plasma proteins as markers of multiple sclerosis

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Background: Neuroinflammation and neurodegeneration are main driving processes in multiple sclerosis (MS) progression at molecular level. Among other changes, expression and quantity of plasma proteins are also influenced. Proteomics offers a great possibilities for deep protein study and searching for novel MS biomarkers. The aim of our work was to realize a preliminary study of changes in plasma protein levels in cases of MS patients and healthy control subjects.

Methods: We analysed plasma protein profiles (4 patients suffering from multiple sclerosis – MS Center, UH and JFM CU Martin, 4 healthy control subjects) using 2-D protein electrophoresis and subsequent MALDI TOF/TOF mass spectrometry for detection of differently expressed, but unknown proteins.

Results: We observed significant changes in acute-phase protein levels - decrease of haptoglobin and increase of alpha-1B-glycoprotein and alpha-1-antitrypsin between MS patients and healthy control subjects.

Conclusions: Based on our promising results, it is suggested to continue and enlarge the groups of examined people focusing on various MS forms.

This work was supported by grants VEGA 128/16 (Ministry of Education, Slovak Republic), 2012/30-UKMA-7 Biological and molecular markers of multiple sclerosis (Ministry of Health, Slovak Republic) and ITMS: 26220220187 Biomedical Center (BioMed Martin) co-financed from EU sources.

13. Antidepressant drugs are involved in the regulation of inflammatory response in the stimulated human cell line HaCaT

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Antidepressant drugs such as fluoxetine and desipramine have proved effective in suppressing contact hypersensitivity (classical example of cell-mediated immune response) in a murine model of contact hypersensitivity. The aim of present study was to elucidate if the antidepressants are involved in the inhibitory effect on proinflammatory cytokines production by keratinocytes. The HaCaT cell line (human keratinocytes) was stimulated by lipopolysaccharide (3 μ M/ml) and mixture of cytokines interferon (IFN)- γ /tumor necrosis factor (TNF)- α (10 ng/ml), cultured 24 hours. Antidepressant drugs – fluoxetine (0.1 and 0.5 μ M) and desipramine (1 and 5 μ M) was added to the culture. Cell lysates and supernatants were collected. The level of proinflammatory cytokines – interleukin (IL)-1 β and IL-6 was measured by ELISA assay. The stimulants significantly increased the secretaion of cytokines and used antidepressants regulated this inflammatory response. It can be concluded that antidepressant drugs are effective in modulation of proinflammatory releasing by human keratinocytes, which may contribute to mechanism of suppression contact hypersensitivity. This study was supported by grant: NCN, PRELUDIUM 7; UMO-2014/13/N/NZ6/00639

14. The expression of ATMIN protein and mRNA decreases in neuronal-like differentiated SH-SY5Y cells after H2O2 and rotenone treatment

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ATM kinase participates inter alia in DNA repair processes, regulation of cellular response to oxidative stress or mitochondrial homeostasis. It has been suggested that ATMIN (one of the ATM interactor) could participate in regulation of this kinase function, although mechanisms of this cooperation are still not well recognized. In order to widen the knowledge about the role of ATMIN in neurodegeneration, we tested its mRNA and protein expression level after treatment of retinoic acid (RA)-differentiated human neuroblastoma SH-SY5Y cells with oxidative stress inducers (hydrogen peroxide (H2O2)- and rotenone (Rot)). Twenty four hours of treatment of cells with Rot (0.1 mM) and H2O2 (1 mM) evoked about 50% decrease in cell viability. Moreover, we observed a significant decrease in the level of ATMIN protein and mRNA after 1 and 4 hour of treatment with Rot and H2O2, respectively. These data suggest that a reduction in ATMIN expression could participate in mechanism of cell damage induced by oxidative stressors, although an explanation of this phenomenon requires additional studies. Acknowledgements: Jakub Chwastek is a holder of scholarship from the KNOW sponsored by Ministry of Science and Higher Education, Republic of Poland.

15. Prenatal stress increases hippocampal levels of pro-inflammatory factors: IL-1 β , IL-18 and CCL2 in young offspring rats

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Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland The disturbances in concentration of pro-inflammatory cytokines and chemokines in CNS may underlie pathological processes leading to mental diseases. In addition multiple data provide evidences that early experiences (e.g. stress during pregnancy) can be crucial for neuronal development and consequently for the health in adulthood. The aim of the present study was to examine the impact of prenatal stress procedure on the concentration of IL-1 β , IL-18 and CCL2 in hippocampus of young offspring rats. Pregnant rats were subjected to restraint stress until the delivery. At 7 days of age, male offspring animals were sacrificed to determine the levels of IL-1 β , IL-18 and CCL2 in hippocampus by ELISA. The obtained data demonstrated that young offspring after prenatal stress procedure exhibit changes in concentration of the cytokines and the chemokine in the examined brain area. Biochemical study showed significantly higher levels of IL-1 β , IL-18 and CCL2 in hippocampus of prenatally stressed offspring. In conclusion, present study demonstrated that prenatal stress procedure leads to brain inflammatory status in young offspring rats. It may be postulated that observed changes if long-lasting may be harmful factor leading to disorders in the following years of life. Supported by the grant no. 2013/09/B/NZ7/04096, National Science Centre, Poland.

16. PINK1 mutation causes synapse dysfunction through the reduction of Bruchpilot protein level

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The hereditary form of Parkinson's disease may be caused by a mutation of PTEN induced putative kinase 1 (PINK1) gene, which encodes a protein kinase involved in mitophagy. Disturbances in this process result in many symptoms like neurodegeneration or synaptic dysfunction. Synapse structure and function depends on the level of synaptic proteins such as Bruchpilot (BRP). This presynaptic protein is a key component of the active zone and is involved in neurotransmitter release to the synaptic cleft. In our study we used Drosophila melanogaster model of Parkinson's disease. Using immunohistochemistry and confocal microscopy we found that PINK1 mutant has reduced BRP level in tetrad synapses in the visual system. We also analyzed BRP level in whole brain by Western Blot, that showed the reduced level in PINK1 mutant. This result suggests that the mutation affects structure of all synapses in the brain. It is also possible that PINK1 mutant affects synapse structure in the peripheral nervous system, because climbing abilities of Parkinson's model flies were reduced. This suggests that the reduction of BRP level impair synaptic functions, which results in decreased climbing ability, life span and perhaps in reduced transmission of visual information from the retina to the brain.

17. LPS pretreatments at different developmental stages modulate differently astroglial transformation following seizures evoked in adulthood

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Emerging experimental evidence indicates that neuroinflammation with activated astrocytes and increased production of proinflammatory cytokines is involved in epileptogenesis. However, it is also suggested that early age inflammation acting as a preconditioning factor may also have protective effects in case of epilepsy. The aim of this study was to examine the long term effects of systemic inflammation induced at different postnatal developmental stages on the range of morphological changes in astrocytes within brain cortex in response to status epilepticus evoked in adulthood. To examine this six- or 30-day-old Wistar rats were injected intraperitoneally with LPS. When became two-month-old, rats which survived inflammation were injected with pilocarpine to evoke status epilepticus and sacrificed 3 days after. Brain sections were then processed for GFAP immunohistochemistry, photographed and the manual mini-Sholl analysis was performed. LPS injection alone on P30 caused a significant increase in number of astrocytic branches (NAB). Seizures induced in non-treated adult rats caused a significant decrease in NAB. However, in both LPS-treated groups the effect of seizures was significantly lowered. This means that morphology of astrocytes in rats pretreated with LPS and reacting to seizures is more similar to morphology of astrocytes in naive rats. Supported by the NSC-grant: UMO-2012/05/B/NZ4/02406.

18. The role of glucocorticoid receptor (Nr3c1) and mineralocorticoid receptor (Nr3c2) in adverse effects of corticosterone and/or glutamate in organotypic hippocampal cultures

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Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland Experimental data indicates that the concentration of glucocorticoids (GCs) during the perinatal period permanently increases the sensitivity of brain tissue to adverse factors acting in the adulthood. The aim of the present study was to find out whether prenatal stress potentiates the adverse effects of corticosterone and/or glutamate on the hippocampal cultures and whether in this action changes in the expression of glucocorticoid (Nr3c1) and mineralocorticoid (Nr3c2) receptors are involved. The hippocampal organotypic cultures prepared from the brains isolated from 7-day-old offspring of control and prenatally stressed rats were treated with corticosterone and/or glutamate for 24 or 72h. It has been found that corticosterone and glutamate present in the medium for 72 h, but not 24 h, damaged hippocampal cells. Expression of Nr3c1 (in control and prenatally stressed groups) and Nr3c2 (in prenatally stressed group only) were increased after 24 h, while after 72 h when cell damage was observed, Nr3c2 mRNA was decreased. The obtained data indicate that during glucocorticoid-induced hippocampal cell damage also decrease in mineralocorticoid receptors expression occurs and that prenatal stress influences the magnitude of these change. Acknowledgements: This work was supported by the NCN, grant No. UMO-2012/05/N/NZ7/00678. A. Kurek, is a holder of scholarship from the KNOW sponsored by MSHE, RP.

19. Photochemically-induced cortical and subcortical models of ischemic stokes in rats – radiological analisys with 9T MRI

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Background: Cerebrovascular diseases are the principal causes of mortality and disability worldwide. 80% of all strokes is ischemic. Magnetic Resonance Imaging (MRI) is widely used technique to image stroke patients for diagnostic and therapeutic purposes.

Aim: The aim of our study was to analyze focal ischemia in photothrombotic cortical and subcortical animal models of stroke with imaging techniques on 9,4T MRI.

Methods: We carried out prospective study, experimental group consists of 7 female Long – Evans rats. 2 rats underwent subcortical and 5 cortical ischemia. All uderwent 24h post-surgery in-vivo MRI-imaging with animal-dedicated 9,4T scanner. We used following MRI techniques: T2-weighted, DWI, PWI, ADC map. We measured size of: an ischemia, "PWI-DWI mismatch" and CBF (cerebral blood flow).

Results: Mean ischemic area size on T2-weighted imaging were 2,1mm ±0,1mm, and was similar on DWI imaging. rCBF of ischemic core was 0 in all cases, rCBF of penumbra was 15-50 ml/100g/min and rCBF of contralateral similar location >80ml/100g/min. Based on the "PWI-DWI mismatch" we precisely located penumbra area.

Conclusions: Our models of cortical and subcortical ischemic stroke are repeatable, very precisely located and lowinvasive. MRI has great potential for studying animal models of brain ischemia as it can provide information on the progression of the brain lesions in vivo.

20. Features of cadmium sulfidenanoparticles neurotoxicity

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The widespread introduction of cadmium nanoparticles (NP) in industry leads to the need for toxicological studies to assess their safety profile. We studied neurotoxic action of cadmium sulfide NP of 5 and 10 nm and cadmium chloride. Wistar rats were injected intraperitoneally every day these compounds in doze 0.08 mg/kg for cadmium. Functional status and pathomorphological changes in the brain were assessed after 30 and 60 injections and 45 days after cessation of exposure. After cadmium exposure increase in relative brain mass, decreased locomotor activity and increased anxiety levels were observed. Biochemical changes in the brain were characterized by an increase in the concentration of diene conjugates, TBA-active products, the superoxide anion and OH-radical, the reduction of catalase activity, which may indicate the development of oxidative stress. There were perivascular and pericellular edema, decrease in vessel diameter, degenerative changes of neurons in the cerebral cortex and slight changes in the calcium, iron and copper content, as well as a significant reduction in the selenium content. In the post-exposure period, intensive cadmium accumulation was detected. The most expressed changes were observed after CdCl2 exposure, but CdS NP of 5 nm were more toxic as compared to NP of 10 nm.

21. 1,8-cineole change activity of nervous system of insect

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Terpenoids are major ingredients of essential oils. They exhibit repellent and neurotoxic action in the insect nervous system. Several mechanisms of its activity are proposed: inhibition of acetylcholinesterase (AChE) activity; positive, allosteric modulation of GABA receptors and binding to octopamine receptors. The aim of our study was to examine 1,8-cineole action in the insect nervous system. We performed a toxicity test using 1,8-cineole at 10-6M as fumigant against Periplaneta americana. The time of insect turning back from dorsal to ventral side was determinant of paralysis. Additionally we examined the activity of nerve cord of cockroach using set-up for extracellular recordings of activity after mechanical stimulation of cerci. 1,8-cineole cause cockroach paralysis. The time of turning back from dorsal to ventral side was statistically longer (2,6±0,5 s) than in control (0,6±0,2 s) 24 hours after application. 1,8-cineole softly increases activity of connective (part of nerve after the last abdominal ganglion). Moreover, it greatly increases (more than 4 times) the activity of cercal nerve (before the last abdominal ganglion). 1,8-cineole seems to be a strong neuroactive agent. Due to its high activity before synapse, the AChE inhibition cannot be its primary effect. One of the other two mechanisms is possible.

22. Genetic and biochemical markers associated with risk and progression of Multiple Sclerosis in Slovaks

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In our study we tried to identify genetic and biochemical markers associated with the risk and disability progression of multiple sclerosis (MS) in Slovaks. We examined 270 MS patients and 303 controls. MSSS score was used to evaluate the disease progression rate. For genotyping, we used restriction analysis. To evaluate calcidiol serum level, chemiluminescent microparticle immunoassay was used. As the risk factor for MS development, we identified a decreased serum level of calcidiol and allele C of rs6897932 in IL-7Ra gene. Allele T was found to decrease the risk of MS in individuals with genotype CT and TT. According to the rapid disability progression, we found minor allele T to be protective, especially in genotype TT, and genotype CC and decreased serum level of calcidiol were found to be negative prognostic factors. The proposed markers could help to identifie individuals predisposed to MS development or rapid disability progression. Acknowledgements: The study was supported by the grants VEGA 128/16 from the Ministry of Education of the Slovak Republic, 2012/30-UKMA-7: Biological and molecular markers of multiple sclerosis from Ministry of Health of the Slovak Republic and Biomedical Center (BioMed Martin)", ITMS code: 26220220187 co-financed from EU sources and European Regional Development Fund.

23. Impact of elastin-derived peptides (EDPs) on cell viability, reactive oxygen species (ROS) formation and apoptotic process in mouse astrocytes in vitro

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Elastin provides elasticity to many connective tissues such as the aorta, lung, cartilage, elastic ligaments and skin. Degradation products of elastin, elastin-derived peptides (EDPs) are involved in various physiological and pathological processes. EDPs are detectable in cerebrospinal fluid of both group of healthy subjects and patients with ischemic stroke. The aim of this research was to investigate the impact of elastin-derived peptide (VGVAPG) on cell viability, reactive oxygen (ROS) production and apoptosis in mouse cortical astrocytes in vitro. The cultures of cortical astrocytes were prepared from Swiss mouse embryos on 17/18 days of gestation. The cells were cultured in phenol red-free DMEM/F12 medium supplemented with 10 % FBS and in the presence of rising concentration (1 nM to 100 μ M) of VGVAPG peptide for 6, 24 and 48 h. Afterwards, cell viability, ROS formation and caspase-3 activity were

measured. The results showed that after 6, 24 and 48 hours of exposure to VGVAPG peptide cell viability is not affected. However, in the same time period the highest μ M concentrations of VGVAPG peptide increase ROS production and activate caspase-3. To conclude, VGVAPG induce ROS-dependent apoptosis in mouse cortical astrocytes in vitro. Support by University of Information Technology and Management in Rzeszow.

24. Neuroregenerative potential of mesenchymal stem cells isolated from various sources

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Mesenchymal stem cells (MSCs) are gaining increased interest of regenerative medicine as a tool in cellular therapies of pathological processes in nervous system, driven by excessive inflammation and neurodegeneration. MSC, which originally populate adult and neonatal tissues, have anti-inflammatory and immunomodulatory properties, which make them perfect candidate as a transplantation material. Moreover, MSCs are known to release many trophic factors, that can mediate extensive tissue repair. This study was to evaluate level of expression of neurotrophic (BDNF, GDNF, NGF, CTNF) and angiogenic (VEGF, HGF, PSTG2) factors as well as immunomodulatory potential (ARG, IDO, IL-4) of MSCs isolated from patients' bone marrow, adipose tissue and Wharton's jelly. Moreover, we have tested media conditioned on MSCs from various sources and their influence on inhibitory GABA interneurons progenitors (MGE) differentiated from human induced pluripotent stem cells. Effect of conditioned media were determined by survival of progenitor cells and their potential to differentiate. Obtained results enable us to compare potential of different MSCs as a source of stem-cells based therapies in injuries of the nervous system.

25. Neuroprotective action of hydroponic Teucrium polium in $A\beta_{25-35}$ - induced neurodegeneration in rats

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BACKGROUND: Neurodegenerative diseases caused by neurons loss lead to devastating effects on patients' lives. Teucrium polium has been used for over 2000 years in traditional medicine due to its hypoglycemic, insulinotropic, antioxidant, and anti-inflammatory properties. Accumulated evidence suggests that phytocompounds, found in herbs may potentially hinder neurodegeneration, and improve memory and cognitive function. Flavonoids can affect A β production and have neuroprotective effects against Alzheimer's disease (AD). The hippocampus, a brain area critical for learning and memory, is especially vulnerable to damage at early stages of AD. The amygdala is another important subcortical region that is severely and consistently affected by pathology in AD. Alzheimer's disease is characterized by the degeneration and loss of cholinergic neurones in the nucleus basalis Meynert.

MATERIALS AND METHODS: In order to investigate whether hydroponic Teucrium polium (enriched with flavonoids) protects against beta-amyloid ($A\beta_{25-35}$)-induced neurotoxicity in rats and explore the electrophysiological effects of Teucrium polium, we prepared an AD model by bilateral intracerebroventricular injection of $A\beta_{25-35}$ and treated with Teucrium polium. We observed the effects on learning and memory. Early and late tetanic, post-tetanic potentiation and depression of neurons to high frequency stimulation of entorhinal cortex was studied.

RESULTS: Under $A\beta_{25-35}$ deeper neurodegenerative changes occur in the hippocampus, basal nucleus of Meynert and amygdala and Teucrium polium ameliorated $A\beta_{25-35}$ -induced learning and memory dysfunction.

CONCLUSION: Hydroponic Teucrium polium may be useful in the prevention of Alzheimer disease and other neurodegenerative diseases.

26. Correction of organic mercury cytotoxicity species in human glioblasts (u-373 mg) by mildronatum

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It is well known that mercury relates to neurotoxic poisons. Thus, more damaged neurons, but the cells of glia react earlier. Therefore, the aim of the study was to evaluate the reaction of glioblastoma in vitro under the conditions of acts of small doses of mercury chloride and the effectiveness of medicine correction of Mildronate. Sensitivity of the cells to the effect of mercury chloride, Mildronate and mercury chloride in the presence of Mildronate was studied by trypan blue staining and in accordance with the method of May-Grunwald. The concentration of Mildronate in culture medium ranged from 10 mg / ml to 0.01 mg / ml. Live cells were counted in hemocytometer. We determined the percentage of live cells. Data compared by a Student's t-test. Study of cell line U-373-MG in the conditions of

Mildronate application and chloride mercury exposure showed a large number densely placed a small polygonal glioblasts, compared with experience without medicine correction. Structurally damaged cells are less frequent observed. Cytological examination revealed cells at different stages of division, compared to the study without pharmacological effects. When exposed Mildronate in doses of 10.0 mg/ml, 1.0 mg/ml and 0.1 mg/ml is observed 73,0 (69,8; 76,2) %, 67,3 (62,8; 71,9) %, 61,8 (59,1; 64,5) % living cells, reduced the decrease in dose and statistically significantly more than in experience with mercury exposure.

27. Contribution of mitochondrial derived reactive oxygen species (ROS) in neurodegenerative diseases

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Clinically, mitochondrial oxidative stress has been demonstrated to be involved in progressive neurodegeneration in many diseases, such as Parkinsons or LHON. Preclinically, the animal models used to study the role of reactive oxygen species (ROS) on neurodegeneration lack the slow progression time course seen in human diseases.

Purpose: The goal of this project is to develop an animal model that results in a slow increase in ROS, followed by a steady and progressive neurodegeneration, in order to mimic as closely as possible the human disease state. Such system allows also investigating how, when, and why mitochondrial ROS induces neuronal death.

Methodology: Deletion of SOD2 gene with the use of Cre-LoxP system in vivo in mice striata and in vitro in primary neuronal cell culture.

Results: In-vivo SOD2 depletion evoke ROS accumulation together with changing striatal connectivity, causing ongoing inflammation and behavioral changes in mice. In-vitro studies, apart from replicating high correlation between SOD2 depletion and ROS accumulation, showed decreased cell viability, increase in apoptosis and changes within cell energetic.

Conclusions: Those data support SOD2 knock-down in vivo mouse model and cell culture system as means of directly studying mitochondrial ROS and progression induced by continuous oxidative stress. This is a substantial improvement over previous models of ROS induced neurodegeneration lacking slow progression time course.

PAIN

28. IL-1 family – how blockage of IL-1beta and IL-18 signalling diminished neuropathic pain and enhanced the efficacy of morphine

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Currently, the low efficacy of antinociceptive drugs for the treatment of neuropathic pain is a major therapeutic problem. Here, we show the potential role of IL-1 family members signaling in this phenomenon. IL-1beta and IL-18 are an important molecules in nociceptive transmission. We have studied the changes in the mRNA/protein levels (qRT-PCR/Western blot analysis) of IL-1beta, IL-1 receptor antagonist (IL-1Ra), IL-18, IL-18-binding protein (IL-18BP) in rats following chronic constriction injury (CCI) of the sciatic nerve. Our study demonstrated upregulation of pronociceptive IL-1beta and IL-18, and downregulation of antinociceptive IL-18BP in the ipsilateral spinal cord 7 days after CCI. Moreover we performed single intrathecal administration of an IL-1Ra or IL-18BP (100 ng i.t., each) on the 7th day following CCI, symptoms of neuropathic pain were attenuated, and the analgesia pursuant to morphine (2.5 μ g i.t.) was enhanced. In summary, restoration of the analgesic activity of morphine by a blockade of IL-1 family members signalling suggests that increased IL-1beta and IL-18 responses may account for the decreased analgesic efficacy of opioids observed in the treatment of neuropathic pain. Acknowledgments: Supported by the National Science Centre, Poland grant Harmonia-2013/10/M/NZ4/00261 and by the Institute of Pharmacology statutory funds.

29. Evaluation of anti-nociceptive potential of dual-target compound OMDM198 in the animal model of osteoarthritis

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Osteoarthritis (OA) is a disease resulting from cartilage degeneration with chronic pain as a main symptom. Lack of satisfactory pain management leads to the search of new therapies. Recent studies suggest endocannabinoid system (ECS) as novel target for OA pain treatment. Presented results discuss the benefits of dual- over single-acting compounds interacting with ECS. Mono-iodoacetate animal model of OA has been investigated in presented studies. Single target compounds (URB-597 – FAAH inhibitor, SB-366791 – TRPV1 antagonist) and dual-acting OMDM-198 (FAAH inhibitor/TRPV1 antagonist) were used in behavioral (PAM test) and molecular (RT-qPCR) assessment. Elevation of pain threshold in PAM test was similar for all tested compounds, although OMDM-198 was used in much lower dose compared to URB-597 and SB-366791. Upregulation of CB1, TRPV1 and FAAH mRNA was observed in neuronal tissue of animals after treatment with OMDM-198. None of other compounds tested did not cause a robust changes in ECS mRNA expression. Results obtained from molecular and behavioral experiments suggests that OMDM-198 is suitable candidate for a novel therapy of OA pain. Our results may lead to improvement in novel OA treatment strategy targeting ECS. Supported by National Science Centre, Poland by grants: OPUS UMO-2014/13/B/NZ7/02311, SONATABIS/NCN/2012/07/E/NZ7/01269, and statutory funds.

30. Pharmacological antagonism of TLR4 and P2X4R potentiates opioid anagesia in rat neuropathic pain model

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Accumulating evidence demonstrate that microglial receptors may play a role in neuropathic pain. Based on available research, we have chosen Toll-like receptor subtype 4 (TLR4), and P2X4 purinergic receptor (P2X4R) to evaluate their contribution in neuropathy development, ability to amplify opioid effectiveness and influence on glia activation. Study consisted of behavioural (von Frey's, cold plate) and biochemical analysis (Western blot) on day 7 after CCI (chronic constriction injury) to the sciatic nerve in rats. We have demonstrated that pharmacological antagonism of TLR4 with LPS-RS Ultrapure as well as P2X4R with CORM-2 significantly attenuated allodynia and hyperalgesia on day 7 after CCI and lowered, upregulated in neuropathy, microglia and astroglia activation markers. Both LPS-RS Ultrapure and CORM-2 enhanced morphine/buprenorphine effectiveness. In summary, results indicate that blockade of TLR4 and P2X4R may have potential therapeutic utility under neuropathic pain conditions. Acknowledgements: Study supported by National Science Centre grant Harmonia2013/10/M/NZ4/00261. AM.Jurga, A.Piotrowska and J.Starnowska are holders of KNOW scholarship sponsored by Ministry of Science and Higher Education, Republic of Poland.

31. The RS504393 (CCR2 antagonist) modulates neuropathic pain via CCR2/CCL2 and glial signaling pathways in CCI-exposed rats

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Neuropathic pain develops as a result of nervous system damage. It is correlated with glial cells activation and neuroimmune interactions. However, optimally efficient treatment is still unknown. Recent studies suggest the crucial role of CCR2 in neuropathy development. The aim was to examine the influence of RS504393 (CCR2 antagonist) on neuropathic pain symptoms development and associated changes in the mRNA level of CCR2, CCL2 and glial markers in chronic constriction injury (CCI) rats. All experiments were performed in accordance with IASP rules. Firstly, animals were implanted with intrathecal catheters, then CCI of the sciatic nerve was performed. Behavioral tests, measured allodynia and hyperalgesia, were conducted 7 days after CCI. The mRNA level was examined by qRT-PCR. We provided evidence that chronic i.t. administration of RS504393 attenuated neuropathic pain symptoms in CCI-exposed rats. Simultaneously, RS504393 significantly reduced the mRNA level of CCR2 and CD40 in the spinal cord and DRG 7 days after CCI. Additionally, we observed lower regulation of CCL2 and GFAP mRNA level in the DRG in RS504393-treated CCI-exposed rats. Our results suggest that pharmacological modulation of CCR2 is a potential novel

approach for neuropathic pain treatment. Acknowledgments: Supported by National Science Centre grant-Harmonia-5-2013/10/M/NZ4/00261, KK-KNOW-scholarship, statutory founds.

32. CB2 receptor as emerging target to prevent and treat osteoarthritis

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Osteoarthritis (OA) is widespread condition characterized by chronic pain and gradual degradation of articular cartilage. There is no disease modifying therapy available therefore studies are focused to propose potential therapies. Active participation of the endocannabinoid system in the pathophysiology of OA has been shown therefore here we investigated JWH-133, CB2 receptor's agonist, as chondroprotective and antinociceptive compound. Human chondrocytes were treated with monoiodoacetate (MIA) to mimic OA. Subsequently cells were treated with JWH-133 to investigate the influence of endocannabinoid system on chondorocytes' proliferation (BrdU assay) and migration (wound healing assay). Chondrocytes demonstrated decreased proliferation and migration capacity after MIA treatment. These effects were reversed by JWH-133 in CB2 dependent manner. Moreover in the MIA rat model of OA we investigated the antinociceptive properties of JWH-133, using behavioral tests: pressure application measurements (PAM) and von Frey. JWH-133 demonstrated CB2-dependent anti-allodynic properties both in PAM von Frey test. Our studies demonstrate therapeutic value of CB2 agonists for pain management associated with osteoarthritis. Furthermore, JWH-133 may act as stimulator of chondrocytes' proliferation, thus would delay OA progression. Our results propose innovative therapy, which could be beneficial for OA patients. Supported by National Science Centre, Poland by grants: OPUS UMO 2014/13/B/NZ7/02311,SONATABIS/NCN/2012/07/E/NZ7/01269, 0044/DIA/2013/42, and statutory funds.

33. The effect of pregabalin on cognition in streptozotocin-induced model of diabetes in mice.

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Cognitive impairments are frequent disorders accompanying many diseases and repeatedly constituting adverse effects of pharmacotherapy. The use of anticonvulsants, especially those of 1st generation, is followed by memory deterioration. In this respect, the 2nd generation of antiepileptic drugs are thought to be safer and lately their application has been expanded to several non-epileptic conditions, including diabetes-related neuropathic pain. Diabetes was induced using a single intraperitoneal injection of streptozotocin (200 mg/kg). Diabetic mice were selected for further in vivo tests that comprised the assessment of the effect of intraperitoneal pregabalin on contextual memory in the passive avoidance task. Streptozotocin significantly (p<0.01) influenced the retention phase of the passive avoidance task, reducing the step-through latency as compared to non-diabetic control, while pregabalin did not impair cognition in streptozotocin-treated mice. The lack of negative influence of pregabalin demonstrated in streptozotocin-treated mice may be crucial for both diabetic patients who are treated with this drug because of neuropathic pain, and physicians deciding on medicines used in neuropathic pain or epilepsy. Supported by Jagiellonian University grant K/ZDS/005546.

34. Influence of honey bee (Apis mellifera) venom on antinociceptive activity of selected drugs in hot plate test in mice

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The aim of the experiment was to investigate the effect of honey bee (*Apis mellifera*) venom on the activity of two analgesics: ketoprofen (nonsteroidal anti-inflammatory drug) and tramadol (opioid drug) in the acute thermal pain model (hot-plate test) in mice. Linear regression analysis was used to evaluate the dose-response relationships between logarithms of drug doses and their resultant maximum possible antinociceptive effects in the mouse hot-plate test. From linear equations, doses were calculated that increased the antinociceptive effect by 20% (ED₂₀ values) for bee venom, ketoprofen, tramadol, and their combination. The interaction between bee venom and selected

anaglesics was evaluated using an isobolographic analysis. Results indicate that all compounds produced a definite antinociceptive effect, and the experimentally-derived ED_{20} values for bee venom, ketoprofen and tramadol, when applied alone, was 2,4 mg/kg, 77,1 mg/kg and 11,9 mg/kg respectively. Isobolographic analysis revealed that the experimentally derived ED_{20} mix value for combinations of bee venom and selected drugs decreased in comparison to theoretically calculated ED_{20} mix value for these combinations. Overall, results demonstrated that the bee venom increases antinociceptive activity of ketoprofen and tramadol in the acute thermal pain mouse model.

SOMATOSENSORY PROCESSING

35. Exploring visuo-tactile crossmodal mechanisms through the frequency-tagging of steady-state evoked potentials

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Multisensory integration is thought to rely on the convergence of sensory inputs from different modalities to associative brain areas. It was also hypothesized that multisensory integration can depend on feed-back influence between sensory-specific areas. Here, we investigate this latter hypothesis using steady-state evoked potentials (SSEP), suggested to reflect (at least partially) cortical processing in primary sensory areas. Using light emitting diodes, two 16s sustained trains of flickering visual stimulation were concomitantly presented in either side of space. Simultaneously, a train of vibrotactile stimulation was applied on one of the participant's hands. In different blocks, the hand was positioned close to either the left or the right diode. Three different frequencies of stimulation were chosen to tag the specific EEG responses to the three different stimuli (visual left, visual right, tactile). Participants were asked to report occasional interruptions in the three streams of stimulation. Surprisingly, the results show no modulation of the amplitude of the visual SSEP when concomitant with the vibrotactile stimulation. This suggests that the crossmodal mechanisms known to modulate the classic ERPs to brief stimuli, might not be reflected in the SSEP.

36. Investigating crossmodal influence between nociception and vision in the peripersonal space of the limb using temporal order judgments

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In order to adapt behaviors to a potentially damaging threat, it is crucial to coordinate the perception of the location of the threat in external space and the perception of the location of the damage on the body surface. In this study, we investigate how a nociceptive stimulus applied to the hand affects the perception of visual stimuli occurring near the hand, placed either near or far from the body trunk according to the anteroposterior axis. In a temporal order judgement task, participants judged which of two visual stimuli had been perceived first. Each pair of visual stimuli was preceded by one nociceptive stimulus applied on one of the two hands (unilateral) or two nociceptive stimuli one applied on each hand at the same time (bilateral). Results show that, as compared to the bilateral condition, participant's judgments were shifted towards the visual stimuli having occurred near the hand on which the nociceptive stimulus was applied, independently of its position in space (near or far from the trunk). These results suggest the existence of cortical representations of each limb that extend slightly from their corporeal boundaries to external space, and are used as an interplay to integrate somatosensory and non-somatosensory information.

37. Cross-modal interactions between pain and vision: Enchanced responses to visual stimuli applied in an area of secondary hyperalgesia

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High frequency stimulation (HFS) applied onto the skin enhances the intensity of perception of mechanical nociceptive stimuli delivered to the skin surrounding the conditioned area. Here we tested if HFS was able to enhance visual evoked potentials (VEPs) applied onto the conditioned arm. High-density EEG (64 channels) was recorded in 26

participants before and after (T1, 20 minutes; T2 45 minutes) HFS. Visual stimuli were generated by two green laser diodes and were projected onto the skin where HFS was applied. The amplitude of the vertex complex (N155) of VEPs elicited by stimuli applied onto the HFS arm was compared across time to VEPs elicited by stimuli applied onto the control arm. All participants developed hyperalgesia for mechanical punctate stimuli applied onto the HFS arm, which was present at both 20 and 45 minutes after HFS. Importantly, we observed that, 20 minutes after the end of HFS, the N155 elicited by stimuli applied onto the sensitized arm was not reduced, in contrast with that elicited by stimuli applied onto the control arm, which underwent habituation. This is the first report showing This is the first report showing that nociceptive sensitization modulates responses to visual stimuli applied in an area showing hyperalgesia.

38. A time-warping method to disentangle sensory- and motor-related brain activities

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Disentangle rhythmic sensory- and motor-related brain activity in electroencephalographic signal is rendered difficult by the fact that both processes can be expected to elicit Steady-State Evoked-Potentials (SS-EPs) at the same frequencies. Previous behavioural studies have shown that when participants are asked to tap along a musical beat, their taps precede the actual occurrence of the beat by 30-50 ms. This phenomenon, referred to as mean negative asynchrony is smaller in musicians than non-musicians. Furthermore, in a pilot experiment (6 participants) we observed significant fluctuations in the tapping period, resulting in some amount of desynchronization between auditory input and motor output. Therefore, we investigated whether the fluctuations in motor output can be used as a "temporal signature" to disentangle sensory- and motor-related periodic brain activity, using a novel approach of time warping in order to separately concentrate those signal in the frequency domain, and measure distincts SS-EPs.

39. Cancer pain is not necessarily associated with enhanced alpha activity in spontaneous EEG

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Background and aims: Previous electroencephalography (EEG) studies have suggested that patients suffering from chronic pain have an increased magnitude of alpha rhythm at rest, as compared to controls and/or patients without pain. However, it remains unclear to what extent: i) this increase is related to pain or concomitant comorbidities; ii) it can be generalized across pain conditions. Methods: We recorded a 3-minute rest EEG in 44 patients suffering from different cancer types, not involving the central nervous system. Patients were divided into two groups on the basis of the presence (N=28) or absence (N=16) of pain, measured on a numerical ratings scale (NRS) and sub-items of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ). Importantly, the two groups were matched for the severity of mood disorders, assessed using the Hospital Anxiety and Depression Scale (HADS). The average amplitude of the alpha response was measured AT posterior electrodes. Results: In contrast with previous findings, we did not observe any significant difference between the two groups in the mean amplitude of the alpha rhythm (8-13 Hz). Conclusion: Our results question the possibility that the previously reported increase of alpha rhythms is strictly pain specific.

40. Is secondary hyperalgesia mediated by type I AMHs?

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Secondary hyperalgesia refers to the increase in pain sensitivity spreading beyond the site of injury. It can be induced experimentally by transcutaneous high frequency electrical stimulation (HFS). Secondary hyperalgesia seems characterized by enhanced pain to mechanical but not heat stimuli and likely mediate by type-I nociceptors. It has been shown that when long duration heat stimuli are used the thresholds of type-I and type-II nociceptors are similar. Therefore one may expect that if type-I mediate secondary hyperalgesia, long duration heat stimuli delivered above the type-II heat threshold, will elicit increased heat pain sensitivity in the area of secondary hyperalgesia. Here we

investigate the intensity of perception elicited by sustained heat stimuli after HFS. Mechanical and long duration heat (30 seconds) stimuli were delivered on both forearms before and 20 minutes after HFS. Intensity of perception was instantaneously recorded during heat stimuli with an analogic rating scale box. While HFS induced a significant increase of the perception of mechanical stimulation, we only observed a significant enhancement of the perception of heat stimuli in the first 4 seconds of the long duration stimulation. It is unlikely that this heat hyperalgesia is mediated by type-I nociceptors.

41. Neural processes involved in directing attention to painful and non-painful stimuli in crossed and uncrossed hand position

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Symbolic central cues which directed tactile attention to the left/right hand elicit: Early Directing Attention Negativity (EDAN) at posterior electrodes contralateral to the direction of attentional shifts (200-300ms after cue onset); Anterior Directing Attention Negativity (ADAN) at frontal cortex contralateral to the cue direction (300-500ms after cue onset); Late Directing Attention Positivity (LDAP) recorded in visual cortex contralateral to the cue direction (300-600ms after cue onset). The aim was to investigate neuronal processes involved in directing attention to painful and non-painful electric stimuli in crossed/uncrossed hand position. Participants crossed/uncrossed their hands at the beginning of each of 16 blocks (8 painful and non-painful blocks). Electric stimuli were preceded by central cues (right/left arrow). ERPs were recorded in response to cues which directed attention to either side. EDAN was observed in painful condition for both hand positions. In non-painful condition EDAN were found only in uncrossed condition. ADAN and LDAP were observed in uncrossed painful condition in contrary to crossed non-painful condition where lack of clear EDAN and LDAP was observed. The ERPs showed double dissociation of Intensity and Hand position effects.

42. Pain, empathy and the link with psychopathic personality traits; an event related potential study

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Pain and empathy are highly interrelated phenomena and are believed to have similar neuronal activation patterns. Current models of empathy for pain suggest that empathy-related processes are derived from bottom-up features, that account for the action-perception coupling resulting in affective sharing, and top-down factors that regulate this experience . Although several modulators of neuronal responses related to pain and empathy processes have been studied, the picture remains incomplete. Most pain and empathy related neuroimaging studies use static, picture-based paradigms that hardly translate to real-life situations. The present study employed a coupled-EEG paradigm that enables to study pain and empathy related processes in a socially interactive setup. Participants were put in the position of the victim and the confederate and were given an active and a passive role in attributing an electrical shock to the victim during different phases of the experiment. Based on literature we assume that position and role of the participant influence pain and empathy related neuronal responses in different phases of the experiment. Results showed that social context and attention are important modulators of pain and empathy related neuronal responses.

INDIVIDUAL DIFFERENCES

43. Electrophysiological correlates of temperament traits measured by Temperament and Character Inventory

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¹Neurobiology Department, Malopolska Centre of Biotechnology ²Department of Cognitive Neuroscience and Neuroergonomics, Institute of Applied Psychology, Jagiellonian University, Krakow, Poland Cloninger's model of personality is based on the assumption that human behaviours are generated by neurobiological processes. To address this we aimed at linking self-report personality measure with electrophysiological markers obtained while performing cognitive task in different experimental conditions. A sample of 56 (27 M) adults (mean age 22.9 \pm 2.3 years) completed the Temperament and Character Inventory measuring 4 temperament traits: Harm avoidance, Novelty seeking, Reward dependence and Persistence. Dense-array EEG (256 channels) was recorded while participants performed the numerical Stroop task in a reward and punishment conditions. Event-related spectral perturbations (ERSPs) aligned to the button press were calculated for erroneous and correct responses. An error resulted in increased frontal theta (3-7Hz) activity and decreased occipital alpha (10-11Hz) activity. Moreover, these two markers for brain error monitoring system were correlated (theta: r=0.30, p<0.05; alpha: r=-0.29, p<0.05) to novelty seeking trait while performing cognitive task in reward condition. These results indicate a neural mechanism of temperamentally-driven sensitivity to rewards and its impact on information processing.

44. Heart Rate Variability dynamics as a psychophysiological marker of temperament and anxiety

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Heart Rate Variability (HRV) is a measure of changes in the time intervals between the consequent heartbeats (beatto-beat). Normal heart rhytm even under resting conditions is in fact irregular.While investigating HRV, it is crucial to take a dynamic approach, having in mind the irregularity of the heart rhytm. In order to study the dynamics of heart rate a non-linear measure of HRV, Sample Entropy, is used as a perfect tool for investigating irregular time series. High HRV values reflect healthy psychophysiological states, while low HRV can be a sign of many abnormalities. In our study, ECG data was collected during resting-state sessions, from a group of 27 healthy young adults. Participants completed beforehand a variety of tests including Formal Characteristics of Behaviour: Temperament Inventory – Revised Version FCZ-KT (R) and State-Trait Anxiety Inventory. EEG signal was registered during the 10-minute resting-state session, in quitet enviroment - well-lit lab room. Sample entropy was calculated from the R-R signal derived from recorded resting ECG. Data collected showed correlation between sample entropy and temperament traits: negative with activity and endurance (FCZ-KT (R)), but positive with perseverativeness. Moreover, low HRV correlated with high states of anxiety. Data collected using sample entropy of the heart showed negative correlation in activity and endurance (FCZ-KT (R)), but positive correlation with perseverativeness. Data also showed negative correlation between HRV values and STAI-S - a scale of anxiety states.

45. Nonlinear complexity measurements of bioelectrical activity of the brain as predictors of individual differences in fluid intelligence: sex as a moderator

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Human brain is the archetype of a complex self-regulatory dynamical biosystem characterized by feedback at multiple levels of organization. Dynamics of these interactions are directly connected with individual adaptive features and form the basis of individual differences between people. These dynamics are manifested in electric field fluctuations generated by the human brain, which in turn translate into complexity of the EEG signal measured. Resting-state bioelectrical activity of the brain is characterized by: 1) coexistence of cumulative effects and neural noise, 2) variability and adaptiveness, 3) emergent phenomena, 4) self-organization, 5) multiscaleness, 6) hierarchism. These features make resting-state EEG measurements a great medium for studies of individual differences in fluid intelligence in absence of cognitive load. To assess the complexity of the resting-state EEG signal Multivariate Multiscale Sample Entropy (MMSE) and Higuchi\'s Fractal Dimension (HFD) indices were calculated for 40 participants (29 women). Obtained values of MMSE and HFD were used as predictors of individual differences in fluid intelligence measured with Raven Advanced Progressive Matrices (RAPM). Analysis was conducted independently for women and men. Preliminary results allow predicting fluid intelligence with 80% accuracy. Sex is a significant moderator of this relation.

46. Supplementary Motor Area activity differences during working memory task performance associated with fluid intelligence scores

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Working memory plays a fundamental role in human cognitive abilities. Studies have found a correlation between fluid intelligence scores and working memory performance. We investigated brain activity differences during working memory task (n-back) between individuals with higher and lower intelligence test scores. Fluid intelligence level was measured using Raven's Advanced Progressive Matrices. We have found significant brain activity difference between higher and lower intelligence group in Supplementary Motor Area (SMA) when comparing 2-back vs 1-back contrast. This region plays a crucial role in controlling motor functions and is typically activated during working memory tasks performance. Our results suggest that individuals with higher intelligence have a higher increase of activity in SMA related to increasing working memory load. This study implicates the potential of neuro-imaging studies for identifying aspects of the neural basis of intelligence and illustrates the importance of its relation to working memory. This study was supported by a grant (2015/17/N/HS6/03549) from the National Science Center, Poland.

47. Default mode network connectivity associated with fluid intelligence level

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Default mode network (DMN) or so called task-negative network remains highly active during resting-state condition, while deactivates during cognitive task performance. There are several hypotheses about the potential role of the resting-state DMN activity such as mind wandering, consciousness or memory consolidation. However, the relationship between DMN and cognitive abilities remains unclear. In this fMRI study, we investigated association between fluid intelligence level and resting-state DMN connectivity of 35 individuals. We found that higher intelligence level was associated with lower connectivity between posterior cingulate cortex (PCC) and precuneus. These results suggest that DMN connectivity may help to explain individual differences such as intelligence. This study was supported by a grant (2015/17/N/HS6/03549) from the National Science Center, Poland.

48. Behavioral control and resting-state EEG complexity

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The purpose of the conducted study was to investigate differences in complexity of resting-state brain activity, taking temperament in account. Our previous study showed that differences in cognitive abilities related to temperament traits could be observed only upon performing demanding attentional task. Presented study was based on a sample of 25 people, aged from 19 to 31 years. FCB-TI(M) survey of Regulative Temperament Theory was used as a measurement of temperament traits. Participants were asked to sit relaxed with their eyes open while electroencephalography was recorded. Higuchi's Fractal Dimension (HFD) was calculated and used as a marker of complexity of time series on the preprocessed EEG data. HFD complexity was estimated for every electrode, subsequently grouped into clusters. Negative correlations were found between behavioural control (measured with

FCB-TI(M)) and complexity of the resting-state EEG signal on frontal and central areas of the scalp. Results shed new light on temperamental differences studies. Unlike other temperament traits, behavioural control is related to complexity of resting-state bioelectrical activity. Complexity of neural networks during resting-state recording can be an indicator of the ability to control future behavioural outcome.

49. Resting-state activity and temperamental traits

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Aim. The aim of this study was to verify the hypothesis that the temperamental traits (briskness, perseveration, sensory sensitivity, emotional reactivity, endurance, activity, rhythmicity, behavioral self-control, social approval) are reflected in the frequency of alpha waves of particular regions in the brain.

Methods. The study involved 28 right-handed, healthy subjects (14 males). Temperamental traits were measured using a Formal Characteristics of Behavior - Temperament Questionnaire, modified version (FCZ-KT(Z)). Subjects were asked to relax with their eyes closed while EEG signal was recorded from 64 electrodes. EEG was subjected to frequency analysis using the Fast Fourier Transform method (FFT).

Results. The results of this study show that in groups of subjects divided by sex there is a relationship between selected temperamental traits and frequency of alpha waves. The results indicate a correlation between self-control, behavioral rhythmicity and frequency of alpha waves in group of women and sensory sensitivity and behavioral self-control in group of men. So, we can conclude that the temperamental traits are reflected in the spontaneous brain activity.

50. Temperament and the brain - what Insular Network can tell us?

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Human brain consists of spatially spread but functionally linked regions. The application of resting-state fMRI (rsfMRI) technique allows identification of various patterns of activation, when spatially spread regions demonstrate synchronous BOLD signal fluctuations during rest. RsfMRI allowed scientists to explore resting state networks, including Default Mode Network (DMN) - the most fundamental, but also Insular Network, linking anterior insula with the middle and inferior temporal cortex and anterior cingulate cortex. Does the Insular Network pattern differ depending on the subjects temperament? Here we present results from the resting-state fMRI study. 61 women (age 20-35) participated in the study. According to FCB-TI, we have distinguished two groups: low (22) and high reactive subjects (23) on which we performed functional connectivity analysis and compared them using two sample T-test. Our procedure comprised of 10 minutes of resting-state scanning session, subjects had their eyes closed. The images were acquired with 3T MRI Scanner (Magnetom Trio, Siemens, Healthcare Germany). SPM8 (http://www.fil.ion.ucl.ac.uk/spm/) was used for data preprocessing and REST software was used for the resting state analysis. Our analysis of the contrast between the resting-state condition in high vs low reactive subjects revealed a robust activation of Insular Network. These results not only stay in line with recent insular connectivity research but also can be contribute to the debate about the neuronal correlates of the temperament in humans.

51. Olfactory performance of early-blind, late-blind and sighted individuals

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Previous examinations of olfactory sensitivity in blind people have produced contradictory findings. Thus, whether visual impairment is associated with increased olfactory abilities is unclear. In the present investigation, I aimed to

resolve the existing questions via a relatively large-scale study comprising early-blind (N=43), and late-blind (N=41) and matched sighted (N=84) individuals. To compare the results with those of previous studies, I combined the data from a free odor identification test, extensive psychophysical testing (Sniffin' Sticks Test), and self-assessed olfactory performance. Further, the participants were matched in terms of gender and age. The analyses revealed no significant effects of sight on olfactory threshold, odor discrimination, cued identification, or free identification scores. Additionally, the self-assessed olfactory abilities of blind people were no different than those of sighted people. These results suggest that sensory compensation in the visually impaired is not pronounced in the olfactory abilities measured by standardized smell tests.

MOTOR ACTIVITY

52. Planning functional grasps of tools vs. non-tools - MVPA searchlight analysis

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Tool use is an inherent part of human functioning. In order to perform such a complex cognitive and motor activity, sophisticated transformations of visual and motor signals have to take place in the brain. Functional magnetic resonance imaging (fMRI) allows us to measure these processes and mechanisms. We conducted Multi-Voxel Pattern Analysis (MVPA) of the fMRI data using a searchlight method - an information-based functional brain mapping - in order to identify brain regions which are involved in the planning of functional grasps of tools. Significant grasp-related clusters of voxels were found predominantly in the left hemisphere along: (1) the ventro-dorsal stream of visuo-motor processing, starting from the mid-to-anterior intraparietal sulcus and the nearby anterior supramarginal gyrus, and terminating in the inferior frontal sulcus and middle frontal gyrus; and (2) the dorso-dorsal stream starting from the superior parieto-occipital cortex (including the parietal reach region), and passing via the sensorimotor cortices trough dorsal premotor area and further to the dorso-lateral prefrontal cortex. These results are consistent with numerous previous studies on tools and show that regardless of the method applied the same brain regions are revealed as contributing to planning tool-related actions.

53. Multiple object tracking affects motor precision

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Multiple object tracking (MOT) experimental paradigm allows to study not only visual attention but also other cognitive processes. For instance, research demonstrated that with increasing number of objects to be tracked perceptual precision declines. In our study we wanted to test if increased MOT load impairs hand motor precision, as neuroscience studies suggest that cortical regions associated with attentional processing are also involved in hand movement control. Thirty women participated in behavioral MOT experiment. The task was to visually track moving target objects (circles) among moving distractors (also circles) displayed on the touchscreen. There were four conditions of attentional load with increasing number of targets and/or distractors. After visual tracking participants performed a motor task of pointing with their index fingers (by touching the screen) the circles that they considered as the targets. As participants were asked to point to the center of each circle, d istance between the touch point and the circle center was used as an indicator of motor precision. Results demonstrated that motor precision decreased as MOT attentional load increased. This supports the notion that visual attention and motor performance are closely related as other behavioral and neuroscience studies demonstrate.

54. Does cross-modal priming can enhance motor skill learning?

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Since the optimal modalities for priming are still being discussed, we examined the effect of cross-modal priming with metaphor on effectiveness of motor skill learning. Two experiments were carried out (n=47), in which we developed

prime stimuli set consisted of visual and auditory modalities, and target stimulus. In the experimental group, the stimuli of different modalities were bound together into unified mental imagery by the metaphor included in the target stimulus. After a short-term, standardized "cup test" training, we assessed learning performance by breaking the set of movements into kinematic sequences and evaluated fluency, smoothness and exquisiteness of performance. The results show that the developed metaphor in the experimental group can enhance motor skill acquisition and therefore lead to higher performance.

55. Handedness and performance of Motor-Imagery BCI

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Brain-computer interfaces (BCI) are systems that enable the conversion of CNS bioelectrical signal to the external reactions of applications or devices without a muscular activity. The most popular BCIs use the oscillations of sensorimotor rhythms registered during movement imagery (Motor Imagery BCI; MI-BCI). There are several obstacles in implementing the common usage of BCIs. The most significant is the poor information transfer rate and large individual differences in acquiring the ability to effectively use BCIs. The latter is due to the physiological and psychological factors. In our study, we wanted to find out how lateralization affects the effectiveness of the MI-BCI control. Based on The Edinburgh Handedness Inventory 19 participants (N female= 15; M age=24,16; SD age=2,52) were selected to take part in the study (10 right-handed, 9 left-handed). The experiment consisted of two stages. First, EEG was registered when participants performed the motor imagery task of the right or left hand movement. Second, participants were asked to apply the same motor imagery task to control the movement of an object presented on the screen by means of MI-BCI. The results revealed significant differences between left- and right-handers in the effectiveness of MI-BCI control and different patterns of sensorimotor rhythms desynchronization.

56. Mirror Movement in children with unilateral Cerebral Palsy: Are mirror movements related to self-perceived bimanual performance?

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Some children with unilateral Cerebral Palsy (uCP) demonstrate a prolonged retention of mirror movements (MM) compared to typically developing children. Previous research has suggested that secondary degeneration of transcallosal axonal colaterales innervating the posterior body of the corpus callosum (CC) might cause these MMs due to reduced collateral inhibition between the motor cortices. This pilot study attempts to investigate this relationship. It is hypothesized that children with uCP and relative thinning of the posterior CC will show enhanced MMs. Twelve children with uCP were included. A repetitive unimanual squeezing task was used to determine the amount of MMs. This was done by cross-correlating the force pattern between hands while either the more affected hand (AH) or the less AH was actively squeezing. The ratio between the posterior and anterior CC was estimated from T1-weighted MRI-scans.Pearson's correlations revealed a trend between the CC-ratio and MM appearing in the more AH when the less AH was actively moving (R2=0.209, p=0.058). No relation was found for MM appearing in the less AH. MMs in the AH may partly be explained by hypogenesis of the posterior CC. A possible alternative underlying factor for MMs may be retention of ipsilateral corticospinal projections during development.

57. Secondary degeneration of the corticospinal tract in relation to complex motor behaviour in adolescents with unilateral cerebral palsy

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Degeneration of the corticospinal tract (CST) is linked with diminished unimanual hand capacity in hemiplegia. However, this relation is less clear with respect to more complex motor performance. This study examined the relation between degeneration of the CST and simple and complex motor behaviour in adolescents with uCP. Peduncle asymmetry was estimated from T1-weighted MRI scans measuring the surface of the cerebral peduncles from the interpeduncular space to the lateral sulcus. Apart from the Manual Ability Classification System (MACS), unimanual hand capacity was determined using the Box & Blocks test (B&B), whereas bimanual performance was estimated by means of the Children's Hand-use Experience Questionnaire (CHEQ). We found that a higher peduncle asymmetry coincides with a more marked disruption of bimanual performance (CHEQ efficacy of grasp: $r^2 = .34$; CHEQ time needed: $r^2 = .45$) and a decreased manual ability (MACS: $r^2 = .24$; all p-values <.05). However, no relation between peduncle asymmetry and B&B was observed. We propose that the amount of secondary degeneration of the CST correlates with difficulties in complex bimanual performance, but less so with unimanual hand capacity. Unimanual hand capacity might be more easily compensated for in children via neuronal plasticity using e.g. the ipsilateral CST.

58. Somatosensory event related potentials and hand capacity in infants at risk of developing unilateral cerebral palsy

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Integration of the central motor and somatosensory systems seems vital for the development of motor skills. The motor system requires feedback from somatosensory system for its development. Indeed, the development of the somatosensory system precedes the development of the motor system during early development (Eyre et al., 2000; 2007). Seven infants with a history of unilateral CVA (and at risk of developing unilateral Cerebral Palsy; uCP) participated in this study. Hand capacity of each hand was determined by means of a semi-structured video-recorded play session. Somatosensory event related potentials (SSERPs) from the ongoing EEG were elicited by delivering tactile stimulation to the palms of each hand. Infants at risk of uCP showed a positive correlation between the differences in hand capacity and SSERPs in response to tactile stimulation, such that larger differences in hand capacity scores between hands correlated with larger differences in SSERP amplitudes between hands. Severity of hand motor impairment seems to be highly correlated with an impairment in somatosensory processing in infants at risk of developing uCP. We propose that the SSERP might be useful as a predictive measure in infants at risk of uCP. In addition, early intervention could be focussed more on the somatosensory development.

SSVEP FREQUENCY RESPONSES

59. Is discrimination of the visual pathways possible using SSVEP?

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Steady State Visual Evoked Potentials (SSVEP) are the steady state responses elicited in EEG by flicker stimulation. Frequency of oscillation of these responses corresponds to the stimulus frequency and its harmonics. In earlier study we showed that time evolution of SSVEP spectral power varies between stimulation frequencies. For low frequencies (5 Hz) the power of the response increases in time while for higher frequencies (15 Hz) the habituation of the power is observed. The possible explanation of this phenomenon is that SSVEP is processed by various visual neuronal pathways (parvo, magno, konio) and characteristics of these paths may not be the same between frequencies. Parvo- and magnocellular cells are localized in different parts of the retina – in its central and peripheral part, respectively. The aim of this study was to investigate the effects of differential activation of parvo- and magnocellural pathways by selectively stimulating centre and periphery of the gaze. The analysis was done using EEG signals recorded during series of 60-seconds long stimulation periods interleaved with 30-seconds rest periods. For each subject 50 trials of signal were collected during stimulation of central and peripheral field of view. The experiment was repeated for each subject for two stimulation frequencies – 5 and 15 Hz. These experiments suggest that distinct SSVEP evolution patterns across frequencies may be related to selective involvement of specific visual pathways but more experimental evidence is necessary to confirm or refute this hypothesis.

60. Time evolution and phase stability of SSVEP harmonics

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Steady State Visual Evoked Potentials are the steady-state responses elicited by flicker stimulation. Frequency of oscillations of these neural responses corresponds to the stimulus frequency. Since the very first reports on SSVEP in 1966, they have been commonly assumed to be stationary (i.e.steady- state) signals which power and other properties are stable over time. In the previous research we showed that SSVEPs are not stable during long term stimulation. For 15 Hz flicker stimulation we observed significant decrease of the instantaneous power during 60 seconds of stimulation. In this work we analyze the evolution of the first harmonic. We show that the decrease of instantaneous power is much smaller for the most of subjects. Additionally we compare the phase stability for basic component and first harmonics and show that while basic component of SSVEP is phase locked with the stimulus the phase of the harmonic is less stable during the stimulation.

61. Evaluation of modulation indexes for assessment of phase to amplitude cross-frequency coupling

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Recent studies indicate that coupling between low- and high-frequency brain rhythms provides valuable information on cognitive processing in humans. One of the methods that are used to measure the strength of the interaction (phase-to-amplitude modulation) across frequencies is so-called modulation index (MI). The purpose of this study was to investigate the influence of properties of simulated signal on the efficacy of the MI proposed by Canolty (2006) and Tort (2008) in terms of detection of simulated cross-frequency coupling. Simulation signal consists of lowfrequency sine (in the range of theta rhythm frequencies) with superimposed spindles of high-frequency (from the gamma band range). Modulation index showed dependence on signal to noise ratio, precision of synchronization of gamma amplitude to theta phase, ratio of gamma to theta amplitude and ratio of theta cycles with gamma spindles to empty theta cycles. The findings suggest the MI have sufficient sensitivity to measure the theta-gamma coupling as measured by high quality EEG.

COMPUTATIONAL MODELS

62. Mechanobiological damage to the structure and function of the brain

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Currently, little is known in neuroscience about the mechanics of damage to tissues and cell brain as well as the impact of physical forces on neurobehavioral dysfunction. The brain is a mechanically sensitive organ, the properties of which enable endogenous forces to regulate many aspects of neuronal function. Unfortunately, substantially greater mechanical forces (e.g. traffic accidents, combat operations) acting on the brain can result in tissue and brain cell degradation and thus cause irreversible cognitive dysfunction, progressive neurodegeneration and even death. One way to identify disorders caused by mechanical forces is to build computer models. In the present study, the authors have undertaken a numerical study of brain fragments based on experimental research. The numerical study was an attempt to analyze changes in the parameters and mechanical characteristics of brain structures in conditions of rapid overload. As a result of the numerical analysis, critical values have been obtained for strain, stress, displacement and energy. These mechanical consequences of head trauma trigger a host of deleterious molecular signaling pathways, which in turn give rise to the clinical manifestations of traumatic brain injury (TBI).

63. Investigation of Beta Generation Mechanisms with Computational Model

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Beta waves (13 up to 30 Hz) can be observed in EEG and LFP signals in different brain regions and under different states, such as attention or in relation to movement. The mechanism of generation of these signals is not well understood. We created a realistic computational model in order to improve our understanding of beta waves origin. The beta oscillations are generated in simulated cortical network under external random drive from other brain areas. The network oscillation emerges from irregular and sparse firing of individual neurons but in phase with the population rhythm. The modeling results suggest that the emergence of oscillatory activity is mediated by reciprocal interactions between pyramidal cells and interneurons. Furthermore the model suggests the continuum of beta/gamma range (13-50 Hz) for wide range of external input strength.

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